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Was it Really a Bupivacaine Toxicity?

Intra-Aortic Balloon Pump for the Treatment of Severe Verapamil Poisoning

**Spontaneous Spinal Epidural Hematoma Causing Paraplegia** 

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# **ACTIVITY RESTRICTION AMONG PENSIONERS OR THEIR WIDOWS ACCORDING TO THE GRONINGEN SCALE\***

Birgül Piyal\*\* Y. Bülent Piyal\*\*\*

# **SUMMARY**

Due to the aging of the population in many countries of the world public health took a serious interest in the problems of aging. In Turkey which was defined a country with a young population data points to an aging population also. To meet this demographic tranformation studies have to start immediately.

To define the activity restriction according to the groningen scale among pensioners or beneficiaries -55 years of age and older- who receive their pensions from a special operation center of a government bank as a first step, this descriptive study is carried out by the application of a questionnaire with face to face interview technique to 461 persons during the first days of pension payment periods on March and April 1998.

Mean scores are calculated for each of activity of daily living (ADL) and instrumental activity of daily living (IADL) items. Minimum, maximum and mean ADL, IADL scales and Groningen Activity Restriction Scale (GARS) sum scores are calculated for the study group and for different sociodemographic subgroups.

The most difficult ADL and IADL items were to go up / down stairs and do heavy cleaning in order. Females, olders, widowed participants, those who have four or more children and those who live with others, those who have more than one chronic medical condition, old-age pensioners scored higher on the GARS as a whole and on the ADL and IADL scales.

The importance of home care services and special support programs for the elderly is emphasized.

Key Words: Activity Restriction, Groningen Scale

Due to the aging population, Public Health in many countries has shown a serious interest in the problems of aging (1). According to the 1985 Population Census 4.2 % of population in Turkey was 65 years of age and over (2); and in 1994, 1995 and 1996, 4.5 %, 4.7 % and 4.8 % respectively. It is estimated that by the year 2000, 5.5 % of population will be 65 years of age and older. The life expectancy at birth in Turkey was 70.5 years for females and 65.9 years for males in 1996 and will be 71.5 and 66.9 in order by the year 2000 (3). This data has to be interpreted very carefully in Turkey which is usually defined as a country with young population. The studies to understand and meet the needs of this demographic transformation have to start immediately.

Definition of activity restriction among different individual groups consisting of elderly (pensioners or their widows or beneficieries in general) or chronically, ill aged people seems as a good first step to clarify the

problem so that professional home help services and aid activities can be planned and actions be taken as soon as possible. One of the main purposes of this descriptive study is to define the activity restriction among pensioners or their widows -55 years of age or older- who receive their pensions from Keçiören special operation center of a government bank by the use of Groningen Activity Restriction Scale (GARS) (4). GARS is a non-disease-specific instrument, very useful for comparative research across countries to measure disability in activities of daily living (ADL) and instrumental activities of daily living (IADL), sometimes referred to as 'housekeeping activities of daily living' (Attachment 1).

Main purposes of this study can be summarized as follows:

- To take interest to aging and its problems,
- To make an attempt to define the activity restriction of a non-institutionalized elderly group,

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<sup>\* 55</sup> years of age or older- who receive their pensions from Keçiören Special Operation Center of a government bank.

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- To open the way for related detailed analytic studies,
- To prepare a sort of baseline for the actions necessary to solve the problem with its limitations.

# **METHODS**

To reach a non-institutionalized elderly group, a government bank's special operation center is chosen. Since most of the pensioners or widows come to the bank to collect their pension payments in the mornings of first few days of each payment period, data is collected in March and April (1998) during these specific periods. A questionnaire prepared by the use of GARS is applied to the pensioners and their widows 55 years of age and older, with face to face interview technique in separate rooms by the researchers and trained last year students of the Faculty of Health Education (Ankara University). Questionnaires of two participants that could not come to the bank were filled by their children. Questions for a participant who could not talk, as a result of a plegia attack, were answered by his wife. The rest are self reported information. The questionnaire -including 18 GARS and 10 sociodemographic- has 28 items. Each GARS item has five response categories presented in Attachment 1. The items refer to what respondents are able to do and not to their actual performance, which is a very important distinction. When an item refers to more than one activity (e.g., item 5), the activity causing the greatest problems to the individual determines the response. This internationally accepted rule was accurate during data collection. Socio-demographic items were about age, sex, marital status, educational status, social-security status, living arrangement, number of living children, social arrangements they need to make to get to the bank, medical conditions (chronic medical conditions) and earned income. Data collected from 461 individuals is analysed with SPSS computer program by the researchers.

# **RESULTS**

Some socio-demographic characteristics of study participants are presented in Table 1 and Table 2. Gender composition is, 51.8 % male and 48.2 % female. Minimum, maximum and mean ages are 55, 90 and 65.11 in order. Married people compose 53.1 % of the study group whereas 45.6 % are widowed. Most of the participants have living children (96.0 %). Those who live alone are only 15.6 %, 51.7 % live with

Table 1. Some Characteristics of Study Participants (n=461)

Characteristic	Number	%
Gender		
Male	239	51.8
Female	222	48.2
Age		
55-59	95	20.6
60-64	136	29.5
65-69	129	28.0
70-74	69	15.0
75>=	32	6.9
Marital Status		
Married	245	53.1
Widowed	210	45.6
Divorced	4	0.9
Never Married	2	0.4
Living Children		
One-Three	194	42.0
Four or More	249	54.0
No Living Children	3	0.7
Never Had a Child	15	3.3
Living Arrangement		
With Husband / Wife	238	51.7
Alone	72	15.6
With a Married Child	102	22.1
With Relatives	6	1.3
Other	43	9.3
Total	461	100.0

the wife / husband, 32.7 % live with a married child, with relatives or with grand children (Table 1). Around one third of the study group is Retirement Fund pensioner, around one third is Social Insurance Institute pensioner and the rest one third is Social Insurance Institute beneficiary. Primary school gradutes compose 34.1 %, illiterates 29.5 %, literates 15.8 % and high school and university graduates 15 % of the study group. Though only one fourth of the participants have no chronic medical condition, about half of them (46.4 %) have one and 28.2 % have more than one chronic medical condition. Most of them come to the bank alone (80.9 %), 18 % come with someone who comes to the bank or with relatives for some reason. Only 5.2 % report that they are still engaged with a sort of income earning activity (Table 2).

When the items are ordered according to their diffuculty, as expressed by the item mean scores (4), the most diffucult activity of daily living (ADL) for the study group is to go up / down stairs (item mean score=1.95) followed by to take care of feet / toenails (item mean score=1.69). The most and second most diffucult instrumental activities of daily living (IADL) are to do heavy cleaning (item mean score=2.63) and to wash / iron clothes (item mean score=2.51) in order (Table 3).

Table 2. Some Characteristics of Study Participants (n=461)

Characteristic	Number	%
Social Security		
Retirement Fund Pensioner	142	30.8
Retirement Fund Beneficiare	22	4.8
Social Insurance Inst. Pension:	137	29.7
Social Insurance Inst. Benefic.	141	30.6
Old-Age Pensioner *	19	4.1
Education		
Illiterate	136	29.5
Literate	73	15.8
Primary School	157	34.1
Middle School	26	5.6
High School	46	10.0
University	23	5.0
Medical Conditions		
No Chronic Med. Condition	117	25.4
1 Chronic Med. Condition	214	46.4
1> Chronic Med. Condition	130	28.2
Soc. Arr. to Get to the Bank		
Alone	373	80.9
With Someone	7	1.5
With a Relative	76	16.5
With a Cab / Auto	4	0.9
Others	1	.0.2
Earned Income		
No	437	94.8
Yes	24	5.2
Total	461	100.0

<sup>\*</sup> Including 7 father/son beneficiaries and 3 disability beneficiaries.

Closer the item mean score to 1 the more the individual is independent. Therefore, 11 ADL and 7 IADL, 18 GARS sum scores are calculated separetely for the total study group and for different sociodemographic subcategories. Minimum ADL, IADL, GARS sum scores have to be 11, 7, 18 in order. Mean and maximum sum scores are presented in Table 4, Table 5, Table 6.

Females, older age-groups, widowed participants, those who have four or more children and those who live with others scored higher on the GARS as a whole and on the ADL and IADL scales (Table 4). Also old-age pensioners, illiterates, those who have more than one chronic medical condition, those who have no earned income other than the pensions scored higher on the all of the three scales (Table 5).

# CONCLUSION

The gender distribution of the study participants is almost equal (51.8 % males, 48.2 % females), half of the group (49.9 %) is 65 years of age and older. Divorced or never married people compose only 1.3 % of the study group and those who live alone are 15.6 % (Table 1).

Table 3. Disribution of Item Mean Scores of Study Participants According to Ordered GARS Items (n=461)

	Ordered GARS Items		Item Mean Scores
1.	Feed yourself	(ADL)	1.08
2.	Wash face / hands	(ADL)	1.09
3.	Get around inside house	(ADL)	1.18
4.	Dress yourself	(ADL)	1.29
5.	Stand up from chair	(ADL)	1.34
6.	Get in / out of bed	(ADL)	1.37
7.	Wash / dry body	(ADL)	1.44
8.	Get on / off toilet	(ADL)	1.50
9.	Prepare breakfast / lunch	(IADL)	1.51
10.	Prepare dinner	(IADL)	1.61
11.	Make beds	(IADL)	1.63
12.	Walk outdoors	(ADL)	1.68
13.	Take care of feet / toenails	(ADL)	1.69
14.	Go up / down stairs	(ADL)	1.95
15.	Do light cleaning	(IADL)	1.96
16.	Do shopping	(IADL)	2.29
17.	Wash / iron clothes	(IADL)	2.51
18.	Do heavy cleaning	(IADL)	2.63

Retirement Fund and Social Insurance Institute pensioners and Social Insurance Institute beneficiaries each compose almost one third of the study participants. The educational level of the study group is rather low, university graduates are only 5 %. One fourth of the participants has no chronic medical condition, 80.9 % come to the bank alone and 5.2 % are engaged to an income earning activity (Table 2).

When the items are scored according to their diffuculty, the most diffucult ADL and IADL are to go up / down stairs and to do heavy cleaning (Table 3). These findings are harmonious with the findings of a study carried out in Etimesgut among 65 years of age and older women and with the findings of a study carried out in different European countries among people with rheumatoid arthritis (5,4).

ADL functions are essential for an individual's self-care (e.g., washing or dressing one-self), whereas IADL functions are more concerned with self-reliant activities in a given environment (e.g., shopping, preparing meals). However, from the perspective of the individual, the ADL functions are no less "instrumental" than the IADL functions, the distinction between these two groups of activities being mainly a consequence of "instrumental" thinking.

Older people and women scored higher on the GARS as a whole and on the ADL and IADL scales (Table 4). These higher scores support the fact that in general, older people are most disabled than younger ones and the fact that sex role-spesific socialization

Table 4. ADL / IADL and GARS Scores of Some Study Participants According to Some Characteristics

ADL IADL **GARS** Characteristic Mean Max. Mean Max. Mean Max. Gender Male 13.71 55.00 11.65 35.00 25.36 90.00 Female 17.66 54.00 16.82 35.00 34.48 89.00 Age 25.68 90.00 55-59 14.18 55.00 11.51 35.00 60-64 14.38 34.00 12.41 34.00 26.79 63.00 15.85 43.00 65-69 14.68 35.00 30.53 78.00 70-74 17.65 36.00 16.90 35.00 34.55 69.00 19.75 54.00 21.19 35.00 40.94 89.00 75>= Marit. Status 13.95 55.00 11.70 35.00 25.65 90.00 Married Widowed 17.64 54.00 17.04 35.00 34.69 89.00 Livin. Childr. One-Three 14.87 54.00 13.03 35.00 27.89 89.00 Four or More 16.17 55.00 15.01 35.00 31.18 90.00 Livin. Arran. With H / Wife 13.99 55.00 11.73 35.00 25.72 90.00 35.00 32.22 62.00 Alone 16.90 34.00 15.32 With Others 17.55 54.00 17.38 35.00 34.93 89.00

patterns effect the physical condition. Living with husband / wife and living alone are generally accepted as advantages those prevent one's activity restriction in some ways. But the data presented in Table 5 have to be interpreted very carefully due to the limitations of this study.

Country wide studies to analyse the spesific needs of different elderly groups have to start immediately. Preparing a detailed profile of this group seems as a crucial start point, including home care services special support programs have to plan accordingly.

Attachment 1- Items and Response Categories of The Groningen Activity Restriction Scale (GARS)

# Response categories for each item

- 1. Yes, I can do it fully independently without any difficulty.
- 2. Yes, I can do it fully independently but with some difficulty.
- 3. Yes, I can do it fully independently but with great difficulty.
- 4. No, I cannot do it fully independently, I can only do it with someone's help.
- 5. No, I cannot do it at all, I need complete help.

# Activities of Daily Living (ADL)

- 1. Can you, fully independently, dress yourself?
- 2. Can you, fully independently, get in and out of bed?
- 3. Can you, fully independently, stand up from sitting in a chair?
- 4. Can you, fully independently, wash your face and hands?
- 5. Can you, fully independently, wash and dry your whole body?
- 6. Can you, fully independently, get on and off the toilet?
- 7. Can you, fully independently, feed yourself?
- 8. Can you, fully independently, get around in the house (if necessary, with a cane)?

Table 5. ADL / IADL and GARS Scores of Study Participants According to Some Characteristics (n=461)

	ADL			DL =	GA	
Characteristic	Mean	Max.	Méan	Max.	Mean	Max.
Soc. Security						
R.Fund Pensi.	13.15	31.00	10.17	34.00	23.32	64.00
R.Fund Benefi.	16.64	34.00	15.27	33.00	31.91	63.00
Soc. I. I.Pensi.	14.58	43.00	13.48	35.00	28.07	78.00
Soc. I. I.Benefi.	18.04	36.00	17.77	35.00	35.81	69.00
OAge Pensi.*	22.16	55.00	20.37	35.00	42.53	90.00
Education						
Illiterate	18.32	55.00	18.46	35.00	36.79	90.00
Literate	17.45	43.00	16.04	35.00	33.49	78.00
Primary School	13.89	36.00	11.89	35.00	25.78	66.00
Middle School	13.73	27.00	11.50	34.00	25.23	61.00
High School	13.04	26.00	10.54	31.00	23.59	50.00
University	12.74	19.00	8.13	13.00	20.87	31.00
Med. Condi.						
No Ch. Med.C.	11.90	26.00	9.45	29.00	21.35	55.00
1 Ch. Med. C.	15.81	55.00	14.46	35.00	30.27	90.00
1> Ch. Med. C.	18.63	36.00	17.84	35.00	36.47	69.00
Getting Bank						
Alone	14.23	34.00	12.29	35.00	26.52	69.00
W Oth / Other	21.47	55.00	21.98	35.00	43.44	90.00
Earned Income						
No	15.80	55.00	14.45	35.00	30.25	90.00
Yes	12.17	22.00	8.46	21.00	20.63	43.00

<sup>\*</sup> Including 7 father/son beneficiaries and 3 disability beneficiaries.

Table 6. ADL / IADL and GARS Scores of Study Participants as a Group (n=461)

	ADL		IA	IADL		GARS	
Study Group	Mean	Max.	Mean	Max.	Mean	Max.	
	15.61	55.00	14.14	35.00	29.75	90.00	

- 9. Can you, fully independently, go up and down the stairs?
- Can you, fully independently, walk outdoors (if necessary, with a cane)?
- 11. Can you, fully independently, take care of your feet and toenails?

# Instrumental Activities of Daily Living (IADL)

- 12 .Can you, fully independently, prepare breakfast or lunch?
- 13. Can you, fully independently, prepare dinner?
- 14. Can you, fully independently, do 'light' household activities (for example, dusting and tidying up)?
- 15. Can you, fully independently, do 'heavy' household activities (for example, mopping, cleaning the windows and vacuuming)?
- 16. Can you, fully independently, wash and iron your clothes?
- 17. Can you, fully independently, make the beds?
- 18. Can you, fully independently, do the shopping?

# **KAYNAKLAR**

- 1. KANE, R.: Making Aging a Public Health Priority. American Journal of Public Health. August 1994; 84: 1213-14.
- 2. Ministry of Health, 1st National Health Congress, Elderly Group Report, Ankara 1992.
- 3. Health Statistics 1996, Ministry of Health Research Planning and Coordination Council, Health Project Coordination Unit's Publication, Ankara October 1997.
- 4. SUURMEIJER, T. P. B. M. et al.: The Groningen Activity Restriction Scale for Measuring Disability: Its Utility in International Comparisons. American Journal of Public Health. August 1994; 84: 1270-73.
- ERGÖR, G. et al.: Etimesgut Sağlık Ocağı Bölgesindeki 65 Yaş Üzerindeki Kadınlarda Günlük Yaşam Aktivitelerinin Değerlendirilmesi. V. Ulusal Halk Sağlığı Kongresi Bildiri Kitabı, Marmara Üniversitesi Tıp Fakültesi Halk Sağlığı Anabilim Dalı Yayını, İstanbul 1996: 655-57.
- 6 MOR, V. et al.: Functional Transitions Among the Elderly: Patterns, Predictors and Related Hospital Use. American Journal of Public Health. August 1994; 84: 1274-80.

# COMPARISON OF TWO DIFFERENT DIABETIC PATIENT EDUCATION PROGRAMS\*

Nilgün Başkal\*\* • Sevim Güllü\*\* • Murat Faik Erdoğan\*\* • Ali Rıza Uysal\*\*
Satı Açıkgöz\*\* • Gürbüz Erdoğan\*\*

### **SUMMARY**

Education of diabetic patients who live far from the diabetes centers is a major problem. Drop-outs from out-patient education programs is very high among such patients. So we conducted a short education program (two days, program 1) and compared the results of it with an eight-day structured program (program 2). Both programs included same topics and performed by the same education team. Fasting(FPG) and postprandial 2-hour(PPPG) plasma glucose levels and lipid profiles of the patients were evaluated before and after education.

FPG levels of patients fell from  $159 \pm 64$  mg/dl to  $128 \pm 36$ mg/dl on program 1 and  $190 \pm 75$  mg/dl to  $149 \pm 51$  mg/dl on program 2. PPPG levels decreased from  $213 \pm 86$  mg/dl to  $159 \pm 49$  mg/dl and from  $233 \pm 88$  mg/dl to  $184 \pm 71$  mg/dl on programs 1 and 2 respectively. A decline in HbA1c from  $8.2 \pm 1.3$  % to  $7.3 \pm 1.2$  % on program 1 and from  $8.7 \pm 2$  % to  $6.4 \pm 1$  % on program 2 was observed. Cholesterol levels fell from  $219 \pm 54$  mg/dl to  $204 \pm 47$  mg/dl with program 1 and from  $234 \pm 16$  mg/dl to  $192 \pm 20$  mg/dl with program 2. Triglyceride levels also decreased with program 1 and 2 ( $222 \pm 109$  mg/dl to  $206 \pm 80$  mg/dl and  $190 \pm 34$  mg/dl to  $170 \pm 31$  mg/dl, respectively).

Statistically significant improvement in metabolic control was observed in both education programs. These results suggest that short-time education programs are as effective as longer programs and can be put into practice for the patients who come to visit diabetes centers from distant parts of the country.

Key Words: Diabetes Mellitus, Education Program.

There is an increased awareness of educating patients not only understand and follow the instructions of their medical team, but to have increased responsibility for their own care. Of all chronic conditions, diabetes mellitus, for which there is no cure, is among the most expensive and education-intensive. Diabetics need to know how to adjust their life-style and activities but also how to take and adjust medications, diet and exercise and how to avoid complications that might be life-threatening. Patient education contributes to reducing the morbidity and mortality of diabetes (1-6). Patient education and follow-up services must be provided on an outpatient basis. In our opinion, dropout from such programs is a major problem. In an unpublished data of ours, we observed a dropout ratio as high as 80 % among our patients who participated an eight-day structured education program given in four weeks. The most striking data of these patients were that most of them were living far

from our diabetes center so they could not able to complete the program. So we conducted a two-day education program in our outpatient clinics.

In the present study we retrospectively evaluated and compared the glycemic and lipid parameters of the patients with non-insulin dependent diabetes mellitus (NIDDM) who attended and completed either a 8-day or two-day structured out-patient diabetes education program.

# **PATIENTS AND METHODS**

Fifty patients with NIDDM who participated the two-day education program (program 1) and 50 patients who participated the eight-day education program (program 2) in our outpatient diabetes teaching unit between March 1995 and February 1997 were evaluated. Topics of the both programs were similar and consisted; survival skills (medications, insulin injection technique, prevention and treatment of

<sup>\*</sup> Presented as poster presentation in "Blacksea Diab Meeting, İstanbul,1997"

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hypoglycemia and hyperglycemia), daily practices (self-monitoring of blood glucose, diet, exercise, hygiene, foot-care) and cognitive issues (general understanding of diabetes, prevention of complications, family and personal coping skills, relationship to other health problems, role of hypertension and hyperlipidemia) Both one-to-one and class interactions by an education team was provided. Nurse educator, dietitian, doctor and psychologist gave the education. Education was supplemented with visual aides, charts, videotapes, transparency and printed materials for home use. Data of the all patients evaluated retrospectively.

Table 1 shows the clinical characteristics of these 50 patients in both groups. Thirty-five of the patients in group 1 and 38 of the patients in group 2 were female and 15 of the patients in group 1 and 12 of the patients in group 2 were male. Mean age was  $51 \pm 12$  in group 1 and  $53 \pm 10$  years in group 2. Duration of the diabetes were similar in both groups (7.9  $\pm$  4.6 in group 1 and  $8.2 \pm 4.1$  years in group 2). All the patients were on diet and on drug treatment either with insulin, insulin plus oral agents or only oral agents.

Fasting plasma glucose (FPG), postprandial 2-hour plasma glucose (PPPG), HbA1c, plasma total cholesterol and triglyceride levels of the patients just before and at least 6 months after the completion of the education program were evaluated. Data are presented as means ± SD. Student's t-test for paired samples was used to determine statistical significance of changes from baseline. p< 0.05 was accepted for statistical significance.

# **RESULTS**

The mean levels of glycemic and lipid parameters of patients on program 1 and 2 are given in table 2.

Table 1. Characteristics of the patients on two structured the diabetes outpatient education programs (percentages are given in paranthesis).

	Program 1	Program 2
Patients (number):	50	50
Female/ Male	35 / 15	38 / 12
Age (mean):	$51 \pm 12 \text{ yrs}$	$53 \pm 10 \text{ yrs}$
Duration of Diabetes	$7.9 \pm 4.6 \text{ yrs}$	$8.2 \pm 4.2 \text{ yrs}$
Treatment:		
Insulin	19 (38 %)	17(34 %)
Insulin+oral agents	18 (36 %)	19(38 %)
Oral agents	13 (26 %)	14(28 %)

The mean fasting plasma glucose (FPG) level of the patients on program 1 was  $159 \pm 64$  mg/dl and on program 2 was  $190 \pm 75$  mg/dl and a statistically significant decrease was observed after the education programs in both groups ( $128 \pm 36$  mg/dl and  $149 \pm 51$  mg/dl, respectively, p<0.05). Mean postprandial 2-hour plasma glucose level also declined from  $213 \pm 86$  mg/dl to  $159 \pm 49$  mg/dl in group 1 and from  $235 \pm 88$  mg/dl to  $184 \pm 71$  mg/dl in group 2; p<0.05). A statistically significant decrease was also detected in mean HbA1c level in both groups ( $7.3 \pm 1.2$  % vs.  $8.2 \pm 1.3$  % for program 1 and  $6.4 \pm 1$ % vs.  $8.7 \pm 2$  % for program 2; p<0.05).

An improvement in total cholesterol and triglyceride levels was also observed with both programs. Total cholesterol decreased from 219  $\pm$  54 mg/dl to 204  $\pm$  47 mg/dl with program 1 and from 234  $\pm$  16 mg/dl to 192  $\pm$  20 mg/dl with program 2. Triglyceride levels of the patients fell from 222  $\pm$  109 mg/dl to 206  $\pm$  80 mg/dl with program 1 and from 190  $\pm$  34 mg/dl to 170  $\pm$  31 mg/dl with program 2, p<0.05).

# **DISCUSSION**

A plan for continuing care is an essential feature in the management of every patient with diabetes. Patients with diabetes need specific education about their disease. Diabetes education improves patient knowledge and diabetes control(1-6). Self-management education is the corner stone of treatment for all people with diabetes.

Diabetes mellitus is a major health problem also in Turkey and nearly 2 million diabetics live in this country. Although conduction of education programs, including patients and educators, were planned throughout the country, a significant amount of diabetics still continue to visit diabetes centers localized in big cities like Ankara for the management of their diseases.

Since education of a diabetic patient is the cornerstone of diabetes self-management, and since structured education programs can not be carried through in every region of the country, increasing the number of participants and patients who complete the education programs in diabetes centers is essential. In our opinion dropout from education programs was the largest potentially correctable problem in this population of patients. For one reason or another, a substantial proportion of patients drop out of the education programs. Several contributing factors have been con-

Table 2. Glycemic levels and lipid profiles of the patients (mean ± SD).

***************************************	Progr	am 1	Program 2	
Parameter	Before	After	Before	After
FPG (mg/dl)	159 ± 64	128 ± 36	190 ± 75	149 ± 51
PPPG (mg/dl)	213 ± 86	$159 \pm 49$	$233 \pm 88$	$184 \pm 71$
HbA1c (%)	$8.2 \pm 1.3$	$7.3 \pm 1.2$	$8.7 \pm 2$	$6.4 \pm 1$
T. Cholesterol (mg/dl)	219 ± 54	$204 \pm 47$	$234 \pm 16$	$192 \pm 20$
Triglyceride (mg/dl)	222 ± 109	$206 \pm 80$	190 ± 34	$170 \pm 31$

<sup>\*</sup> Changes in all parameters labeled as before and after education, in both groups, has statistically significance.

sidered for these dropouts. One of these factors is the distance from the patients residence. A study from Mt. Sinai Hospital diabetes clinic demonstrated significant number of dropouts from follow-up, and they attributed this to living farther away and economic reasons(7). Graber et al. also found that distance from home to clinic was a factor associated with dropouts(7).

Patients are less likely to return for education program if they live far from the clinic. Most of the patients can not maintain the transportation and/hotel costs. Therefore, ongoing care of a chronic medical condition such as diabetes should take place within the patients residence. But as mentioned above it is not possible, at least now a days, in Turkey. So shorter education programs, in which the patient can par-

ticipate during his/her routine clinical control, can be taken into consideration. But the efficacy of such short programs can be questioned.

In the present study we evaluated the efficacy of two diabetes education programs (one given in eight days in four weeks and one in two consecutive days). Our results show that both glycemic and lipid parameters of the patients improved with both education programs.

In conclusion these results indicate that short-time education programs are as effective and satisfactory as longer programs in improving glycemic control and life quality in diabetics. Such programs can be put into practice for the patients who come visit diabetes centers from distant parts of the country.

# REFERENCES

- The Diabetes Control and Complication Trial Research Group: The effect of intensive treatment of diabetes on the development of long term complications in insulindependent diabetes mellitus. N Engl J Med 329:977-986;1993
- Kaplan RM., Davis WK. Evaluating the costs and benefits of out-patient diabetes education and nutrition counseling. Diabetes Care 9:81-86;1986
- 3. Anderson RM: Is the problem of compliance all in our heads ? Diabetes Educ 11: 31-34;1985
- Brown S.A. Studies of educational intervention and outcomes in diabetic adults: a meta-analysis revisited. Patient Ed Counsel 16:189-215;1990

- 5. American Diabetes Association; Third-Party reimbursement for diabetes care, self- management, education and supplies. Diabetes Care 20 suppl 1; 61;1997
- Padgett P., Mumford E., Hynes M., Carter R. Meta analysis
  of the effects of educational and psychological interventions on management of diabetes mellitus. J Clin
  Epidemiol 41: 1007-1030;1988
- 7. Graber AL., Davidson P., Brown AW., McRae JR., Wooldridge K. Dropout and relapse during diabetes care. Diabetes Care 15(11): 1477-1483, 1992

<sup>\*</sup> FPG: fasting plasma glucose; PPPG: postprandial plasma glucose

# PLASMA MALONDIALDEHYDE AND CATALASE LEVELS BEFORE AND AFTER ELECTROCONVULSIVE THERAPY\*

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# **SUMMARY**

Molecules that serve in biologic systems as electron acceptor are referred to as "oxidants" or "free radicals". Oxidative stress can be considered as a disturbance in the pro-oxidant - antioxidant balance in favor of the pro-oxidant.. Malondialdehyde (MDA) is a cleavage product of fatty acid peroxidation. The antioxidant defence is largely provided by overall enzymes (e.g. superoxide dismutase, glutathione peroxidase, catalase, glucose-6- phosphate dehydrogenase etc.) which tend to neutralize the oxidants  $(O_2^-$ , superoxide anion;  $HO_2$ , perhydroxyl radical;  $H_2O_2$ , hydrogen peroxide;  $OH^-$ , hydroxyl radical etc). In order to evaluate the effect of electroconvulsive therapy (ECT) on antioxidant enzyme status and lipid peroxidation, we measured the levels of MDA and activities of catalase in 15 patients before and after ECT. MDA levels decreased and catalase levels increased significantly after ECT. We concluded that ECT shows antioxidant activity with an unknown mechanism.

Key Words: Catalase, Electroconvulsive therapy, Malondialdehyde

Free radicals are chemical species possessing an unpaired electron that can be considered as fragments of molecules and which are generally very active (1). Toxic free radicals can be produced by many reactions required for the maintenance of normal metabolism and the production of energy in cell (2). Generation of free radicals in biological systems is mostly the result of radiolysis, photolysis, thermal degradation of organic material and redox reactions catalyzed by metal ions and enzymes (3). Polyunsaturated fatty acids are particularly vulnarable to free radical attack. This oxidative damage is termed lipid peroxidation and causes a reduction in membrane fluidity and permeability. Free radical induced damage to proteins may result in fragmentation, cross-linking, aggregation of protein (4). Strand scission, destruction and fragmentation of bases and deoxyribose sugars have all been reported to occur following free radical (mainly hydroxyl) attack on DNA. The resulting cytotoxicity, mutations and potential for malignant change occurs as a result of induced chromosomal aberrations (5). Much of evidence is based on experimental data indicating increased rates of lipid peroxidation in diseased tissues,

evaluation of therapeutic procedures, ameliorating effect of antioxidants, etc.

The mechanism underlying therapeutic effect of ECT is still unknown (6). Although most effects of ECT have been investigated, we were unable to find any documentation including the effect of ECT on lipid peroxidation. The primary aim of this study was to evaluate the effect of single-dose ECT on lipid peroxidation and antioxidant enzyme status.

# **MATERIALS AND METHODS**

15 schizophrenic patients, without another chronic systemic disturbance, hospitalized on the inpatient psychiatry department of Medical Faculty of Ankara University who were planned to undergo ECT were chosen for the study. As is generally the case, failure to respond to the other therapeutic procedures and development of intolerable side effects of drugs were major reasons for patients' being referred for ECT. Each patient gave written information for participation in the study. Although the planned course of ECT treatments ranged from 4 to 12 sessions over an 8 to 32 day

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period, blood samples were drawn before and after the first ECT. All patients received conventional bilateral ECT with bifrontotemporal electrode placement. Mean age was 43.6 ranging from 21 to 52. Venous blood samples were drawn from a peripheral vein at the beginning and 5 minutes after the first ECT session between 7 to 9 am. for the determination of MDA and catalase.

The catalase mediated decomposition of  $\rm H_2O_2$  was followed directly at 240 nm. The results were calculated from the extinction coefficient of  $\rm H_2O_2$  at 240 nm., spectrophotometrically (7).

The thiobarbituric acid (TBA) assay is the most popular and easiest method used as an indicator of lipid peroxidation and free radical activity in biological samples. The assay is based upon the reaction of TBA with MDA, one of the aldehyde products of lipid peroxidation (8).

# **RESULTS**

Fifteen patients (11 women and 4 men) participated in the study. As mentioned before, all blood samples were taken before and 5 minutes after the first ECT. The results of patients before ECT and the comparison of results before and after ECT were given at Table-1. MDA levels decreased and catalase levels increased significantly after ECT. The statistical analyses were made with 'paired t-test'. The differences between the groups were statisti-cally meaningful.

### DISCUSSION

Pathologic dysfunctions suggested to involve oxygen radicals include conditions affecting several organ systems like inflammatory-immune injury (e.g. glomerulonephritis, vasculitis) (9), ischemia-reflow injury

# **REFERENCES**

- Davies KJA, Goldberg AL. Proteins damaged by oxygen radicals are rapidly degraded in extracts of red blood cell. J Biol Chem 1987; 262/17:8227-8234
- Bosaga HS. Biochemical aspects of free radicals. Biochem Cell Biol 1990; 68:989-998
- 3. Cochrane CG. Cellular injury by oxidants. Am J Med 91 (suppl.3C): 235-305
- Clark RA, Stone PJ, Hag AE, Calore JO, Franzblau C. Myeloperoxidase catalysed in activation of alpha-1-protease inhibitor by human neutrophils. Biol Chem 198;1; 256: 348-53
- Aruoma OI, Halliwell B, Gajewski E, Dizdaroğlu M. Copper ion-dependent damage to bases in DNA in the presen-

Table 1. Plasma MDA and catalase levels in Pre- and Post-ECT patient groups.

n=15 for all	MDA (nmol / ml.)	Catalase (c / gHb.)
Pre-ECT	8.1 ± 1.3	77.5 ± 9.2
Post-ECT	$4.7 \pm 1.1$	$125.2 \pm 21.3$
Paired t test	p < 0.001	p < 0.001

(10), drug and toxin induced reactions (11), alcohol, radiation injury, iron overload (12), aging and cancer (13), lungs (e.g. cigarette smoking) (14), heart and cardiovascular system (e.g. Doxorubicin toxicity), kidney (e.g. renal graft rejection) (15), brain (e.g. hyperbaric oxygen) (16,17). In the light of this information, we can easily understand that lipid peroxidation and antioxidant defense systems play an important role in the mechanism of many pathologic events of body, like in CNS (18).

In our study, we aimed to observe the effect of ECT on lipid peroxidation (MDA) and antioxidant defense systems (catalase). As a result, we observed a meaningful alteration in catalase and MDA, between preand post-ECT groups. There was an increase in catalase (with a ratio of % 61) and a decrease in MDA (with a ratio of %58). We conclude that, ECT prevents lipid peroxidation and free radical damage and strengthens antioxidant defense systems of the body.

Probably, such studies may lead to new approaches in therapeutic mechanism of ECT and underlying etiology of mental disorders. Still, these initial observations need to be confirmed in a large number of subjects with advanced techniques those have the ability to evaluate, even minor brain changes. Further investigations should also involve longterm follow-up studies and animal experiments those give the chance to directly observe the target tissue.

- ce of hydrogen peroxide. Biol Chem 1991; 273: 601-604
- Milstein V, Small JG, Miller, MJ, Sharpley PH, Small IV. Mechanisms of action of ECT: Schizophrenia and schizo-affective disorder. Biol Psychiatry 1992; 27:1282-1292
- Grankvist K, Marklund S. Superoxide dismutase, catalase and scavengers of hydroxyl radicals protect against the toxic action of alloxan on pancreatic islets cells in vitro. Biochem J 1979;182: 17-25
- Esterbaur H, Cheeseman K. Determination of aldehydic lipid peroxidation products: malondi-aldehyde and 4-hydroxynonenal. Methods Enzymol. 1990;186:407-421

- Chaudri G, Clark IA, Hunt NH, Cowden WB, Ceredig R. Effect of antioxidants on primary alloantigen-induced T-cell activation and proliferation. J Immunol 1986; 137: 2646-52
- Becker LC, Ambrossia G. Myocardial consequences of reperfusion. Prog In Cardiovasc Dis 1987; 30/1:23-44
- Garcia-Escrig M, Martinez J, Fernandez-Ponsati J, Diaz J, Soto O. Severe central nervous system toxicity after chronic treatment with cyclosporine. Clin Neuro-pharm 1994; 17/3:298-302
- 12. Dillard CJ, Downey JE, Tappel AL. Effect of antioxi dants on lipid peroxidation in iron loaded rats. Lipid 1984; 19:127-33
- Ames BN. Dietary carcinogens and anticarcinogens: oxygen radicals and degenerative diseases. Science 1983; 221:1256-64
- Brigham KL. Role of free radicals in lung injury. Chest 1986;
   89:859-63

- Boud L, Ardaillau R. Reactive oxygen species: Production and role in the kidney. Am J Physiol 1986; 251 (5 pt 2): 765-76
- Avaret N, Coussemacq M. Thiobarbituric acid-reactive material content and enzymatic protection against peroxidative damage during the course of cryogenic rabbit brain edema. Neurochem Research 1990; 15/8:791-795
- Ellis EF, Dodson LY, Police RJ. Restoration of cerebrovascular responsiveness to hyperventilation by the oxygen radical scavenger-acetylcysteine following experi-mental travmatic brain injury. J Neurosurg 1991; 75:774-779
- 18. Halliwell B, Gutteridge JMC. Metal ions and oxygen radical reactions in human inflammatory joint disease. Philos Trans R Soc Lond (Biol.) 1985; 311:659-71

# ARE URAEMIC CHILDREN IMMUNOLOGICALLY DISTURBED?\*

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### **SUMMARY**

In this study, peripheral blood total white blood cell count, total granulocytes, total lymphocytes, lymphocyte subsets were evaluated, skin tests with PPD and Candida antigens were performed, serum immunoglobulin (Ig) and complement levels were measured in thirty children with end-stage renal failure (10 predialysis, 10 continuous ambulatory peritoneal dialysis-CAPD and 10 hemodialysis) and 15 healthy controls. The data showed significant lymphopenia in uraemic children except CAPD group (predialysis: p<0.05; hemodialysis: p<0.0005), when compared with the controls. Absolute values of lymphocyte subsets were significantly lower than controls in all groups and there was no difference in the ratio of CD4/CD8 lymphocytes between the groups. Patients in the predialysis group showed significantly decreased response to Candida skin test (p<0.05). Serum Ig levels were significantly decreased in CAPD group compared with the control group (p<0.01).

Key Words: uraemia, children, immune system, hemodialysis, CAPD.

Chronic renal failure (CRF) affects many organ systems in humans including the immune system. The degree of the abnormalities in the immune system at uraemic stage correlates well with the severity of renal failure (1-5). Most studies reported so far, are concerned with the immune status in adult patients with CRF while there are only few studies in paediatric age group. Paediatric textbooks are also comprised of data from adult uraemic patients with immune system abnormalities.

The aim of the present study is to evaluate the changes in the immune system of paediatric patients with CRF using certain immunological parameters. Patients receiving hemodialysis, or continuous ambulatory peritoneal dialysis (CAPD) and those without dialysis treatment were grouped separately in order to analyse the effects of renal replacement therapy on the immune system.

# MATERIALS AND METHODS

Thirty patients (19 boys and 11 girls) admitted to the University of Ankara Medical School, Department

of Paediatric Nephrology with a diagnosis of CRF were included in the study. The age distribution of the patients was between 5 and 18 years (mean age = 12.4±3.3 years). Of these, 20 were receiving renal replacement therapy (10 CAPD and 10 hemodialysis) while remaining 10 patients showing a creatinin clearance of 9.4±5.2 ml/min/ 1.73 sqm body surface, were designated as "predialysis" group. CAPD lasted for 7-25 months whereas hemodialysis was continued for 12-73 months. None of the patients had an underlying renal disease that is particularly known to cause immunological abnormalities. The patients were seen on an ambulatory basis and thus, were not hospitalised during the study. Fifteen healthy subjects (8 boys and 7 girls) between 6-16 years of age (mean age= 10.1±2.4 years) comprised the control group.

Peripheral blood total white blood cell count (TWBC), total granulocyte count (TGC), total lymphocyte count (TLC) were measured using coulter-counter. Lymphocyte phenotypes were evaluated in the Immunology Laboratory of Department of Paediatric Immunology with indirect immunofluorescence

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using monoclonal antibodies (CD3 for total T cells, CD4 for T-helper/inducers, CD8 for T cytotoxic/ supressors, CD16 for Natural Killer cells, CD19 for total B cells; Cymbus Bioscience Ltd., Southampton, UK). All cell counts were presented as relative values (percentage of lymphocyte phenotypes) and absolute numbers (percentage x total lymphocytes/ 100) in cubic millimetres (mm3). In the hemodialysis group the blood samples were collected prior to the dialysis treatment. Skin tests were performed in every patient using PPD and Candida Albicans antigens intradermally to analyse delayed type hypersensitivity (6). All patients in the study had previous BCG vaccination. Serum levels of IgG, IgA, IgM, C3, C4 were measured using a Behring Nephelometer in the Immunology Laboratory of Ibni Sina Hospital.

Results were presented as mean values ± SEM for each patient group and unpaired Student's T test, and Mann-Whithey U test were used for parametric and nonparametric comparisons, respectively. A p value less than 0.05 was regarded as significant. The results of all the immunologic tests performed in each patient group were compared with the control group and also comparisons were made between the patient groups.

# **RESULTS**

The results of immunological tests are presented in Table 1A and B.

Both predialysis and hemodialysis patients showed significant lymphopenia while CAPD patients did not show any significant change in TLC when compared with the control group (p<0.05 and p<0.0005, respectively). Patients receiving hemodialysis had signi-

Table 1. Immunologic data from children with CRF

A.

Subjects	TWBC (/mm³)	TGC (/mm³)	TLC (/mm³)	(%)	D3+ (/mm <sup>3</sup> )	(%)	D4 <sup>+</sup> (mm <sup>3</sup> )	(%)	(/mm³)	CD4/ CD8	CD1 (%)	6+ (mm³)		)20+ (mm³)
Predialysis (n=10)	8140 ±926	4835 ±718	2854 <sup>a</sup> ±342	52.1	1490ª ±196	32.9	925ª ±106	26.7	782 ±139	1.27 ±0.11	13.5	422 ±108	10.7	310 ±66
CAPD (n=10)	8160 ±899	4767 ±534	3039 ±475	49.9	1463ª ±233	29.2	848 <sup>a</sup> ±127	25.3	742ª ±122	1.23 ±0.13	10.1°	289 <sup>d</sup> ±39	9.4	288 ±71
Hemodialysis (n=10)	7070 <sup>b</sup> ±629	4377 ±490	2379 <sup>d</sup> ±232	52.9	1255 ±126	33,2	785° ±84	24.3 <sup>b</sup>	584* ±70	1.35 ±0.11	12.3	291 <sup>d</sup> ±35	8.9	205 <sup>d</sup> ±30
Control (n=15)	9387 ±470	4849 ±437	3800 ±200	53.6	2050 ±146	32.3	1248 ±112	28.6	1089 ±79	1.14 ±0.05	13.6	519 ±38	11.9	456 ±51

B.

Subjects	lgG (g/L)	IgA (g/L)	IgM (g/L)	C3 (g/L)	C4 (g/L)	PPD (%)+	Candida (%)+
Predialysis (n=10)	11.65 ±1.60	1.605 ±0.278	1.411 ±0.261	0.710 ±0.048	0.338 ±0.058	30	50ª
CAPD (n=10)	9.47 <sup>d</sup> ±0.94	1.375° ±0.188	0.935 <sup>b</sup> ±0.232	0.752 ±0.042	0.280 ±0.047	30	70
Hemodialysis (n=10)	16.11 ±2.34	1.499 ±0.148	1.911 ±0.205	0.692 ±0.063	0.262 ±0.024	20	70
Control (n=15)	14.84 ±0.68	1.841 ±0.123	1.852 ±0.176	0.796 ±0.034	0.248 ±0.016	53.3	93.3

Data are presented as means ± SEM

All comparisons are made between patient groups and control group

 $^{a}$  p < 0.05;  $^{b}$  p < 0.01;  $^{c}$  p < 0.005;  $^{d}$  p < 0.0005;  $^{e}$  p < 0.0001

ficantly reduced number of TWBC (p<0.01) but no significant change was found in TGC. All patient groups had significantly lower numbers (absolute values) of nearly all lymphocyte subsets (CD3+, CD4+, CD8+, CD16+ and CD19+ cells) while only a few of the percentages (relative values) were significantly different from those of control subjects. There was no change however, in the ratio of CD4/CD8 in either group studied.

There were normal responses to PPD and Candida skin tests in CAPD and hemodialysis patients but poor response was observed with Candida antigen in predialysis group compared with the control group (p<0.05).

Serum Ig levels did not show any significant change in neither predialysis nor hemodialysis patients whereas CAPD patients had significantly lower serum Ig levels compared with the control subjects (p<0.0005 for IgG; p<0.05 for IgA; p<0.01 for IgM).

Serum C3 and C4 values showed no significant change in any of the groups studied.

The CAPD group had significantly lower serum Ig levels than the hemodialysis group (p<0.05 for IgG; p<0.005 for IgM). There was no significant difference between the patient groups for any of the other immunological parameters studied.

# DISCUSSION

Uraemia may cause lymphopenia the degree of which correlates with the decrease in Glomerular Filtration Rate (GFR) (1-4). The present study showed that uraemic children except those receiving CAPD, may develop lymphopenia. There was no significant change in TLC in the CAPD group. Hisano et al. (7) also showed that uraemic children on CAPD therapy had total lymphocyte counts similar to the controls. Our results showed that TWBC was significantly reduced in the uraemic patients receiving hemodialysis when compared with the control subjects. Since no significant change was found in TGC, the decrease in TWBC was considered to be the result of the significant lymphopenia observed in this group.

Most of the studies concerned with adult uraemic patients showed decreased numbers of T cell subsets

without any change in the relative (percentage) values or in CD4/CD8 ratio (1-4). In contrast, paediatric studies have demonstrated that patients receiving CAPD therapy showed no change in either absolute or relative values (7,8). In one other study, similar results on the relative values of lymphocyte subsets were reported in predialysis, hemodialysis and CAPD patients in paediatric age group (9). Our results on the relative values of 1 lymphocyte subpopulations correlated well with these studies. The CD4 / CD8 ratio of the patients was also similar to those of control subjects. The low values in the absolute number of lymphocyte subpopulations found in our patients were in accordance with some studies in adult patients (2,4).

Though not uniform, the data is sufficient to suggest that skin test response is decreased in uraemic adult patients (4). There is only one study in paediatric patients where skin test response was decreased (5). In our study patients in predialysis group had poor response to Candida skin test. Hemodialysis and CAPD patients showed a nonsignificant decrease in their skin test response. This finding may have two possible explanations; firstly, CAPD and hemodialysis treatments might have corrected the abnormality partially, hence the decrease is not marked (nor significant), and secondly, the small number of patients included in the study might have effected the statistical analysis.

It is well known from the previous studies that serum Ig levels may be low due to the loss of immunoglobulins by peritoneal route in paediatric uraemic patients (7,11). Similarly, in our CAPD group, the levels of IgG, IgA and IgM were decreased compared with the controls. Also in accordance with the literature, the fall in IgG was more significant.

In summary, the results of the present study suggest that the effects of uraemia may only slightly change some of the components of the immune system, particularly cellular immunity in children with CRF. However, since the parameters used here are mostly quantitative, it is difficult to state at this stage, whether these changes are sufficient to cause functional impairment in the immune system of uraemic children.

### REFERENCES

- 1. Schollmeyer P, Bozkurt F. The immune status of the uraemic patient: hemodialysis vs CAPD. Clin Nephrol 1988; 30 (Suppl. 1): S37-40.
- 2. Chatenoud L, Herbelin A, Beauran G, et al. Immune deficiency of the uraemic patients. Adv Nephrol 1990; 19: 259-74.
- 3. Drukker A, Schlesinger M. The immune system in uraemia. Child Nephrol Urol 1990; 10: 61-4.
- Benfield M, Michael AF. Immunology of uraemia. In: Edelman CM, ed. Paediatric Kidney Disease. 2nd ed. Boston/Toronto/London: Little, Brown and Co, 1992: 783-90.
- 5. Chatenoud L, Jungers P, Descamps-Latscha B. Immunological considerations of the uraemic and dialysed patient. Kidney Int 1994; 45 (Suppl. 44): S92-6.
- Lawlor GJ, Fischer TJ. Immunologic methods useful in the diagnosis of infectious disease. In: Manual of Allergy and Immunology. 2nd ed. Boston/Toronto: Little, Brown and Co, 1988: 384-7.

- 7. Hisano S, Miyazaki C, Hatae K, et al. Immune status of children on continuous ambulatory peritoneal dialysis. Pediatr Nephrol 1992; 6: 179-81.
- 8. Ettenger RB, Blifield C, Prince H, et al. The paediatric nephrologist's dilemma: growth after renal transplantation and its interaction with age as a possible immunologic variable. J Pediatr 1987; 111: 1022-5.
- Drachman R, Schlesinger M Shapira H, et al. The immune status of uraemic children/adolescents with chronic renal failure and renal replacement therapy. Pediatr Nephrol 1989; 3: 305-8.
- Rister M, Roth B, Skopnit H, et al. Prüfung der Hautreaktion vom Spat-Typ chronisch kranker. Kinder Klin Pediatr 1986; 198: 316-20.
- Fivush BA, Case B, May MW, et al. Hypogammaglobulinemia in children undergoing continuous ambulatory peritoneal dialysis. Pediatr Nephrol 1989; 3: 186-8.

# THE EPIDEMIOLOGICAL CHARACTERISTICS OF WOMEN DIAGNOSED TO HAVE EPITHELIAL OVARIAN CANCER IN A TURKISH POPULATION: A PRELIMINARY REPORT OF 129 CASES

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# **SUMMARY**

The purpose of this study is to determine the epidemiological characteristics of women with epithelial ovarian cancer in a Turkish population. A prospective study was performed on 129 women who were diagnosed to have epithelial ovarian cancer between January 1,1997 and March 30, 1998 at SSK Ankara Maternity and Women's Health Teaching Hospital. Most of the women included were found to belong to low socioeconomic group (n:81, 62.8%), whereas 58.9% were illiterate. Grandmultiparity was identified in 35 subjects (27.1%) while 16 patients reported to have ever used oral contraceptive pills (12.4%). Sixteen patients had got simple hysterectomy (12.4%) while five women (3.9%) were found to have either tubal ligation or unilateral oophorectomy (n:2, 1.6% and n:3, 2.3%, respectively). Sixty-two women had got spontaneous menopause at the diagnosis of ovarian cancer (48.1%) and the mean age at spontaneous menopause was found to be 46.3±6.4 years. Our data suggest that established protective factors for epithelial ovarian cancer such as increasing parity, hysterectomy, sterilization by tubal ligation and oophorectomy do not seem to protect an absolute proportion of Turkish women from epithelial ovarian cancer. In order to confirm these preliminary data, a larger, case-controlled study is needed.

Key Words: Epithelial Ovarian Cancer, Epidemiology.

Ovarian cancer is the most common fatal cancer of the female reproductive tract in the western world and is a leading cause of cancer deaths in North American and European women (1). About 4200 new cases of ovarian cancer in England and Wales (2) and 21000 in the United States (U.S.) (3) are diagnosed each year. The life time risk of ovarian cancer for women in industrialized countries is about 2% (4). Mortality rates are only slightly lower than the incidence rates and are a reflection of the poor prognosis.

Increasing research attention has been given to the epidemiology of ovarian cancer for the last twenty years (1). Although numerous studies have examined ovarian cancer risk factors and many attempts were given to identify the epidemiology of ovarian cancer, several studies revealed conflicting or inconsistent results. Broadly speaking, ovarian cancer incidence increases with age, and is more common in women with a family history of the disease. Nulliparity and infertility can be also classified as established risk conferring

factors (5). Risk decreases with increasing parity, oral contraceptive use, hysterectomy and sterilization by tubal ligation.

The purpose of this paper is to determine the epidemiological characteristics of women diagnosed to have epithelial ovarian cancer in a Turkish population.

# MATERIAL AND METHODS

The women diagnosed to have epithelial ovarian cancer at SSK Ankara Maternity and Women's Health Teaching Hospital were identified prospectively between January 1, 1997 and March 30, 1998. A total of 129 cases of epithelial ovarian cancer were identified during this period and all were included in the study. The socioeconomic and educational status of the patients were analyzed. Patients coming from families that had an income less than 50 million Turkish liras per month were identified in the low socioeconomic group, whereas women from families having a monthly income of 50-100 million Turkish liras were identified

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in the moderate socioeconomic status. Patients from families that had an income more than 100 million Turkish liras per month were identified in the high socioeconomic status. Educational status of the patients were analyzed by dividing them into five groups such as illiterate, educated for five years, for eight years, for eleven years and women having university degrees.

History of oral contraceptive use, reproductive history, age at the birth of the first child, breast feeding, duration of lactation, history of tubal ligation, oophorectomy and hysterectomy, family history of ovarian, endometrial and breast cancer, history of infertility, fertility drug use, age at menarche and spontaneous menopause, talc use, smoking and saturated fat intake and milk consumption in the diet were also investigated.

The statistical analysis of the data was performed by using SPSS programme for MS Windows Release 6.0.

# **RESULTS**

Nulliparity was identified in 18 patients (14%), whereas 9 patients were primiparae (7%) and 102 cases were found to have two or more parities (79%). The mean number of parities was found to be 3.6±2.6 (range:0-12) for all the patients included in the study. Sixty-one women had a history of either spontaneous or induced abortions (47.3%) while 68 patients reported to have no abortions (52.7%). The mean number

Table 1. Demographic characteristics of women diagnosed to have epithelial ovarian cancer.

	No	%
PARITY		
0	18	14
1	9	7
2+	102	79
SPONTANEOUS AND/OR		
INDUCED ABORTIONS		
Yes	61	47.3
No	68	52.7
EDUCATION		
Illiterate	76	58.9
Educated for 5 years	44	34.1
Educated for 8 years	4	3.1
Educated for 11 years	4	3.1
University degree	1	0.8
SOCIOECONOMIC STATUS		
Low	81	62.8
Moderate	41	31.8
High	7	5.4

of abortions was found to be 2.2±1.8 (range:1-12) for women reported to have abortions.

When the educational status of women included were analyzed, it was found out that 58.9% of them were illiterate (n:76), whereas 44 women reported to have been educated for five years (34.1%). The remainders were found to be educated for 8 years or more (n:9, 9.7%). Most of the women included in the study were found to be from either low or moderate socioeconomic group (n:122, 94.6%) while only seven subjects reported to have high socioeconomic status (5.4%) according to the criteria explained in the Material and Methods. Table 1 demonstrates demographic characteristics of women diagnosed to have epithelial ovarian cancer.

Sixteen women included reported to have used oral contraceptive pills (12.4%). The mean duration of oral contraceptive use was found to be 33.2±22.8 months (range:3-72) for oral contraceptive users. When patients were analyzed in terms of increasing parity, grandmultiparity was identified in 35 cases of epithelial ovarian cancer (27.1%). On the other hand, 12.4% of our patient population had got hysterectomy (with ovarian conservation) (n:16) while five women (3.9%) were found to have had either tubal ligation or unilateral oophorectomy (n:2, 1.6% and n:3, 2.3%, respectively). The mean duration between hysterectomy and diagnosis of epithelial ovarian cancer was found to be 6.75±7.7 years (range:1-25) for the hysterectomized patients. The percentages of the establis-

Table 2. Established protective factors for ovarian cancer in 129 women diagnosed to have epithelial ovarian cancer.

-	No	%
Oral Contraceptive Use		
Yes	16	12.4
No	113	87.6
Grandmultiparity		
Yes	35	27.1
No	94	72.9
Hysterectomy		
Yes	16	12.4
No	113	87.6
Sterilization (Tubal Ligation)		
Yes	2	1.6
No	127	98.4
Unilateral Oophorectomy		
Yes	3	2,3
No	126	97.7

Table 3 Duration between hysterectomy and diagnosis of epithelial ovarian cancer in terms of years.

Years	No	%
1	2	12.5
2	3	18.8
3	4	25
4	2	12.5
5	1	6.3
10	1	6.3
20	2	12.5
25	1	6.3

hed protective factors for epithelial ovarian cancer (1) is shown in Table 2, whereas Table 3 demonstrates the duration between hysterectomy and the diagnosis of epithelial ovarian cancer in terms of years.

Family history of endometrial cancer, breast cancer and ovarian cancer was found to be in a total of 18 cases of epithelial ovarian cancer (14.1%). It should be emphasized that each patient with a family history of the mentioned cancers reported to have only one of the diseases in the family history. Family history of endometrial cancer, breast cancer and ovarian cancer in women diagnosed to have epithelial ovarian cancer is shown Table 4.

The mean age at the birth of the first child was found to be 20.2±4.9 years (range: 14-38) for the parous women included in the study. Only two cases of epithelial ovarian cancer had their first child after 35 years of age (1.8%). Twenty-three v/omen reported to have never breast fed (17.9%), whereas 106 women had ever performed breast feeding (82.1%). The mean duration of lactation was found to be 47.6±36.4 months (range:0-158) for the parous women included in our series.

The mean age at menarche was found to be 13.6±1.4 years (range:10-17) for the women diagnosed to have epithelial ovarian cancer. However, 62 women had got spontaneous menopause at the time of diagnosis of epithelial ovarian cancer (48.1%) while 67 patients were found to be still menstruating (51.9%). The mean age at spontaneous menopause was found to be 46.3±6.4 years (range: 36-55).

On the other hand, 3.1% of our patient population had got perineal talc application (n:4) while 18 women were found to be smokers (14%). High intake of saturated fat and milk consumption in the diet was identified in 23 women in our series (17.8%). Table 5 demonstrates equivocal factors for epithelial ovarian cancer (1) identified in our patient population.

Table 4. Family history of endometrial cancer, breast cancer and ovarian cancer among 129 women diagnosed to have epithelial ovarian cancer\*.

	No	%
Endometrial Cancer		
Yes	6	4.7
No	123	95.3
Breast Cancer		
Yes	6	4.7
No	123	95.3
Ovarian Cancer		
Yes	6	4.7
No	123	95.3

<sup>\*</sup>Each patient had only one type of the mentioned diseases in the family history.

# DISCUSSION

It has been known for some time that reproductive factors influence a woman's risk of developing ovarian cancer. Interest in the role of parity and gravidity in the development of ovarian cancer started with the observation of high rates of ovarian cancer among nuns (6) and low rates among groups with generally high parity (7,8). Both case-control studies and cohort studies have clearly demonstrated the protective effect of births. Recent large collaborative studies involving

Table 5. Equivocal factors for ovarian cancer in 129 women diagnosed to have epithelial ovarian cancer.

	No	%
Breast feeding		
Yes	106	82.1
No	23	17.9
Menopause at diagnosis		%
Yes	62	48.1
No	67	51.9
History of infertility		
Yes	23	17.8
No	106	82.4
Perineal talc application		
Yes	4	3.1
No	125	96.9
Smoking		
Yes	18	14
No	111	86
Saturated fat intake		
Low	47	36.4
Moderate	59	45.7
High	23	17.8
Milk consumption		
Low	48	37,2
Moderate	58	45
High	23	17.8

the re-analysis of data from several centers in the U.S. (9) and Europe (10) and a large national Swedish study (11) have confirmed a decreasing risk with increasing parity. In general, published results tend to show a 40% reduction in ovarian cancer risk associated with the first term pregnancy and overall trends consistent with a 10-15 % average reduction in risk with each term pregnancy (9). In our study, it was found out that 14% of the epithelial ovarian cancer cases had been nuns. However, it was a surprising finding that 27.1 % of our patient population were grandmultiparous.

Some studies report significant decreases in ovarian cancer with incomplete pregnancy (10,12,13) while many have failed to find any effect (14-16). In our series, 47.3% of epithelial ovarian cancer cases had got either spontaneous or induced abortions, whereas the mean number of abortions was found to be 2.2±1.8. Negri et al. (10) reported a decreasing trend in risk with number of abortions, whereas Whittemore et al. (9) found that gravidity did not affect risk.

Studies in Britain and China have found an elevated risk of ovarian cancer among women of higher socioeconomic status (17-19). This relationship is believed to be the result of lower fertility rates among these more educated and affluent groups (20). Although Beral et al. (20) reported that ovarian cancer tended to be less common in lower socioeconomic groups, we found out that 62.8% of our patient population had belonged to low socioeconomic group, whereas 58.9% of our cases were illiterate. This finding doesn't agree with the previously reported studies (17-20) but it should be emphasized that our institution generally serves for women from low socioeconomic status.

On the other hand, studies over the last twenty years have shown consistently lowered risks of ovarian cancer for ever- versus never-use of oral contraceptives (12,17,21-23). Risk in ever-users range from 40-60% of that in never-users and the degree of protection increases with the duration of use among ever-users. Women who use oral contraceptives for five years or more experience about a 60% reduction in risk. Although a 5-10% decrease in risk with each year of use is reported (9,24), we found out that 12.4% of our patient population had been ever-users with a mean duration of 33.2±22.8 months of oral contraceptive use.

Recent studies have suggested that tubal ligation or simple hysterectomy(with bilateral ovarian conservation) as well as previous unilateral oophorectomy reduce the risk of subsequent ovarian cancer (9,25,26). In our series, 12.4 % of our patient population had got simple hysterectomy, whereas 3.9% of women included in the study had got either tubal ligation or unilateral oophorectomy. That is to say; a total of 16.3% of women in our patient population have got established protective factors (1) for ovarian cancer. This finding is striking although it has been neither controlled nor adjusted for other variables such as age and parity.

Family history of endometrial cancer, breast cancer and ovarian cancer was found to be 4.7% for all the patients included in this study. A review of observational studies report that women with a family history of ovarian cancer are three to four times more likely to develop ovarian cancer than those without such a history (27-29). Segregation analysis of families with a clustering of both ovarian and breast cancer cases had led to the suggestion that a single dominant gene may be responsible for both (28). Genetic linkage studies have identified a marker gene on chromosome 17, called BRCA-1 which predisposed those with gene to both ovarian and breast cancer (27,29). Although the presence of such a gene may confer a greatly increased risk, it must be pointed out that the proportion of all ovarian cancer cases which are of the familial ovarian carcinoma type may be as little as 1% (30).

Whittemore et al.(9) and Adami et al.(11) demonstrated that the risk of epithelial ovarian cancer decreased with increasing age at the first birth (after adjustment for parity itself). It was reported that a 10% reduction in risk occurred for each five-year increment in age at first birth (11). However, these findings are contradicted by those of the pooled European studies which found a significantly increased risk in those women having their first child at ages greater than 35 years compared with those first giving birth age 25 or younger (10). In our study, the mean age at the birth of the first child was found to be 20.2±4.9 years. However, 90.2% of the parous women included in this study were found to give their first births at age 25 or younger (not shown), whereas 1.8% of the parous women in our patient population had given their first births after 35 years of age. To date, there are inconsistent findings as to how the age of a woman at the birth of her first child affects ovarian cancer risk.

Risch et al.(31) were the first to report a protective effect of lactation. In an analysis based on six US case control studies, Whittemore et al.(9) found a reduced risk of ovarian cancer in women who breast fed com-

pared to those who had not, after controlling for parity and oral contraceptive use. Studies outside the U.S. (China, Japan, Australia, WHO) do not support these findings (14,15,17,18,32). Although a 1% reduction in risk for each month of breast feeding was suggested (9), we found out that 82.1% of our patient population had breast fed while the mean duration of breast feeding was found to be 47.6±36.4 months for the parous women in our study.

Although Whittemore et al. (9)reported a weak trend of decreasing ovarian cancer risk with increasing age at menarche, most studies have found no significant effect of age at menarche on ovarian cancer risk (12,14,15,18,21,33). Franceschi et al. (33) reported of doubling in the relative risk associated with an age at menopause of 53 or greater compared with menopause at under 45 years old and noted a significant trend of increasing risk of ovarian cancer with later age at menopause. On the other hand, Purdie et al. (14) found no significant effect of age at menopause on ovarian cancer risk in Australia. We found the mean age at menarche as 13.6±1.4 years for women diagnosed to have epithelial ovarian cancer whereas the mean age at spontaneous menopause was found to be 46.3±6.4 years in this study. The exact nature of the relationship between menarche, menopause and ovarian cancer is by no means clear.

Whittemore et al.(9) reported that infertile women who took fertility drugs were estimated to have a three-fold increase in risk (95% confidence interval 1.3-6.1) of epithelial ovarian cancer compared to women without a history of infertility. Studies questioning women directly about their difficulty in conceiving have generally found increased relative risks of ovarian cancer (13,18,34,35), however, few achieved statistical significance (13,35). On the other hand, Risch et al.(15) found the risk of ovarian cancer to be unaffected by infertility, after controlling for parity. Rosing et al.(36) demonstrated that the use of the drug clomiphene citrate for 12 months or more was associated with an increased risk of ovarian cancer (relative risk 11.1, 95% confidence interval 1.5-82.3). In the present study, we found out that 17.8% of our patient population had a history of either primary or secondary infertility whereas 7% of all women included had ever used fertility drugs. The mean duration of exposure to fertility drugs was found to be 22.8±18.3 months among the fertility drug users. Investigating the effects of infertility on ovarian cancer, above and

beyond the elevated risk conferred by low parity and other factors has proven problematic and its role in the epidemiology of ovarian cancer remains unclear.

The suggestion that talc may be involved in the etiology of ovarian cancer was made over 20 years ago when talc particles were detected in ovarian tumors (37). Many studies have shown significantly increased ovarian cancer risk with use of talc on the perineum or sanitary napkins (14,17,18) while the others have not found a significant association (38-40). In our patient population, only 3.1% of the women were found to use perineal talc. The evidence in favour of a causal link between talc and ovarian cancer is not conceiving (37).

On the other hand, 14% of our patient population reported to have ever smoked. Although Purdie et al.(14) reported a significantly raised relative risk of 1.38 among smokers compared to non-smokers, numerous studies in this area showed no association (12,17-19,32,38).

Cramer et al.(41) have highlighted the role of milk consumption in the etiology of ovarian cancer and has proposed that increased dietary galactose consumption and low serum levels of galactose-1-phosphate uridyl-transferase (which prevents degradation of galactose to glucose) is causal. Recent studies, however, have not confirmed these findings (42,43). In our study, 17.8% of our patients reported to have highly consumption of milk in their diets.

Several studies have indicated that dietary fat may be a direct causal factor (42,44). Intake of saturated fat and lower intake of vegetables and/or vegetable fiber are associated with an elevated risk of ovarian cancer (45,46). In the present study, saturated fat intake was identified to be high in 17.8% of our patient population but evidence about the association between dietary fat and epithelial ovarian cancer does not seem to be strong.

Our study is limited since it is not a large, population-based and a case-control one. But we believe that some of the data reported in this study is striking such as the high percentage of grandmultiparous women (27.1%), high percentage of patients from low socioe-conomic group (62.8%), long duration of breast feeding among the patients and high percentage of women undergoing pelvic surgery before the diagnosis of ovarian cancer (16.3%) which seem to conflict with the previously reported data in literature. Our data

suggest that established protective factors for epithelial ovarian cancer such as increasing parity, hysterectomy, sterilization by tubal ligation, oophorectomy and breast feeding do not seem to protect an absolute

proportion of Turkish women from epithelial ovarian cancer. In order to confirm these preliminary data, a larger, case-controlled study is needed.

# REFERENCES

- Banks E., Beral V., Reeves G. The epidemiology of epithelial ovarian cancer: a review. Int J Gynecol Cancer. 1997; 7: 425-438.
- Swerdlow AJ and Dos Santos Silva. Atlas of cancer incidence in England and Wales, 1968-85. 1993; pp.11. Oxford: Oxford University Press.
- 3. Yancik R. Ovarian cancer. Age contrasts in incidence, histology, disease stage at diagnosis and mortality. Cancer 1993; 71: 517-523.
- Parkin DM, Muir CS, Whelan SL, Gao YT, Ferlay J and Powell J, eds. Cancer Incidence in five continents. Lyon: IARC Scientific Publications, 1992; 770-773.
- Ayhan A. Epitelyal Over Kanseri. In Kişnişçi, Gökşin, Durukan, Üstay, Ayhan, Gürgan, Önderoğlu eds.. Temel Kadın Hastalıkları ve Doğum Bilgisi. 1996; pp.982. Ankara, Güneş Kitabevi Yayınları.
- Fraumoni JF Jr, Lloyd JW, Smith EM, Wagoner JK. Cancer mortality among nuns: Role of marital status in the etiology of neoplastic disease in women. J Natl Cancer Inst. 1969; 42: 455-68.
- Enstrom J. Cancer mortality among Mormons in California during 1968-1975. J Natl Cancer Inst. 1980; 65: 1073-1082.
- 8. Philips RL. Role of life-style and dietary habits in risk of cancer among Seventh-Day Adventists. Cancer Res. 1975; 35: 3513-3522.
- Whittemore AS, Harris R, Itnyre J & Collaborative Ovarian Cancer Group. Characteristics relating to ovarian cancer risk: Collaborative analysis of 12 U.S. case-control studies: II. Invasive Epithelial Ovarian Cancers in White Women. Am J Epidemiol. 1992; 136: 1184-1203.
- Negri E, Franchesci S, Tzanou A. et al. Pooled analysis of 3
   European case-control studies: I. Reproductive factors
   and risk of epithelial ovarian cancer. Int J Cancer. 1991;
   49: 50-56.
- 11. Adami H.O., Harieh CC, Lambe M et al. Parity- age at first childbirth and risk of ovarian cancer. Lancet. 1994; 344: 1250-54.
- 12. Newhouse ML, Pearson RM, Fullerton JM, Boesen EAM, Shannon HS. A case control control study of carcinoma of the ovary. Br. J. Prev. Soc. Med. 1977; 31: 148-153.
- Mc Gowan L, Parent L, Lednar W, Norris HJ. The woman at risk for developing ovarian cancer. Gynecol Oncol. 1979; 7: 325-344.

- Purdic D, Green A, Bain C, et al. Reproductive and other factors and risk of epithelial ovarian cancer: An Australian case-control study. Int J Cancer. 1995; 62: 678-684.
- 15. Risch HA, Marrett LD, Howe GR. Parity, contraception, infertility and the risk of epithelial ovarian cancer. Am. J. Epidemiol. 1994; 140: 585-597.
- Hildreth NG, Kelsey JL, Li Volsi VA, et al. An epidemiologic study of epithelial carcinoma of the ovary. Am. J. Epidemiol. 1981;114:398-405.
- 17. Booth M, Beral V, Smith P. Risk factors for ovarian cancer: A case control study. B J Cancer. 1989;60:592-598.
- 18. Chen Y, Wu PC, Lang JH, Ge WJ, Hartge P, Brinten LA. Risk factors for epithelial ovarian cancer in Beijing, China. Int. J. Epidemiol. 1992; 21: 23-29.
- 19. Shu XO, Brinton LA, Gao YT, Yuan JM. Population-based case-control study of ovarian cancer in Shanghai. Cancer Res. 1989; 49: 3670-3674.
- 20. Beral V, Fraser P, Chilvers C. Does pregnancy protect against ovarian cancer? Lancet. 1978;20:1083-1087.
- 21. Rodriguez C, Calle EE, Coates RJ, Miracle Mc Mahill HL, Thun MJ, Heath CW, Jr. Estrogen replacement therapy and fatal ovarian cancer. Am J Epidemiol. 1995; 141: 828-835.
- 22. Rosenberg L, Palmer JR, Zauber AG, et al. A case-control study of oral contraceptive use and invasive epithelial ovarian cancer. Am. J. Epidemiol. 1994; 139: 654-661.
- 23. Vesay MP, Painter R. Endometrial and ovarian cancer and oral contraceptives: Findings in a large cohort study. Br. J. Cancer. 1995; 71: 1340-42.
- 24. Francheschi S, Parazzini F, Negri E, et al. Pooled analysis of 3 European case-control studies of epithelial ovarian cancer: III. Oral contraceptive use. Int. J. Cancer. 1991; 49: 61-65.
- 25. Irwin KL, Weiss NS, Lee NC, Peterson HB. Tubal sterilization, hysterectomy and the susequent occurrence of epithelial ovarian cancer. Am. J. Epidemiol. 1991; 134: 362-369.
- Parazzini F, Negri E, La Veochia, et al. Hysterectomy, oophorectomy and subsequent ovarian cancer risk. Obstet Gynecol. 1993; 81: 363-366.
- 27. Amos CI, Struewing JP. Genetic epidemiology of epithelial ovarian cancer. Cancer. 1993; 71: 566-572.

- 28. Lynch HT, Schulke GJ, Wells IC, et al. Hereditary ovarian carcinoma: biomarker study. Cancer. 1985; 55: 410-415.
- 29. Narod JA. Genetics of breast and ovarian cancer. Br. Med. Bull. 1994; 50: 656-76.
- Herbst AL. The epidemiology of ovarian carcinoma and the current status of tumor markers to detect disease. Am. J. Obstet. Gynecol. 1994; 170: 1099-1107.
- 31. Risch HA, Weiss NS, Lyon LJ, et al. Events of reproductive life and the incidence of epithelial ovarian cancer. Am. J. Epidemiol. 1983; 117. 128-139.
- 32. Mori M, Harabuchi I, Hirotsugu M, et al. Reproductive, genetic and dietary risk factors for ovarian cancer. Am. J. Epidemiol. 1988;128: 771-777.
- 33. Franceschi S, La Vecchia C, Booth M, et al. Pooled analysis of 3 European case-control studies of ovarian cancer: II. Age at menarche and at menopause. Int. J. Cancer. 1991; 49: 57-60.
- 34. Harlow BL, Weiss NS, Roth GJ et al. Case-control study of borderline ovarian tumors: Reproductive history and exposure to exogenous female hormones. Cancer Res. 1988; 48: 5849-5852.
- 35. Hartge P, Schiffman MH, Hoover R, et al. A case-control study of epithelial ovarian cancer. Am. J. Obstet. Gynecol. 1989;161:10-16.
- 36. Rossing MA, Dalling JR, Weiss NS, et al. Ovarian tumors in a cohort of infertile women New Fng J Med. 1994; 331: 771-776.
- 37. Wehner AP. Biologic effects of cosmetic talc. Fd. And Chem. Toxic. 1994; 32: 1173-1184.

- 38. Whittemore AJ, Wu ML, Paffenberger RJ Jr, et al. Personal and environmental characteristics related to epithelial ovarian cancer: II. Exposures to talc powder, tobacco, alcohol and coffee. Am.J.Epidemiol. 1988; 128. 1228-1240.
- 39. Hartge P. Hoover R, Leiher LP, Mc Gowan L. Talc and ovarian cancer (letter). JAMA. 1983; 250:1844.
- 40. Tzonou A, Polychionopolou A, Hsieh CC, et al. Hair dyes, analgesics, tranquilizans and perineal talc application as risk factors for ovarian cancer. Int. J. Cancer. 1993; 55: 408-410.
- 41. Cramer DW, Harlow BL, Willett WC, et al. Galactose consumption and metabolism in relation to the risk of ovarian cancer. Lancet. 1989; 2: 66-71.
- 42. Risch HA, Jain M, Mairett LD, Howe GR. Dietary lactose intake, lactose intolerance and the risk of epithelial ovarian cancer in Southern Ontario, Canada. Cancer, Causes and Control. 1994; 5: 540-548.
- 43. Herrington LS, Weiss NS, Beresford SA, et al. Lactose and galactose intake and metabolism in relation to the risk of epithelial ovarian cancer. Am. J. Epidemiol. 1995; 141: 407-416.
- 44. Shohem Z. Epidemiology, etiology and fertility drugs in ovarian epithelial carcinoma: Where are we today? Fertil Steril. 1994; 62: 433-448.
- 45. Risch HA, Jain M, Marrett LD, Howe GR. Dietary fat intake and risk of epithelial ovarian cancer. J. Natl. Cancer Inst. 1994; 86: 1409-1415.
- 46. Shu XO, Gao YT, Yuan JM, Ziegler RG, Brinton LA. Dietary factor and epithelial ovarian cancer. Br. J. Cancer. 1989; 59: 92-96.

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# FACTORS AFFECTING STONE CLEARENCE FOR INFERIOR RENAL POLE CALCULI

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# **SUMMARY**

Factors affecting stone clearance were investigated on intravenous urograms obtained from 119 patients having single unilateral lower calyceal stone. On intravenous urograms lower infundibulopelvic angle, lower infundibulum diameter and inferior calyceal length were measured for calculous and noncalculous kidneys and compared with 40 patient control group. When we consider lower infundibulopelvic angle statistically significant difference was not present between calculous kidneys and the control group whereas lower infundibulum diameter and inferior calyceal length were significantly (p<0.05) higher in calculous kidneys. Similary in the patient group lower infundibulum diameter and inferior calyceal length of calculous kidneys were greater than noncalculous kidneys which was significant (P<0.05). The difference in lower infundibulum diameters was thought to be due to dilatation. As a conclusion inferior calyceal length could be a good index in determining stone clearance for lower calyceal stones.

Key words: Lower calyceal stones, stone clearance

Recently the introduction of extracorporeal shock wave lithotripsy (ESWL) has provided an effective and noninvasive method for treatment of urinary tract calculi. However lower success rate in inferior calyceal calculi is still a problem when compared to renal pelvis and other calyceal stones (1,2). There is a common consensus that high incidence of residual fragments in lower calices is due to the effect of gravity which decreases the stone clearance (3,4,5). Despite that, it is not clear why some patients become stone free while the others not. A new anatomical approach has been put forward by some authors using parameters such as infundibulopelvic angle and lower infundibulum diameter to explain renal stone clearence (6,7,8). In this respect we examined intravenous urograms of patients with lower calyceal stone using parameters such as lower infundibulum diameter, lower infundibulopelvic angle and inferior calyceal length and tried to determine the factors affecting renal stone clearence.

### MATERIAL AND METHODS

The study was based on examination of intravenous urograms obtained from 119 patients with single

unilateral inferior pole stone during 1993- 1997 at Gülhane Military Medical Academy Hospital. The number of male patients was 104 and female 15. On intravenous urograms lower infundibulopelvic angle (defined as the angle between lower infundibulum and renal pelvis), lower infundibulum diameter and inferior calyceal length harboring the stone (defined as the distance between the most distal point of calculous calyx and the proximal point of renal pelvis) were measured and recorded (Figure 1). Intravenous urograms were obtained using standard roentgen device and all films were taken from 1 meter distance.

The same parameters were also measured on normal urograms from 40 patients (35 male, 5 female) who were donor candidates for renal transplantation.

In addition lower infundibulopelvic angle, lower infundibulum diameter and inferior calyceal length were compared between calculous and noncalculous kidneys among the patient group.

Considering the possible effect of dilatation on working parameters patients having grade 3,4 hidro-ureteronephrosis and anomalous kidneys were not included in the study. Statistical analysis was performed by Mann-Whitney U-Wilcoxon Rank Sum test.

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Table 1. Lower infundibulopelvic angle (LIPA), lower infundibulum diameter (LID) and inferior calyceal length (ICL) in the patient group having calculous and the control group.

	Patient group	n:119	Control group	n:40
	Mean	S.D.	Mean	S.D.
Left LID (mm)	10.48	6.39	6.00	2.76
Right RID (mm)	9.49	4.90	5.94	2.72
Left LIPA	85.41	22.56	82.03	21.23
Right LIPA	86.94	12.23	91.88	24.55
Left ICL (mm)	32.13	8.45	21.28	5.80
Right ICL (mm)	32.95	8.95	20.70	5.56

# **RESULTS**

Mean stone size was 1.2 cm (0.6-1.5). Fifty three patients had left side stone while 66 had right. In patients having left side stone, mean lower infundibulum diameter was 10.48 mm (SD, 6.39), for right side calculi as 9.49 mm (SD, 4.90) while for the control group mean diameters were 6 mm (SD, 2.76) for the left and 5.94 mm (SD, 2.72) for the right and the difference was significant for both kidneys (p<0.05) (Table 1).

When we consider the lower infundibulopelvic angle the mean angle was 85.41° (SD, 22.56) for the left and 86.94° (SD, 12.23) for the right side calculi whereas the same measurement in the control grup revealed 82.03° (SD, 21.23) and 91.88° ((SD, 24.55) respectively. Difference between the groups was not significant (p>0.05) (Table 1). Inferior calyceal length harboring the calculi was significantly longer in the patient group than the control group (p<0.05). The mean inferior calyceal length for calculous kidneys

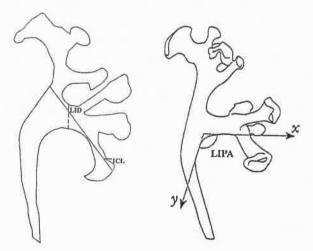


Figure 1. Schematic presentation of lower infundibulopelvic angle (LIPA), Lower infundibulum diameter (LID) and inferior calyceal legth (ICL).

Table 2. Overall comparison of the lower infundibulopelvic angle (LIPA), lower infundibulum diameter (LID) and inferior calyceal length (ICL) between the patient group and the control group.

	Patient group n:119		Control gro	up n:80
	Mean	S.D.	Mean	S.D.
LID (mm)	9.95	5.64	5.97	2.73
LIPA	84.28	15.58	86.95	23.34
ICL (mm)	32.58	8.70	20.99	5.65

was 32.13 mm (SD, 8.45) on right side stone and 32.95 mm (SD, 8.95) for left. In the control group the results were 21.28 mm (SD, 5.80) and 20.70 mm (SD, 5.56) respectively (Table 1).

Overall consideration of patient group showed that mean infundibulopelvic angle was 84.280 (SD, 15.58), mean lower calyceal length as 32.58 mm (SD, 8.70) and mean lower infundibulum diameter 9.95 mm (SD, 5.46) and the corresponding measurements were 86.95° (SD, 23.34), 20.99 mm (SD, 5.65) and 5.97 mm (SD, 2.73) in the control group. Statistical analysis revealed that difference between infundibulopelvic angles was not significant (p>0.05) while lower infundibulum diameter and inferior calyceal length were significantly higher in the patient group (p<0.05) (Table 2).

Calculous and noncalculous kidneys among the patient group revealed similar results showing no difference (p>0.05) between infundibulopelvic angles and significant difference (p<0.05) between infundibulum diameters and inferior calyceal lengths. (Table 3).

# DISCUSSION

Current treatment of urinary tract calculi is largely based on ESWL and endourology. However numerous clinical reports present a problem in clearence of lower calyceal residual fragments (2,4). Although gravity

Tablo 3. Comparison of the lower infundibulopelvic angle (LIPA), lower infundibulum diameter (LID) and inferior calyceal length (ICL) between calculous and non-calculous kidneys the patient group.

	Patient gro	oup n:119	Control group n:1		
	Mean	S.D.	Mean	S.D.	
LID (mm)	9.95	5.64	5.86	3.36	
LIPA	82.28	15.58	78.41	28.48	
ICL (mm)	32.58	8.70	24.71	7.74	

is accusen for retention of calculi in lower pole !ithiazis it is not clear why some patients become stone free while the others not (3,4,5).

To increase the success rate of ESWL a new anatomical approach to renal pelvic and calyceal anatomy is needed. Nevertheless studies conducted for this purpose revealed great variation in the position, configuration and number of calices (6,9). Sampaio pointed out that lower infundibulopelvic angle and lower infundibulum diameter were important factors affecting stone clearence on his studies performed on normal cadaver kidneys and normal urograms (7,8). In the same reports lower infundibulopelvic angle was greater than 90° in 74 % of normal cadaver kidneys which was thought to ease stone clearence (7,8). In our study there was no significant difference (p>0.05) between lower infundibulopelvic angle of the patient group (84.28° - SD, 15.58) and the control group (86.95 - SD, 23.34).

Another parameter by Sampaio was lower infundibulum diameter which was thought to lower stone clearance when lower than 4 mm (7,8). At the patient group we measured the mean infundibulum diameter as 9.95 mm (SD, 5.64) and at the control group as 5.97 mm (SD, 2.73) which was significantly different (p<0.05). The difference between infundibulum diameters was attributed to calyceal dilatation but whether this affects peristaltism and stone clearence is a point of discussion. Sampaio's studies could be critisized as no control group was present (7,8).

In our study inferior calyceal length was found to be significantly larger in kidneys harboring the calculi (32.58 mm - SD, 8.70) when compared to the control group (20.99 mm - SD, 5.65). Increase in inferior calyceal length could increase gravity affect and the distance fragments should course. Nevertheless the critical inferior calyceal length far stone clearence is for to be determined necessitating further studies. As a conclusion inferior calyceal length could be a good index for estimating clearence of inferior calyceal calculi.

# REFERENCES

- Drach,G,W., Dretler,S., Fair,W, et al: Report of the United States Cooperative study of Extracorporeal Shock Wave Lithotripsy, J Urology 135: 1127-33, 1986.
- Siegel, Y,I., Lingeman,J,E., Steek,B.: The management of lower pole nephrolithiasis: Meta analysis, J Urol 149:219A, 1993.
- 3. Graft, J., Diedericks, W., Schulze, H.: Long term follow up in 1,003 ESWL patients. J Urology 140:1479, 1989.
- Mc Cullough, D, L., Extracorporeal shock wave lithotripsy and residual stone fragments in lower calix (letter): J Urology 141:140, 1989.
- Brownlee, N., Foster, M., Griffith, D.P., Carlton, C.E. jr: Controlled inversion therapy: an adjunct to the elimination of

- gravity dependent fragments following extracorporeal shock wave lithotripsy. J Urology 143: 1096, 1990.
- 6. Kaye, K, W., Reinke, D, B.: Detailed caliceal anatomy for endourology. J Urology 132:1085-88, 1984.
- Sampaio,F,J,B., Aragao A,H,M.,: Inferior pole collecting system anatomy: Its probable role in extracorporeal shock wave lithotripsy. J Urol 147: 322-4, 1992.
- Sampaio,F,J,B., Aragao A,H,M.,: Limitation of extracorporeal shock wave lithotripsy for lower caliceal stones: Anatomic Insight. J Endourology, 8(4): 241-7, 1994.
- Sampaio,F,J,B., Mandarim-de Lacerd,CA.: 3 dimensional and radiological pelviocaliceal anatomy for endourology. J Urol 140: 1352-5, 1988.

# POSTERIOR FUSION IN-SITU IN CONGENITAL SCOLIOSIS A STUDY OF 107 PATIENTS

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#### SUMMARY

Congenital scoliosis is an abnormal curvature of the spine. In congenital scoliosis conservative or surgical treatment can be performed. In this study we analysed the results of 107 patients, retrospectively, who were operated between January 1984 - June 1995. Posterior fusion in-situ was the performed surgical treatment in all patients. Patients who were instrumented or who had kyphotic deformities were excluded. The mean angle of the curve was 52.6 degrees before the operation. 10 months later, after the cast was taken off there was an average of 9.8 degrees correction where as after an average of 42 months (range 24-144 months) follow-up period the mean angle correction was 9.0 degrees. According to Srirama's scala in 72% of patients the results were good, in 15.9% moderate and in 12.1% poor. Thoracolumbar curves and unilateral unsegmented bars have the worst prognosis. In 72% of our patients we had a solid fusion and the progression of the curve diminished. In 15.9 % of our patients fusion mass bending occured. We believe that the goal of the treatment is not to correct the deformity but to prevent the progression of the curve. So the surgical technique has to be combined with a cast application until the fusion heals.

Key Words: Congenital Scoliosis, Posterior fusion In-situ.

Congenital scoliosis is a developmental curvature of the spine caused by vertebral anomalies that occurs in the membraneous phase of embrionic period (1, 2). Congenital spine abnormalities can be classified into failures of formation, failures of segmentation and a mixture of them. This classification is based on the appearance of the spine on a roentgenogram. The embriologic development of the spinal column coincides with the development of numerous other organs and systems. As many as 60% of individuals with vertebral malformations have associated malformations that may be present as anomalies outside the spinal column, elsewhere in the bony structure of the spine or within the spinal canal and the neural tissue. The type of vertebral anomaly that occurs does not predict the type or location of any associated anomalies (3, 4, 5). Since 1972 the term VATER association has been used to describe the non-random association of multiple malformations of the vertebrae, lower GIT, trachea and eosophagus, renal tract, lungs, heart, radius, ear, lip and palate. This association confirms the importance of a thorough physical examination of children who have congenital vertebral anomalies (6).

## **MATERIALS AND METHODS**

In this study we analysed the results of 107 patients who were operated for congenital scoliosis between January 1984- June 1995, retrospectively. Posterior fusion in-situ was the performed surgical treatment in all these patients and the patients who had kyphotic component or instrumented were excluded.

76 patients were female, and 31 were male. The mean age at the operation was 13.0 (range 1.5-23 years old). The mean follow-up period was 42 months (range 24-144 months).

16 patients worn Boston or Milwaukee brace before surgery, but because the bracing did not prevent the progression of the curve, surgery was needed. In the other 91 individuals posterior fusion in-situ was the first choice of treatment options.

The localization of the scoliosis was thoracic in 75 (70.09%) patients, thoracolumbar in 26 (24.30%) pati-

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	Thoracic	ThorLum.	CerThor.	Lumbar	Total
Hemivertebrae	22	11	_	_	33
Unsegmented Bar	11	7	2	_	20
Complex Anomalies	32	8	1	1	42
Block Vertebrae	5	_	1	-	6
Wedge Vertebrae	5	_	-	1	6
Total	75	26	4	2	107

Table 1. Localisation of scoliosis according to the type of anomaly.

ents, cervicothoracal in 4 (3.74%) patients and lumbar in 2 (1.87%) patients.

In 39 (36.45%) patients there was a formation failure (33 hemivertebrae, 6 wedge vertebrae), whereas in 26 (24.30%) patients there was a segmentation failure (20 unsegmented bars, 6 block vertebrae) and in the other 42 (39.25%) there was a mixed type of formation and segmentation failure. The curves of 62 (57.94%) patients had a concavity to the right and 45 (42.06%) to the left. Locations according to the type of anomaly can be seen in Table 1.

The angle of the curve is measured by using Cobb method. The mean angle of the curve was 52.6 degrees (range 14-86 degrees) before the operation. (Table 2).

In our patients costa anomalies were the most common abnormality coexisting with the congenital scoliosis in 34 (31.7%) individuals and spina bifida was the second in 20 cases (Figure 1). The other associated deformities with congenital scoliosis can be seen in Table 3.

The patients were operated regardless of their ages. All the vertebraes in the curve and one normal vertebra from both the upper and lower parts were also included in the fusion area. Transverse processes and bilateral laminas were decorticated and the region was filled with cortico-cancellous iliac otogen bone grafts.

The sutures were taken at the second week postoperatively and the patients were ambulated with localised Risser casts. The cast was changed after 6 months. 4 months later the patients were allowed to be free or braced with Milwaukee brace according to their age. The patients were followed up then yearly.

## **RESULTS**

The mean angle of curve before the operation was 52.6 degrees (range 14-86 degrees). Ten months later after the cast was taken off it was 42.8 degrees (range 14-79 degrees) and mean angle in the last visits was 43.6 degrees (range 14-80 degrees)

When we look at the curve progression according to their localisations, it can be seen that the thoracolumbar curves are the worst because there is a mean of 5.2 degrees correction in the curve. There is a 9.6 degrees correction in the thoracal curves so their prognosis seems to be the better. (Table 2).

When the type of the anomaly is taken into consideration, unilateral unsegmented bars and complex anomalies have the worst prognosis because there is only an average of 3.8 degrees curve correction in these patients (Figure 2). In scoliosis depending on hemivertebrae, block vertebrae or wedge vertebrae there can be only slight correction with 3 to 4 degrees in the curve.

Srirama's scala was used to determine our results (7). In 77 (72%) patients the results were good (Good stability of the spine according to a solid fusion), in 17 (15.9%) moderate (Inspite of a solid fusion, there was

Table 2. Mean angle of curves.

	Number	Preop.	10 M. Postop.	Last Visit	Percentage
Thoracic	75	53.2°	42.8°	43.6°	18 %
Thoracolomber	26	51.2°	45.0°	46.0°	10 %
Cervicothoracic	4	52.0°	43.0°	43.2°	17 %
Lumbar	2	50.0°	44.0°	44.0°	12 %
Total	107	52.6°	43.4°	44.2°	15.9 %

Table 3. Associated anomalies seen in congenital scoliosis.

	# Patient	Percentage (%)
Costa Anomaly	34	31.7
Spina Bifida	20	18.6
Tethered Cord	16	14.8
Urinary Tract Anomaly	16	14.8
Diastomatomyelia	12	11.1
Syringomyelia	8	7.4
Pelvic Obliquity	8	7.4
Anomalies Of Lower Extremity	8	7.4
Congenital Heart Anomalies	4	3.7
Dural Ectasia	4	3.7

#: Number



Figure 1. An eight years old girl with congenital scoliosis presented a curve with a Cobb angle of 60D. She had an associated costal synostosis in addition to her wedge vertebra at the level of T7. The patient underwent a fusion in situ operation, which included all the thoracal vertebra from T12 to T3. In her last follow-up no progression of the deformity beyond 60 degrees could be demonstrated.

progression of the curve or positive radiologic criteries of pseudoathrosis) and in 13 (12.1%) poor (Progression of the curve with instability and complaints). In curves of patients with good Srirama scores there was an average of 8 degrees correction in their last visits. In 74% of thoracal curves (55 Patients), 70% of thoracolumbar curves (18 patients) and 87.9% of hemivertebrae the results were rated as good. In curves of patients with moderate scores there was an average of 9.7 degrees progression whereas in poor result group the progression in the curve was 10 degrees. 9 of the 13 poor resulted patients had unsegmented bars and the other 4 had mixed type of segmentation and formation defects.

In 11 cases second operation was needed because of the progression more than 10 degrees in the curve. Posterior fusion was repeated in all of them but in one

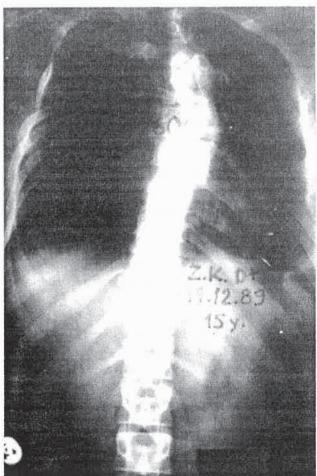


Figure 2. A 15 years old girl with thoracal scoliosis underwent an operation of posterior fusion in situ. She had a curve correction of 10D. Although curves with unilateral unsegmented bars have poor prognosis, the result in this patient with the established stability was good.

the progression persisted, so an anterior fusion was done also. After these operations, progression stopped in all of them. 7 of these cases had unsegmented bars and 4 of them had mixed type of anomalies. 6 of them were in thoracolumbar region and 5 in thoracal.

In three patients the wound was infected but treated with suitable antibiotherapy. Any neurological complications were not recorded in our patients.

## **DISCUSSION**

The prognosis of congenital scoliosis depends on three parameters. The type of scoliosis is one of them. The unilateral bar with the associated contralateral hemivertebrae leads to be the most severe and rapidly progressive deformity of all types of congenital scoliosis (2, 8). Prognosis of the hemivertebrae depends on localisation, type and number of vertebraes included (8, 9). Our results are also similar. In our patients the unilateral unsegmented bars and complex anomalies have the worst prognosis. Whereas in patients with hemivertebrae the results are satisfactorily, because most of them are single or balanced.

Second important parameter is the location of the abnormality. A hemivertebrae in the thoracic spine causes a curve that, with a compensatory curve above and below, may remain fairly well balanced. However a similar vertebrae at the lumbosacral junction may cause severe trunk shift and promotes the development of a rather large structural compensatory thoracolumbar curve. Just as in our patients congenital scoliosis is more frequent in thoracal region as can be seen in literature (2, 10, 11). Thoracolumbar localised scoliosis have the worst prognosis (2) according to McMaster and Ohtsuka, and our results support this fact.

The third important process that the progression depends on, is the number of vertebrae that participates in the curve. Female patients are more likely to have larger curves than male patients (12).

In our 81 (76%) patients there is one or more associated malformations rather than scoliosis. This is more than Beal's (3). Intraspinal abnormalities are found in 18% to 38% of individuals with congenital spi-

ne deformities (4, 5, 13). In our series this is more frequent, about 55.6%. Structural abnormalities of the urinary tract occur in 18% to 37% in different series (3, 14) whereas in ours it is 14.8%. This is probably because of the reason that some do not have an IVP investigation.

The prognosis of the congenital scoliosis has been reported by several investigators. Winter says that in 25% of his patients progression was stopped, 25% had mild progression (less than 30 degrees) and 50% had significant progression (more than 30 degrees) (15). McMaster and Ohtsuka showed that approximately 75% of patients required treatment before reaching maturity (2).

Posterior spine fusion is the oldest surgical technique, as well as the simplest and the safest, and is the benchwork against which to compare all other methods. The posterior spine fusion technique should include fascetectomy and cupious bone grafting so that the result is a thick, wide fusion mass that will resist later growth deformity. When the technique is combined with a cast application, until the fusion heals, some curve correction can be expected without risk of neurologic deficit. Although correction of most curves appears to be desirable, in some areas such as the cervical-thoracic area, attempts at correction probably represents an unacceptable risk. In these situations, the in-situ fusion is probably the preferred procedure. Even in series with best results the range of correction is not more than 25-30% (11, 16). Comparing with the Winter's 26% and Moe's 28% correction notes, our results seems to be bad. But we believe that the goal of the treatment is not to correct the deformity but to prevent the progression of the curve. In our 77 (72%) patients we had a solid fusion and the progression of the curve diminished. Depending on these results we think that our surgical technique is acceptable but there are some problems about casting postoperatively.

Fussion mass bending is the most important reason for progression of the curve in 17 (15.9%) patients. Inspite of a solid fusion there is progression of the curve. This result is similar of Winter's study (16). In 77 patients whose Srirama score's are good, there is an average correction of 8 degrees.

- Gillespe R, Faithfull D, dRoth A, Hall JE: Intraspinal anomalies in congenital scoliosis. Clin Orthop 1973; 93: 103-109
- 2. McMaster MJ, Ohtsuka K: The natural history of congenital scoliosis; A study of 251 patients. J Bone Joint Surg 1982; 64 (8) A: 1123-1147.
- Beals RK, RobinsJR, Rolfe B: Anomalies associated with vertebral malformations. Spine 1993; 18: 1329-1332.
- 4. McMaster MJ: Ocuult intraspinal anomalies and congenital scoliosis. J Bone Joint Surg 1984; 66 A: 588-601.
- Miller A, Guilee JT, Bowen JR: Evalution and treatment of diastomatomyelia. J Bone Joint Surg 1993; 75 A: 1308-1317.
- Beals RK, Rolfe B: VATER association: A unifying concept of multiple anomalies. J Bone Joint Surg 1989; 71-A: 948-950.
- Sriram K, Bobechko WP, Hall JE: Surgical management of spinal deformities in spina bilida. J Bone Joint Surg 1972; 54 (4) B: 666-676.
- McMaster MJ, David CV: Hemivertebrae as acause of scoliosis: A study of 104 Patients. J Bone Joint Surg 1986; 68 B; 588-595.
- 9. Nasca RJ, Stelling FH, Stell HM: Progression of congenital

- scoliosis due to hemivertebrae and hemivertebrae with bars. J Bone Joint Surg 1975; 57 (4) A: 456-466.
- Bunnel WP, McEven GD: Congenital deformities of spine, In: Surgery Of The Musculo-skeletal System (Ed. Evarts MC) Churchill-Livingston Co. New York 1983; 4: 363-409.
- Winter RB, Moe JH, Eilers VE: Congenital scoliosis: A study of 234 patients treated and untreated. J Bone Joint Surg 1968; 50 (1) A: 1-47.
- 12. WinterRB: Congenital scoliosis. Clin Orthop 1973; 93: 75-
- 13. Bradford DS, Heithoff KB, Cobren M: Intraspinal abnormalities and congenital spine deformities: A radiographic and MRI study. J Pediatr Orthop 1991; 11: 36-41.
- 14. Drvoric DM, Rodermen RJ, Conrad RW, et al: Congenital scoliosis and urinary tract abnormalities. Are IVP necessary? J Pediatr Orthop 1987; 7: 441-443.
- 15. Winter RB: Congenital Deformities Of The Spine. New York, Thieme-Stratton, 1983.
- Winter RB, Moe JH, Lonstein JE: Posterior spinal arthrodesis for congenital scoliosis; An analyses of the cases of 290 patients, 5 to 19 years old. J Bone Joint Surg 1984; 66 (8) A: 1188-1195.

# SKULL BASE PROCEDURES FOR ORBITAL PATHOLOGIES

## Haluk Deda\*

#### **SUMMARY**

There are many approaches for intraorbital tumors. Skull base approaches allow direct visualization of the pathology. So the masses are removed with protecting the important neural and vascular structures without any cosmetic defects. Between 1993-1997, 19 orbital tumors were operated on in University of Ankara, Department of Neurosurgery. Orbitozygomatic approach was used for tumors located at the orbital apex and deep orbital compartment. Medial orbital approach was used for tumors located medial to the optic nerve but not deep in the apex. In most of the patients, satisfactory cosmetic and functional results were achieved.

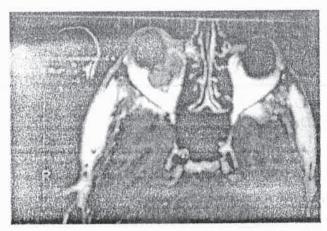
Surgical access and radical removal of lesions located in the orbita presents a formidable challenge. Standard neurosurgical approaches to these areas often provide only limited exposure. In recent years, advances in microsurgery, neuroradiology and microneuroanatomy have provided the development of new approaches which are based on aggressive and radical removal of bony skull structures, in order to gain access to orbital lesions. (1,2) There are two main new skull base approaches to orbita. One of them is orbitozygomatic approach and the other is medial orbitotomy with external ethmoidectomy. (3,4)

Orbitozygomatic approach allows direct visualization from orbital apex to depth of the infratemporal fossa, so superior, posterior and lateral area of the orbita are undercontrol. Among the intraorbital tumors, neurosurgeons have to manage huge tumors or tumors that invade into the intracranial space. The most important thing in skull base surgery is that surgeons should retract the brain as little as possible, since excessive retraction causes cerebral contusion, intracerebral hemorrhage, neuronal damage. The most ideal manipulation does not need brain retraction. (5) So many neurosurgeons think of new approaches to the skull

base lesions. One of them is orbitozygomatic approach.

Retrobulbar tumors within the medial orbital space especially in anteromedial space are difficult to remove with other neurosurgical procedures because of their position. Other neurosurgical procedures do not allow easy removal of masses on the medial side of the optic nerve so the precise location is very important to choose the surgical approach. The precise location of orbital tumors in relation to the optic nerve and orbit is determined by clinical findings of the patient, highresolution CT scanning, MRI and ultrasonic scanning. The most direct surgical approach to the lesion is then planned. Most important direct approache for tumors in this location is medial orbitotomy with external ethmoidectomy. In the literature, the principal uses of the medial orbitotomy are the drainage and evacuation of mucocele with orbital extension or orbital invasion by benign or malignant lesions of the paranasal sinuses. (6,7,8,9) But in the mean time, medial orbitotomy with external ethmoidectomy provides adequate exposure for removing most masses located in the medial retrobulbar space.

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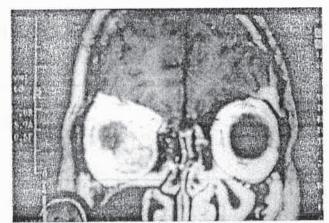


Fig. 1, 2. MRI showed that the tumor was located inferomedial part of the orbita.

# MATERIAL AND METHOD

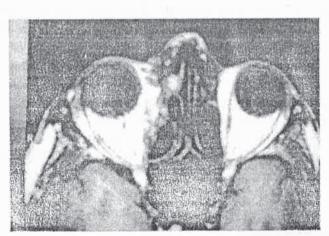
Between 1993 and 1997, 6 cases were operated on with anteromedial approach in the University of Ankara, Department of Neurosurgery. Pathologies were as follows; 2 cases were ossifing fibroma, 2 cases were mucocele, 1 case was dermoid cyst and 1 case was cavernous hemangioma. (Fig 1,2) Total excision was achived in 5 cases.(Fig 3,4) There was no morbidity and mortality. Satisfactory cosmetic and functional results were achieved in all patients.

Between 1993-1997, 12 patients underwent operation via orbito-zygomatic approach for tumors of the orbit. Eight patients were female and 4 patients were male. Diagnoses included; cavernous hemangioma in 3, lacrimal gland adenoma in 2, schwannoma in 2 (Fig 5), adenoid cystic carsinoma in 2, plasmacytoma in 1, cyst hidatic in 1 and nöroepithlioma in 1. The clinical symptoms included ophthalmological symptoms;

exophthalmos in 12 patients, oculomotor damage in 3 patients and decrease visual acuity in 9 patients, one of whom suffered from blindness. Total tumor excision was performed in 10 patients (Fig 6) and gross total excision in 2 cases. The follow-up periods ranged from 9 to 42 months, and to date only 1 patient has shown evidence of recurrence. 3 patients had radiation therapy. In the early postoperative period 4 patients had slightly ophtalmoplegia; 3 months after surgery. Two of these patients recovered without any deficit. There was no mortality.

## **DISCUSSION**

There are many approaches to intraorbital tumors. They are mainly divided into five groups: anterior, anterolateral, lateral, superior or transcranial and transantral.(2,10,11,12) The approach of choice depends on tumor location, tumor size, surrounding structures,



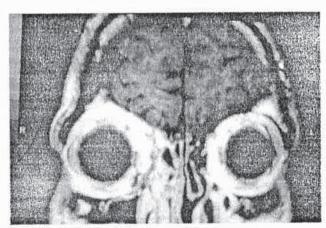


Fig. 3, 4. After anteromedial approach to orbita, MRI showed that the tumor was removed totally.

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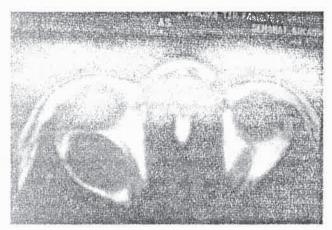


Fig. 5. The tumor was located posterolateral part of the orbita on MRI.

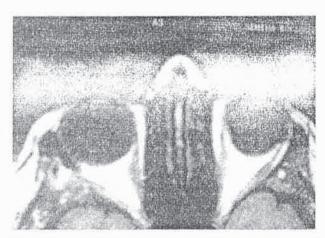


Fig. 6. After orbitozygomatic approach, there was no tumor on MRI.

neurological status, etc. Neurosurgeons use superior or transcranial approach mostly. There are several merits for the transcranial approach: easy decompression of the orbital roof, popular approach for neurosurgeons, etc. But there are some demerits for the transcranial approach. First, the space for manipulation of an intraorbital tumor is narrow so that the operation often ends with biopsy. If the operator needs a wider working space, he must retract the base of the frontal lobe upwards. As a result, brain contusion may occur and in many cases the superior levator palpebrae muscle is injured causing blepharoptosis which is one of the most important cosmetic problems in periorbital surgery. In contrast, with the orbitozygomatic approach, the frontozygomatic bony flap is removed and the lateral wall of the orbit is almost totally removed so that the working space is wider than in the subfrontal approach.(13,14) In addition, brain retraction is not essentially needed. If the tumor invades the greater wing of sfenoid and intracranial space, intradural management must be done in a safe manner. The extra and intradural approach is necessary. In this situation, the frontotemporal approach with orbitozygomatic craniotomy is recommended and the tumor can be resected from the clinoid and cavernous sinus. In some extensive malign orbital tumors it is almost impossible to find 3., 4., and 6. nerves in the tumor. But with orbitozygomatic approach it is possible to find these nerves in the begining of the SOF and it can be able to follow, protect and dissect these nerves from the tumor safely. The orbitozygomatic approach does not give us enough space to resect inferomedial tumors. This approach is an excellent operative technique for meningiomas with an en plaque character

involving the sfenoid wing and at the same the orbit and intracranial structures.(11) Reconstruction has not caused any problems.

Access to medial orbital space is not easy even neurosurgical skull base procedures such as orbitozygomatic approach. Because visualization of whole medial orbital wall without any damage orbital structures and achievement enough space to remove the mass is very difficult with standart neurosurgical procedures. In the other hand it takes a long time to reach this area with these tecniques. So the better plan in this area is the most direct surgical approach with protecting the important neural and vascular structures without any cosmetic defects. One of these direct approaches is antero-medial approach. There are three main medial approaches to orbita and main difference between each these tecniques is external ethmoidectomy. So there are some advantages and disadvantages of medial orbitotomy without external ethmoidectomy. Medial orbitotomy without external ethmoidectomy advantages include ready access to the medial retrobulbar space.(4) Disadvantages, it is possible that excessive amounts of lateral traction on the globe could exceed the ocular perfusion pressure leading to visual loss. To prevent this complication especially if the lesion is in the medial portion of central surgical space it is necessary to perform a lateral orbitotomy to obtain increased lateral retraction of the globe. If additional exposure is required, a lateral orbitotomy may be carried out so that the globe can be retracted further laterally for excellent visualization. Optic nerve can be injured when dissecting posteriorly. Because central retinal artery enters the medial portion of the optic nerve approximately 1 cm behind

the globe. These disadvantages are never seen with our approach. The globe is retracted only a little so no complication is seen and visualization and prevention of optic nerve is excellent. If the mass is located antero-inferior space of the orbita, the incision can also be extended below the medial canthal tendon for better exposure of the lacrimal fossa. But the nasolacrimal duct is not allow for more retraction. At this time I prefer to cut the nasolacrimal duct to gain more exposure. At the end of the operation the nasolacrimal duct was anastomosed end to end with 10/0 sutures.

#### CONCLUSION

The orbitozygomatic approach for orbital tumors causes many benefits because it provides the wide working space needed for manipulation of the important structures under direct view with no retraction of the brain and no disturbance of extraocular movement and medial orbitotomy with external ethmoidectomy is easy and effective procedure to reach to medial orbital space without craniotomy. So useage of this technique is easy, effective and economic.

- 1. Hakuba A, Liu S, Nishimura S. The orbitozygomatic infratemporal approach: A new surgical technique. Surg. Neurol. 1986; 26: 271-276.
- 2. Maroon JC, Kennerdell JS. Surgical approaches to the orbit. J Neurosurg 1984; 60: 1226-1235.
- Alaywan M, Sindou M. Fronto-Temporal approach with orbito-zygomatic removal. Acta Neurochir. 1990; 104: 79-83.
- 4. Leone CR. Surgical Approach to the medial retrobulbar space. A J Ophthalmology 1993; 96: 1-5.
- 5. Al-Mefty O. Supraorbital-Pterional approach to skull base lesions. Neurosurgery 1987; 21: 474-477.
- 6. Johnson LN, Krohel GB, Yeon EB, Parnes SM. Sinus tumors invading the orbit. Ophthalmology 1984; 91: 209-217.
- 7. Weaver DT, Bartley GB. Malignant neoplasia of the paranasal sinuses associated with mucocele. Ophthalmology 1991; 98: 342-346.
- Delfini R, Missori P, Lannetti G et al. Mucoceles of the paranasal sinuses with intracranial and intraorbital extension: Report of 28 cases. Neurosurgery 1993; 32: 901-906.

- 9. Ciappetta P, Delfini R, Lannetti G. Surgical strategies in the treatment of symptomatic osteomas of the orbital walls. Neurosurgery 1992; 31: 628-635.
- Osguthorpe JD. Surgical access to primary orbital tumors.
   Otolaryngologic Clinics of North America 1988; 21: 135-153.
- 11. Mcdermott M.W, Durity F.A, Rootman J, Woodhurst W.B. Combined frontotemporal-orbitozygomatic approach for tumors of the sphenoid wing and orbit. Neurosurgery 1990; 26: 107-116.
- 12. Lee J.P, Tsai M.S, Chen Y.R. Orbitozygomatic infratemporal approach to lateral skull base tumors. Acta Neurol Scand. 1993; 87: 403-409.
- 13. Lesoin F, Pellerin P, Villette L, Dhellemmes P, Jomin M. Monobloc of the fronto-temporo-pterional bone flap. Acta Neurochir. 1986; 82: 68-70.
- Lesoin F, Thomas III C.E, Pellerin P, Villette L, Autricque A, Jomin M. An orbital-zygomatic-malar bone flap approach: a technical note. Acta Neurochir. 1986; 83: 154-156.

# GIANT SEMINAL VESICLE STONES: REPORT OF 2 CASES

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Murat Dayanç\* • İbrahim Yıldırım\*

#### SUMMARY

Seminal vesicle stones are a very rare condition. Here we present two cases with single and multiple seminal vesicle calculi. Common symptom for both cases was perineal pain. Diagnosis was established by digital rectal examination, abdominal X ray and transrectal ultrasonography. Patients were treated with seminal vesiculotomy and stones were extracted.

Key words: Calculi, Seminal vesicle,

Stones in the seminal vesicles are an extremely rare event and only few cases were reported in the literature(1,2). Here we present two cases of vesiculoseminalis calculi one of which is single while the other being multiple.

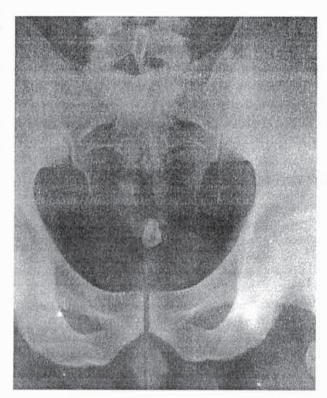
#### CASE 1

A 45 years old man having perineal pain radiating to both testicles was found to have a 2x1 cm shadow in the region of left seminal vesicle on pelvic X Ray (Figure 1). His rectal examination revealed a normal prostate and a stony hard left seminal vesicle. Transrectal ultrasonography (Acuson 128 X p/10, Mountain USA) was performed and at longitudinal - linear plane an acoustic shadow and dilatation in left seminal vesicle was observed (Figure 2). A 20.7 x 19.3 x 17.8 mm sized calcium oxalate stone (weight: 13.5 gr) was extracted from the left seminal vesicle by perineal left seminal vesiculotomy.

## CASE 2

A 30 years old man with perineal pain and hemospermia was found to have right stony hard mass unrelated to prostate by rectal palpation. On pelvic X ray multiple shadows were present at midline in front of the coccyx (Figure 3). Transrectal USG (Sonolayer SSA-270A Toshiba, Tokyo, Japan) revealed dilatation

of right seminal vesicle harboring multiple acoustic shadows at longitudinal - linear and axial sector plane. Multiple stones were extracted from the right seminal



**Figure 1.** Pelvic X-Ray shadow releated to left seminal vesicle calculous (Case-1).

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Figure 2. Transrectal ultrasonography longutidunal- linear plane. Dilatation and acoustic shadow releated to calculus present in left seminal vesicle (Case- 1).



**Figure 3.** Pelvic X-ray showing multiple shadows (arrows) in front of the coccyx related to right seminal vesicle calculi, oblique plane (Case-2).

vesicle by perineal approach. The largest stone diameter was 18 mm and chemical analysis was magnesium ammonium phosphate calculi.

## **DISCUSSION**

Only few reports of seminal vesicle calculi are available in the literature by White, Wesson, Uchijima, Li and Amona (1,3-6). Although more frequent in elderly it was observed in infants and young adults also (2-4). The usual symtomps are perineal pain, testi-

cular pain, hemospermia and painful ejaculations although it could be asymptomatic(2,6). Rectal examination typically confirms a stony hard seminal vesicle apart from the prostate(2,6). Best diagnostic tool is transrectal ultrasonography(4,6,7). Opaque calculi can also be revealed by roentgenographic study. Treatment depends on the age of the patient. In young patients stone extraction by seminal vesiculotomy is advised while vesiculectomy can be considered in the elderly(2).

- 1. White, J.L.: Stones in the prostate and seminal vesicles. Texas J. Med. 23:581, 1928.
- Drach, G,W.: Urinary Lithiasis, in Campbell's Urology Edited by Walsh, Gittes, Perlmatter, Stamey. W.B. Saunders Company. Philadelphia. Chapter 25: 1167-70, 1986.
- 3. Wesson, L., Steinhardt, G.: Case profile: Seminal vesicle stones. Urology. 22(2): 204-5, 1986.
- 4. Uchijima, Y., Hiirage, S., Akutsu, M., Yoshida, K., Hobo, M., Okada, K.: Stones of the seminal vesicles ands ejecula-

- tory duct in infant: Report of a case. Hinyokika- Kiyo, 30(12): 1843-9, 1984.
- 5. Li, Y,K.: Diagnosis and management of large seminal vesicle stones. Br. J. Urol. 1991 68(3): 322-23.
- Amano, T., Kanimi, K., Ohkawa, M.: Transrectal ultrasonography of the prostate and seminal vesicles with hemospermia. Urol- Int. 53(3): 139-42, 1994.
- Marmol- Navarro, S., Nagal- Lecumburi, S., Rajab, R.: Calcification of seminal vesicles and deferent duct. Arch-Esp- Urol, 45(10): 1043-4, 1992.

# SINUS NODE DYSFUNCTION ASSOCIATED WITH HYPOTHYROIDISM

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#### SUMMARY

Sinus node dysfunction (SND) is defined as any disturbance or abnormality of the function of the sinus node and is rare in children. In order to assess the association of SND and thyroid disease, we have prospectively evaluated cardiac status of patients with hypo and hyperthyroidism presenting to our department of pediatrics in a year. Among the 135 hypothyroidic patients, a 12 year old girl who complained of fatigue and dizziness; a routine electrocardiogram (ECG) suggested sinus node dysfunction with severe bradycardia, sinus arrythmia, sinus pause and junctional rhythm periods. The diagnosis was confirmed by Holter monitoring and exercise test. Thyroid hormone replacement therapy was started. However two months later permenant pacemaker was implanted for persisting clinical and ECG findings.

This patient represent an example for the rare association of SND with thyroid disfunction children and indicates, this arrythmia is not always reversible with appropriate therapy of thyroid disease.

Key words: Sinus node dysfunction, hypothyroidism

SND is defined as any disturbance or abnormality of the function of the sinus node (1,2,3). The ECG shows irregular and slow sinus rates with a variety of escape rhythms, sinoatrial exit block varying in severity, bradytachyarrhythmias, sinus pause or arrest, paroxysmal supraventricular tachyarrhythmia episodes (1,2,3). Diagnosis is somewhat difficult, since, sinus arrhythmia is found in normal children, as well (8,9,10).

There are only few reports of SND associated with thyroid dysfunction in children (3,4,5). In order to assess the association of SND and thyroid disease, we have prospectively evaluated cardiovascular status of patients with hypothyroidism presenting to our department of pediatrics.

## **MATERIALS AND METHODS**

135 hypothyroidic patients with an age range of 45 days-16 years old (mean  $4.33 \pm 4.15$  years) were evaluated by clinical (history, physical examination) and laboratory (chest x-ray, surface ECG, Holter, exer-

size test) for the presence of arrhythmia. One child was diagnosed as having SND.

#### Case report

A 12 year old girl was admitted to the hospital with fatigue, dizziness, abdominal distention and constipation. On physical examination, she had a puffy face with dry and rough skin. She had severe bradycardia (heart rate 36-42/min.) and marked growth failure (below 3th percentile). The blood pressure was 90./65 mmHg. Physical examination was normal except for the irregular and slow heart rate.Laboratory examinations yielded a normal urinalysis, hemoglobin 12,3gr/dl, hematocrit 38 percent, white blood cell count 7600/mm3, a normal peripheral blood smear. On surface ECG, severe sinus bradycardia along with sinus arrythmia, low amplitude of P waves and QRS complexes, flattened T waves, frequent sinus pauses and junctional escape rhythm were found, 24 hour Holter monitorisation revealed severe sinus bradyarrhythmia, frequent sinus pauses and junctional

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rhythm periods (Figure 1). Maximal heart rate was 8 'min. during the exercise test which performed to modified Bruce protocol. Chest x-ray showed cardiomegaly and M-Mode, Doppler echocardiographic study revealed depression of left ventricular systolic function and myocardial contractility with asymmetric septal hypertrophy.

Eight weeks after thyroid hormone replacement therapy, the girl was in euthyroid status but no significant change was obtained in the cardiac findings. She still suffered from dizziness, fatigue, and heart rate still was nearly 40-42/min., but had no attacks of syncope.

According to AHA/.ACC criterias, she was defined as Class I for permenant pacemaker implantation (6), DDDR pacemaker (mode DDD, Medtronic) was implanted. She has been followed up with regular intervals with thyroid hormone replacement and permanent pacemaker without any complaints for two years.

## DISCUSSION

Thyroid hormones have positive inotropic and chronotropic effects on myocardium (5). The thyroid hormone, catalyzes the formation of cyclic 3'5'AMP from ATP. The hormone probably exerts its influence on the conduction system through a similar mecha-

nism. It markedly facilitates the impulse transmission through the atrioventricular conduction system. The action appears to be direct and independent of the sympathetic activity (5,7) Some ECG changes such as increased voltage of QRS, sinus tachycardia, atrial fibrillation, complete atrioventricular block can be found in hyperthyroidism (7). On the other hand, in hypothyroidism, low voltage of QRS complexes, flattened or inverted T waves, prolongation of PR interval and sinus bradycardia are generally found on surface ECG (2,8). It has been reported that, these ECG abnormalities usually disappear with appropriate endocrine therapy of thyroid dysfunction. Rarely, they can persist and this may be because of the myocardial necrosis due to the progressing widespread thyrotoxic heart disease or myxedema of the myocardium (2,3,8).

SND related to endocrine and metabolic problems has been rarely reported in children. The clinical symptoms are directly related to the hemodynamic state and to the function of the remaining conduction system (2). If there is adequate AV-nodal-His-Purkinje escape rhythm, it is usually uncommon to see the signs of uncompromised hemodynamic function.

The treatment decision is straightforward when syncope/presyncope occur or symptoms of congestive heart failure and severe fatigue are determined during

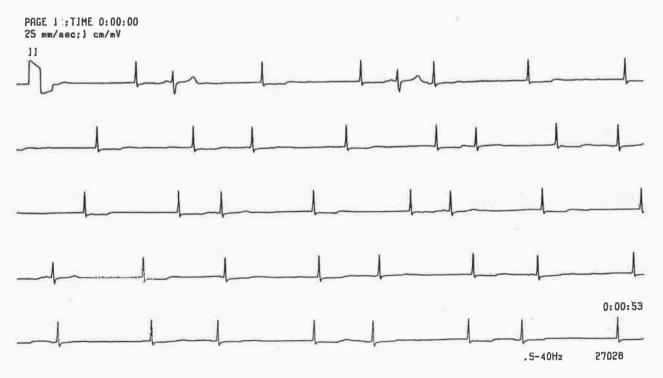


Figure 1. Junctional escape rhythm on rhythm stripe.

documenteal arrhythmias of SND(2). Recommendations for symptomatic patients with undocumentable SND and asymptomatic patients are somewhat controversial(2,3). Generally, it is accepted that asymptomatic patients do not warrant treatment. However the decision of treatment is complicated when symptoms can not be documented during SND. In some patients, requirement of antiarrhythmic therapy or the presence of underlying disease may direct to apply pacemaker implantation. Kugler reported that there are no data to show which sudden death is prevented by pacemaker implantation in asymptomatic patient. But, he speculated that increasing cardiomegaly resulting from chronic bradycardia could predispose to life threatening ventricular arrhythmias(2).

In this case, improvement of the symptoms, cardi-

ac and ECG findings could not be obtained after appropriate thyroid hormone replacement therapy. Any increase of the heart rate and change of the heart size could not be determined. According to AHA/ACC criterias, she was applied a permanent pacemaker. The type of the pacemaker was fixed to the type of the arrhythmia, ventricular function, her age and size. She has been followed free of symptoms with thyroid hormone replacement and permanent pacemaker.

Although SND with hypo or hyperthyroidism has been found in adults, it is rather rare in children(1,3). This case is also remarkable, since it is associated with thyroid dysfunction and keeping on in spite of appropriate endocrine treatment. We conclude that SND should be sought for and carefully followed up in children with thyroid problems.

- 1. Bashour TT: Classification of sinus node dysfunction. Am Heart J 1985;110:1251-1256.
- Kugler JD: Sinus node dysfunction. In: Gilette PC, Garson A jr, eds. Pediatric Arrhythmias: Electrophysiology and Pacing. Philadelphia, W.B.Saunders Co., 1990:250-300.
- 3. Swiryn S, McDonough T, Hucter DC: Sinus node function and dysfunction. Med Clin N Am 1984;68:935-954.
- 4. Alter CA, Moshang T: Diagnostic dilemma, the goiter. Ped Clin N Am 1991;38(3):567-578.
- 5. Goel BG, Hanson CS, Han JH: AV conduction in hyper and hypothyroid dogs. Am Heart J 1972;83:504-511.
- 6. Dreifus LS, Fisch C, Griffin JC et al: Guidelines for implanta-

- tion of cardiac pacemakers and antiarrhythmia devices. A report American College of Cardiology American Heart Association Task Force on assessment of diagnostic and therapeutic cardiovascular procedures. (Committee on Pacemaker Implantation) JACC 1991;18:1-3.
- Kramer MR, Shilo S, Heishho C: Atrioventricular and sinoatrial block in thyrotoxic crisis. Br Heart J 1985;54:600-602.
- Balducci G, Acquafredda A, Amendola F et al: Cardiac function in congenital hypothyroidism: Impairment and response to L-T4 therapy. Pediatr Cardiol 1991;12:28-32.

# WAS IT REALLY A BUPIVACAINE TOXICITY?

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#### **SUMMARY**

Regional anaesthetic techniques have potential risks of complications due to technique and local anaesthetic solutions. We present a case of spinal anaesthesia complication in a patient with incomplete right bundle branch blockade (RBBB) who had been scheduled for inguinal hernia operation. Subarachnoidal puncture was performed from L3-4 interspace at the first attempt and 3 ml 0.5% bupivacaine solution was injected intrathecally without any complication in our patient. Eleven minutes after injection and a few minutes after initiation of surgery a deep bradycardia (10 bpm) occurred and followed by generalised convulsions. Convulsions and bradycardia were controlled with thiopentone sodium and atropine and this period of bradycardia took approximately 7 minutes. The anaesthesia level was observed at T10 and T8 before and after this period, respectively. Thereafter, operation was completed under spinal anaesthesia and without any additional complication.

Clinical presentation of our case mimics systemic toxic reaction as a result of rapid absorption of local anaesthetic solution to the systemic circulation. In spite of possible low plasma concentration of bupivacaine, the perexistance of incomplete RBBB in our patient may be the reason which facilitating the cardiac toxic symptoms, bradycardia, before con-

vulsions.

In conclusion; anaesthesiologists have to be aware of that delayed bupivacaine toxicity may occur after nontraumatic spinal anaesthesia, possibly because of the vascular absorption of the local anaesthetic drug, even in small doses especially in susceptible patients.

Key Words: Regional, anaesthesia, bupivacaine, toxicity.

## **CASE REPORT**

A 39-year-old man was admitted to Ankara University Faculty of Medicine Hospital for recurrent right inguinal hernia repair. Routine pre-operative physical and laboratory assessments had no abnormality except incomplete right bundle branch block (RBBB) in the ECG.

On the morning of the operation, the patient was premedicated with atropine 0.5 mg and diazepam 10 mg intramuscularly, and admitted to the operating room. The patient's initial blood pressure, heart rate and arterial oxygen saturation were 140/95 mmHg (18.5/12.5 kPa), 65 bpm and 96%, respectively (Fig. 1). Normal saline infusion was started following intravenous cannulation with an 18 G cannula. Subarachnoid puncture was achieved in the left lateral position with midline and perpendicular approach in the first attempt from L3-4 interspace by using a 25 G spinal

needle. Three ml of 0.5% bupivacaine was injected slowly into the subarachnoid space without barbotage after observation of free and bloodless crystalline clear cerebrospinal fluid flow and confirmation of it was made with aspiration test. The patient was given in a 30 (semifowler position, immediately. No haemodynamic alteration was observed with the establishment of bilateral anaesthesia at T10 level. A few minutes after initiation of surgery, during subcutaneous bleeding control, and on the 11th minute of subarachnoid injection, bradycardia occurred and progressively decreased to 10 bpm in a short time. Atropine 0.5 mg was injected intravenously. Before observing the response to atropine, generalised convulsions began which were controlled by intravenous injection of 2.5% thiopental sodium 250 mg while respiration was controlled with 100% O2 by a face mask. After convulsions subsided, atropine 0.5 mg was again injected int-

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ravenously because of persisting bradycardia. Subsequently, heart rate increased to 50 then to 60 bpm, and the blood pressure was recorded as 120/90 mmHg (16/12 kPa). The time between the beginning and the end of bradycardia was 7 minutes. Blood pressure could not be measured because of the ineffectiveness of the automatic blood pressure measuring monitor in the situation of the bradycardia during this time, however any decrease in the depth of the pulse could not be observed. The patient regained consciousness in a short time and the operation was completed under spinal anaesthesia without any additional complications. The anaesthesia level was observed at T8 level following regaining of consciousness. Although a venous blood sample was collected, a suitable laboratory that is capable of determining the plasma concentration of bupivacaine could not be found. As no other complications related to anaesthesia and surgery occurred postoperatively, the patient was discharged in one week.

## **DISCUSSION**

There are some reports of bradycardia and cardiac arrest after spinal anaesthesia (3, 4, 5). This clinical presentation may be seen because of:

- a) vasovagal attacks;
- raising of injected local anaesthetic in the cerebrospinal fluid to cardiac accelerator fibers or to brain stem; and
- c) high plasma local anaesthetic concentrations due to inadvertent intravascular injection or rapid absorption of subarachnoidally injected bupivacaine to systemic circulation.

A vasovagal attack may induce bradycardia during or after spinal anaesthesia (6). This reason is not valid for our case because of the bradycardia that began before peritoneal manipulation, eleven and a few minutes after the subarachnoidal puncture and surgical incision, respectively, and during control of subcutaneous bleeding.

The loss of cardiac sympathetic stimulation and a decreased venous return because of spinal anaesthesia higher than T3-4 levels can induce bradycardia, conduction defects and hypotension (4, 5). Raising of the spinal anaesthesia to medlar level initiate persistent apnea, loss of consciousness, fixed and dilated pupils in addition to cardiotoxic symptoms (1). Although anaesthesia was not higher than T8 level in our case, according to the traditional idea the level of sympathetic

blockade would be markedly more cephalad than the sensory blockade and may induce bradycardia. However, it has been clearly shown that sympathetic activity is present far below the level of anaesthesia; the extent and intensity of the sympathetic blockade are less than analgesia; and the duration of the sympathetic blockade is shorter than the analgesia and motor blockade (7). These findings can exclude the possibility of high sympathetic blockade as a reason of bradycardia in our case.

There have been several reports on the development of neuro- and cardiotoxicity after regional anaesthesia because of high plasma local anaesthetic concentrations following inadvertent intravascular injections or rapid absorption of used local anaesthetic drugs into the systemic circulation (1,2,8). Neurotoxic symptoms have been the primary symptom in several of these cases and the central nervous system effects of used local anaesthetic drugs have been questioned (2). However, in the toxicity cases occurring with relatively newer amide local anaesthetics, bupivacaine and etidocaine, cardiotoxicity symptoms have been observed as simultaneously and vigorously as neurotoxicity symptoms (1,2,9). Although neurotoxic doses of bupivacaine are a bit lower than its cardiotoxic doses, it has also been shown that subconvulsant doses of bupivacaine and etidocaine can precipitate cardiac arrhythmias (9). More powerful cardiotoxic effects of

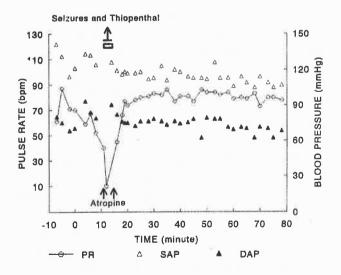


Figure. Pulse rate, systolic and diastolic blood pressure trends before and during spinal anaesthesia. Subarachnoidal injection time is shown located at the zero point. Medical treatment related with haemodynamic changes are shown in the figure. Abbreviations: PR: Pulse rate; SBP: Systolic blood pressure; DBP: Diastolic blood pressure.

these local anaesthetics are correlated with their anaesthetic potencies. Cardiac toxic effects of bupivacaine and etidocaine are bradycardia, conduction defects, arrhythmias and cardiovascular collapse (8). However, the initial cardiac symptom of their cardiac toxic effects is bradycardia and bradycardia could be followed by other symptoms which is related with the doses (10). There have been some reports of severe neuro- and cardiotoxicity after spinal anaesthesia with bupivacaine as with other regional techniques (3). Bradycardia, which occurs with spinal anaesthesia is slow in onset, and generally easily treated (4). These specifications of the systemic toxic effects of bupivacaine are similar to the clinical presentation in our case. Observation of no blood in the cerebrospinal fluid during aspiration before the subarachnoid bupivacaine injection, and an 11 minute interval between the subarachnoid injection and the clinical symptoms in our case, are the reasons for the elimination of intravascular injection possibility and are the reasons for introducing the fast bupivacaine absorption possibility from subarachnoid space to systemic circulation. Low bupivacaine dose used for spinal anaesulesia, high affinity of bupivacaine molecules to bind plasma proteins (2), slow absorption profile of the bupivacaine from subarachnoid space to circulation (11) are factors which are prohibiting to accept occurrence of high free bupivacaine plasma concentration possibility to initiate cardiac toxic effects. However, it has been reported that cardiac conduction defects, hypoxia, hypercarbia, acidosis and hyperkalaemia are the factors which are potentiating cardiac toxicity in the use of local anaesthetic drugs (2,5,12). In spite of possible low plasma bupivacaine concentrations, the preexistence of incomplete RBBB in our patient may be the reason which is facilitating the initiation of cardiac toxicity symptom, bradycardia, before convulsions.

In conclusion; anaesthesiologists have to be aware of that delayed bupivacaine toxicity may occur after nontraumatic spinal anesthesia, possibly because of the vascular absorption of the local anaesthetic drug, even in small doses especially in susceptible patients.

- Edde RR, Deutsch S. Cardiac arrest after brachial-plexus block. Anesth Analg 1977; 56: 446-447.
- Albright GA. Cardiac arrest following regional anesthesia with etidocaine or bupivacaine. Anesthesiology 1979; 51: 285-287.
- 3. Matta BF, Magee P. Wenckebach type heart block following spinal anaesthesia for caesarean section. Can J Anaesth 1992; 39(10): 1067-8.
- Mackey DC, Carpenter RL, Thompson GE, Brown DL, Bodily MN. Bradicardia and asystole during spinal anesthesia: A report of three cases without morbidity. Anesthesiology 1989; 70: 866-868.
- Caplan RA, Ward RJ, Posner K, Cheney FW. Unexpected cardiac arrest during spinal anesthesia: A closed claims analysis of predisposing factors. Anesthesiology 1988; 68: 5-11.
- 6. McConachie I. Vasovagal asystole during spinal anesthesia. Anaesthesia 1991; 46: 281-282.
- 7. Touminen M. Bupivacaine spinal anaesthesia. Acta Anaesthesiol Scand 1991: 35: 1-10.

- Cottrell WM, Schick LM, Perkins HM, Modell JH. Hemodynamic changes after intercostal nerve block with bupivacaine-epinephrine solution. Anesth Analg 1978; 57: 492-495.
- De Jong RH, Ronfeld RA, DeRose RA. Cardiovascular effects of convulsant and supraconvulsant doses of amide local anesthetics. Anesth Analg 1982; 61: 3-9.
- Widman B. Some circulatory and respiratory effects of intravenous local anaesthetics. Acta Anaesthesiol Scand Suppl 1966; 25: 34-36.
- 11. Veering BT, Burm AGL, Vletter AA, Van den Hoeven RAM, Spierdijk J. The effect of age on systemic absorbtion and systemic disposition of bupivacaine after subarachnoid administration. Anesthesiology 1991; 74: 250-254.
- Eledjam JJ, De La Coussaye JE, Colson P, et al. Is epidural anaesthesia using bupivacaine safe in patients with atrio-ventricular conduction defects? Acta Anaesthesiol Scand 1989; 33: 402-404.

# INTRA-AORTIC BALLOON PUMP FOR THE TREATMENT OF SEVERE VERAPAMIL POISONING

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Mehmet Özkan\*\* • Oya Özatamer\*

#### SUMMARY

A 15-years-old girl was admitted to the intensive care unit 9 hours after ingesting 7.2 gr of sustained-release verapamil (144 mg/kg). The electrocardiogram revealed complete atrioventricular block with prolonged QRS duration and ventricular rate of 40 beats/min. The patient was intubated and received artificial ventilation. Gastric lavage was initiated with charcoal by nasogastric tube. A transvenous pacemaker and a 7 Fr thermodilution catheter was inserted via internal juguler and left subclavian vein, respectively. The cardiac index was 1.7 liters/m²/min. Oliguria persisted at this stage. Despite vigorous fluid resuscitation, cardiac pacing, calcium and high doses of vasopressor administration, blood pressure and cardiac index did not increase. Therefore, 48 hours after ingestion, intra-aortic balloon pump (IABP) was used to restore cardiac output and to allow sufficient time for liver detoxification. The IABP increased systolic blood pressure to 95 mm Hg and cardiac index to 2.9 liters/m²/min within 30 minutes time and initiated diuresis. The patient was discharged 9 days after admission without sequale. In the present case, the value of IABP was emphasized in verapamil induced circulatory failure which is unresponsive to aggresive gut decontamination and high dose inotropic therapy.

Key words: overdose, calcium channel blocker, verapamil-SR, circulatory failure, intra-aortic balloon pump.

Calcium channel antagonists are frequently prescribed drugs that are useful in the treatment of a variety of conditions including angina, hypertension, and paroxysmal supraventricular tachycardia. With the greater use of and widening indications for calcium antagonists, there has been an increase in the number of cases of poisoning with these drugs accidental or intentionally (1-5).

Verapamil is a slow channel calcium entry blocker that exerts its pharmacologic effects by blocking calcium influx in arterial smooth muscle as well in conductible and contractile myocardial cells; it depresses sinus node fuction and the atrioventricular conduction system and causes arterial vasodilation. Slow release verapamil is a relatively new preparation and overdose with this drug is not uncommon (6-10). Verapamil intoxication can lead to hypotension, atrioventricular nodal conduction defects, idioventricular rhythms, and asystole. The treatment is generally supportive and includes the administration of fluid, calcium, ca-

techolamines and ventricular pacing to counter the adverse cardiovascular actions of verapamil.

We report a case of severe verapamil overdose with a sustained-release formulation in a girl who did not respond to the standart treatment and required an intra-aortic balloon pump (IABP) to reverse circulatory failure.

# **CASE REPORT**

A 15-years-old, 50-kg girl was admitted to the intensive care unit approximately 9 hours after ingesting 7.2 gr of sustained-release verapamil (144 mg/kg) intentionally. On admission, the patient was semiconscious but answering questions appropriately. She had bilateral mydriasis, cyanosis and bradypnea, low and weak pulse, a systolic blood pressure of 55 mmHg. Her chest was clear to auscultation and chest x-ray was normal. The electrocardiogram revealed complete atrioventricular block with prolonged QRS duration and ventricular rate of 40 beats/min (Figure 1a). The

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patient had no other diseases except a previous history of suicidal attempt.

Laboratory studies on admission were sodium, 146 mEq/L; potassium, 2.8 mEq/L; chloride, 116 mEq/L; glucose, 349 mg/dL; total serum calcium, 8.2 mg/dL; phosphate, 1.9 mg/dL; total protein, 4.7 g/dL; albumin, 3.5 g/dL; alkaline phosphatase, 127; biluribin, 0.4 mg/dL, SGOT, 36 U/L; SGPT, 55 U/L; BUN 26 mg/dL; creatinine, 1.7 mg/dL; CPK, 84 U/L; hemoglobin, 12.8 g/dL; WBC, 12.000, platelet count, 273.000 prothrombin time, 12.5 seconds; partial thromboplastin time, 25.7 seconds. Arterial blood gases showed metabolic acidosis and hypoxemia (pH: 7.16, pO2: 39 mmHg, pCO2:44 mmHg). Therefore, the patient was intubated and received artificial ventilation. An echocardiogram performed on admisson demonstrated depressed biventricular function.

The patient was administered 1 mg atropine, 2 mg adrenaline, 1 gr calcium chloride, 50 mEq/L sodium bicarbonate and 1 L normal saline IV, but there was no improvement in blood pressure. A transvenous pacemaker was inserted via internal juguler vein, set at a rate of 80 and demonstrated 100% capture (Figure 1b). A dopamine infusion was started (2 to 50 (μg/kg/min). Blood pressure stabilized at 90/60 mmHg. Gastrointestinal decontamination was performed with activated charcoal solution through a nasogastric tube at a rate of 2 L/hr and then 1 L/hr. A dextrose-insulin solution was started to maintain at a normal serum glucose level. The patient remained stable for the next 29 hours, and total serum calcium was closely monitored; calcium chloride was given to maintain total serum calcium at 9.5 mg/dL.

Approximately 20 hours after the patient's admisson to ICU, her sytolic blood pressure decreased to 55 mmHg. The pace maker was working well at the rate of 80/min and still demonstrated 100% capture. Despite epinephrine and dobutamine infusions were started (0.01 to 5 (g/kg/min and 5(g/kg/min, respectively), the patient was worsened, blood pressure remained 70/50 mmHg and urinary output was 0.2 ml/kg/hr. A 7 Fr thermodilution catheter was inserted via left subclavian vein. Mean pulmonary artery pressure was 35 mmHg, pulmonary capillary wedge pressure was 27 mmHg, and cardiac index by thermodilution technique was 1.7 liters/m²/min.

Despite vigorous fluid resuscitation, cardiac pacing, calcium and high doses of vasopressor administration, blood pressure and cardiac index did not increase. Therefore, 48 hours after ingestion, IABP (Datas-

cope System 95, Datascope corp, Paramus NJ 07653) was used via right femoral artery to restore cardiac output and to allow sufficient time for liver detoxification. The IABP resulted a dramatic increase in blood pressure to 95/65 mmHg and augmented cardiac index to 2.9 liters/m<sup>2</sup>/min within 30 minutes time and initiated diuresis. 2 hours after the insertion of IABP. blood pressure increased to 115/65 mmHg and Cl increased to 3.4 liters/m<sup>2</sup>/min. Heart rate remained 100% paced at a rate of 80. At that time, the dopamine was infusing at a rate of 50 (µg/kg/min, and the epinephrine was infusing at a rate of 5 (µg/kg/min; no changes were made in these infusion rates or in the ventilator settings. Supplemental calcium in the form of calcium chloride was continued to maintain total serum calcium at 9.5 mg/dL.

The patient's hemodynamic status continued to improve over the next 15 hours. Her inotrope levels were incrementally decreased. Blood pressure remained in the range of 115/65 mmHg, urinary output increased to 3.2 ml/kg for 15 hours and Swan Ganz measurements returned to normal. As a result of this, it allowed adequate time for liver to detoxicate the drug. When the patient's cardiac performance improved, the balloon augmentation was reduced in steps from 1:1 counterpulsation to 1:2 then 1:3 with appropriate intervals by assessing hemodynamic stability in 2 hours' time. The IABP was discontinued 15 hours after insertion. The pacemaker also was removed on the fourth hospital day, and the patient returned to a normal sinus rhythm with narrow QRS complexes (Figure 1c). Serial ECG's were performed and did not demonstrate an acute myocardial infarction: cardiac enzymes remained at a normal level. The patient was extubated on the fifth hospital day and discharged without sequale from the intensive care unit 9 days after admission.

#### DISCUSSION

Verapamil overdose is occasionally reported and responds mainly to standart treatment (5-10). In the present case, high doses of dopamine and epinephrine did not reverse shock, whereas the IABP definetly reversed the circulatory shock in a short period. We found the use of IABP effective in reversing verapamil induced heart failure.

Verapamil is a benzenacetonitrile that was first introduced as a coronary dilator. The drug subsequently was found to have antiarrhythmic and antihypertensive qualities. Verapamil is a potent calcium antagonist

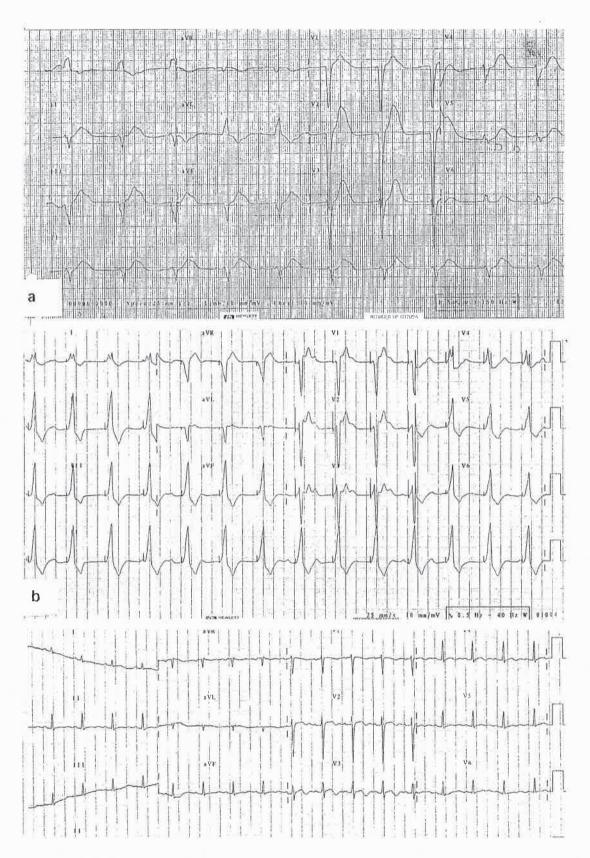


Figure 1. a) Patient's 12-lead ECG on arrival shows complete atrioventricular block, enlarged QRS complexes and a ventricular rate of 40 beats/min., b) Ventricular pacemaker at 80 beats/min just after the placement of pacemaker, c) Sinus rhtym with narrow QRS complexes was achieved simultaneously on the fifth hospital day.

with 90% absorbtion and large first pass hepatic extraction (70%). Verapamil is metabolized to norverapamil, which has mild hemodynamic effects. The drug has a half-life of seven to nine hours in therapeutic doses (11).

The sustained-release preparations of verapamil have an onset of action of six hours and duration of action of 14 hours (12). However, little is known about the pharmacokinetics of sustained-release verapamil in overdose situations (13,14). A variety of conditions may effect the duration of action of verapamil. For example, the presence of food produced a longer peak plasma concentration than the fasting state (15). There may also considerable inter- and intraindividual variations in plasma concentrations due to the biotransformation of the drug in the liver. Therefore, the duration of effect is probably greater than 14 hours for sustained-release verapamil in our patient and her rate of absorbtion is indeterminable. The prolonged condition of circulatory shock in our patient to 48 hours after ingestion is best explained by continued absorbtion of the drug. Buckley et al (16) indicated that sustained-release verapamil absorbtion was continuing at least 22 hours. We suggest that despite gastric lavage and charcoal administration, the prolonged absorbtion with the slow-release preparation delayed toxicity in our patient and highlighted the seriousness of an overdose SR verapamil.

The relationship of serum verapamil levels to cardiotoxic effects is not direct. A non linear correlation exists between the verapamil dose administered and plasma concentration observed. Patients with fatal cases of verapamil overdose have had a wide range of values (17). Ramoska et al (3) found that the threshold dose of verapamil that caused cardiovascular toxicity was 960 mg, while ingestion less than this were always asymptomatic. They also indicated that overdosage in excess of 2.0 g routinely caused major effects. Although no plasma concentrations were available in our patient, several pharmacologic and clinical considerations support the presence of high concentration of the drug at that moment. Additionally, total dose of verapamil which our patient had taken was much more higher than the thresold that cause cardiovascular toxicity according to Ramoska's report.

Verapamil can influence cardiovascular hemodynamics by its three principal actions: coronary arterial dilatation, peripheral arterial dilatation, and negative inotropic effect. The net hemodynamic effect will vary depending on the relative strength of each action.

Hypotension, cardiac conduction abnormalities, and biventricular heart failure are the primary effects of verapamil toxicity. In spite of pacemaker use, however, a number of patients with massive verapamil ingestion die from cardiovascular collapse (18,19). The reason for this hemodynamic decompensation is not clear; however, massive verapamil ingestion may lead to complete inhibition of ventricular contraction (20). As mentioned above, cardiovascular collapse occured also in our patient who was refractory to the conventional therapy.

Many different therapeutic modalities have been suggested for calcium channel blocker overdoses (21,22). The use of calcium to reverse the hypotension and conduction abnormalities associated with calcium channel blocker overdoses, although recommended usually is minimal. Most catecholamines have been used alone or in combination for the treatment of calcium channel blocker overdoses with variable results (7,23). Isoproterenol, glucagon and amrinon have been used with promising results in humans (4,5). However, in severe cases, most of the inotropes are inadequate to reverse the circulatory failure in verapamil overdose. Treatment with 4-aminopyridine may effectively reverse circulatory failure because of the ability of this agent to increase transmembrane calcium influx (24).

The strategy of sustaining the circulation while hepatic detoxication continues is supported by reports of recovery from asystole after five (25) and eight (26) hours of external cardiac massage in cases of tricyclic anti-depressant overdose and in the use of cardiopulmonary bypass (CPB) in overdoses in human beings (27) and experimental animals (28). Hendren et al (9) used CPB in a baby with severe SR verapamil overdose with partial success. His patient's cardiac status improved after CPB initially, but continued absorbtion of drug after bypass resulted in death.

Intra-aortic balloon counterpulsation has been the standart method of providing mechanical circulatory support for over 25 years (29,30). The IABP consists of a 30-cm polyurethane balloon attached to one end of a large-bore catheter. Once inserted, the catheter is advanced up the aorta until the tip lies just beyond the origin of the left subclavian artery. The intraaortic balloon is rapidly inflated with helium or carbondioxide at the onset of ventricular systole, just before the aortic valve opens (31). Inflation of the balloon increases the peak diastolic pressure and displaces blood toward periphery. The increase in diastolic pressure increases

the mean arterial pressure and thereby increases mean blood flow in the periphery. It also incraeses coronary blood flow. Deflation of the balloon reduces the end-diastolic pressure, which reduces the impedance to flow when the aortic valve opens at the onset of systole. This decreases ventricular afterload stroke output (32).

The results of the IABP in our patient was quite dramatic. In this case, IABP decreased myocardial work and increased cardiac output and mean arterial pressure. IABP also improved perfusion pressure to vital organs such as central nervous system, kidneys, mesenteric circulation and as a consequence neurologic and hemodynamic stabilization and normal urine output were obtained. In clinical applications, IABP is used with combination of pharmacologic inotropes in circulatory failure (33,34). Frierson et al (10) used intra-aortic balloon pump and multiple high-dose pressor agents for hemodynamic stabilization in a patient with unsuspected verapamil-SR and atenolol overdose. However, total dose of verapamil which his pati-

ent had taken is much less than our patients'. Initially, during the insertion of IABP, dopamine and epinephrine were infusing at maximum rates to improve hemodynamia in our patient. However, as the patient's hemodynamia was stabilized in 2 hours' time, the administration of inotropic agents was discontinued step by step according to the performance of the cardiac status.

To our knowledge, this is the first clinical report of IABP in the treatment of circulatory failure due to severe verapamil SR overdose with full success. In the present case, IABP provided the needed time for successful hepatic detoxication. Such therapy should be considered when sustained - release verapamil has resulted in hypotension, bradycardia and circulatory failure. We believe that IABP when combined with aggresive catharsis and use of other conventional therapy, will be beneficial in the treatment of severe verapamil overdose. However, more clinical reports are needed to confirm our observation.

- Litovitz TL, Bailey KM, Schmitz BF, et al. 1990 Annual Report of the American Association of Poison Control Centers National Data Collection System. Am j Emerg Med 1991; 9:461-509.
- 2. Pearigan PD, Bentowitz NL. Poisoning due to calcium antagonists. Drug Safety 1991; 6:408-430.
- 3. Ramoska EA, Spiller HA, Myers A. Calcium channel blocker toxicity. Annals of Emergency Medicine 1990;19(6):55-59.
- Goenen M, Col J, Compere A, Bonte J. Treatment of severe verapamil poisoning with combined amrinone-isoproterenol therapy. Am J Cardiol 1986;58:1142-43.
- 5. Doyon S, Roberts JR. The use of glucagon in a case of calcium channel blocker overdose. Annals of Emergency Medicine 1993; 22(7): 1229-1233.
- 6. Immonen P, Linkola A, Waris E. Three cases of severe verapamil poisoning. Int J Cardiol 1980;1:101-105.
- Enyeart J, Price WA, Hoffman DA, Woods L.Profound hyperglycemia and metabolic acidosis after verapamil overdose. JACC 1983;2:1228-1231.
- 8. Krick SE, Gums JG, Grauer G, Cooper GR. Severe verapamil (sustained release) overdose. The annals of pharmacotherapy 1990;24:705-707.
- Hendren WG, Schieber RS, Garettson LK. Extracorporeal Bypass for the treatment of verapamil poisoning. Annals of Emergency Medicine 1989;18(9):984-987.

- Frierson J, Bailly D, Shultz T, Sund S, Dimas A. Refractory cardiogenic shock and complete heart block after unsuspected verapamil-SR and atenolol overdose. Clin Cardiol 1991;14:933-935.
- 11. Hirotoshi E, Eichelbaum M. Clinical pharmocokinetics of verapamil, nifedipine and diltiazem. Clin Pharmocokinet 1980:11:425-449.
- Schlepper M, Thorman J, Schwarz F: The pharmacodynamics of orally taken verapamil and verapamil retard as judged by their negative dromotropic effects. Arzneim Forsch 1975;25:1452-1455.
- 13. Ellenhorn M, Barceloux D: Medical Toxicology Diagnosis and Treatment of Human Posioning; ed 1. 1988, p:195-200.
- Mitchell B, Schroder J, Mason J: Comparative clinical electrophysiologic effects of diltiazem, verapamil and nifedipine: A review. Am J Cardiol 1982;49:629-635.
- Package insert. Calan SR (verapamil sustained release). Skokie IL. Searle and Company, May 1988.
- Buckley N, Dawson AH, Howarth D, Whyte IM. Slow-release verapamil poisoning: Use of polyethylene glycol whole-bowel lavage and high-dose calcium. The Medical Journal of Australia, 158;202-204.
- 17. Gelbke HP, Schlicht HJ, Schmidt G: Fatal Poisoning with verapamil. Arch Toxicol 1977;37:89-94.

- 18. Horowitz BZ, Rhee KJ. Massive verapamil ingestion: a report of two cases and a review of the literature. Am J Emerg Med 1989;18:984-7.
- Orr GM, Bodanski HJ, Dymond DS, Taylor M. Fatal verapamil overdose. Lancet 1982;2:1218-9.
- Hariman RJ, Mangiardi LM, McAllister RG, Surawicz B, Shabetai R, Kishida H. Reversal of the cardiovascular effects of verapamil by calcium and sodium: differences between electrophysiologic and hemodynamic responses. Circulation 1979;59:797-804.
- 21. Antman E, Stone P, Muller J, et al. Calcium blocking agents in the treatment of cardiovascular disorders: Part I. Basic electrophysiologic effects. Ann Intern Med 1980; 93: 886-904.
- 22. Neugebauer G: Comparative cardiovascular actions of verapamil and its major metabolites in the anaesthetized dog. Cardiovasc Res 1978;12:247-254.
- 23. McMillan R: Management of acute severe verapamil intoxication. J Emerg Med 1988;6:193-96.
- 24. Agoston S, Maestrone E, Van Hezik EJ, Ket JM, Houwertjes MC, Uges DRA. Effective treatment of verapamil intoxication with 4-aminopyridine in the cat. J Clin Invest 1984;73:129-6.

- 25. Parmley W, Glick G, Sonnenblick E. Cardi wascular effects of glucagon in man. N Eng J Med 1968;279:12-17.
- 26. Farah A, Tuttie R. Studies on the pharmacology of glucagon.
  J Pharmacol Exp Ther 1960;129:49-55.
- 27. Westile L, Andersen A, Jervell J. et al. Cardiovascular effects of glucagon. Acta Med Scand 1971;189:179-184.
- 28. Armstong PW, Gold HK, DaggettWM, et al. Hemodynamic evaluation of glucagon in symptomatic heart disease. Circulation 1971:44:67-73.
- 29. Golding LAR. Postcardiotomy mechanical support. Semin Thorac Cardiovasc Surg 1991;3;29-32.
- 30. Kantrowitz A, Cordona RR, Freed PS. Percutaneous intraaortic balloon counterpulsation. Crit Care Clin 1992;8:819-837.
- 31. Marino PL. The ICU Book. 2nd ed. Williams & Wilkins, Baltimore 1997, chap. 16, pp:252-54.
- 32. Kaplan JA. Cardiac Anesthesia. 3rd ed. W. B. Saunders Philadelphia 1993, chap. 34, pp:1126-1134.
- 33. Gibbon JH. Application of a mechanical heart and lung apparatus to cardiac surgery. Minn Med 1954;37:171.
- 34. DeBakey ME. Left ventricular bypass pump for cardiac assistance. Clinical experience. Am J Cardiol 1971;27:3.

# SPONTANEOUS SPINAL EPIDURAL HEMATOMA CAUSING PARAPLEGIA

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#### **SUMMARY**

We report a case of Spontaneous Spinal Epidural Hematoma (SSEH) extending from C7 to Th2 in a 21 years old man diagnosed by magnetic resonance imaging and with complete recovery after immediate surgical treatment. Diagnoses and treatment of SSEH are discussed in this report.

Key Words: Spinal epidural hematoma, spontaneous hematoma, magnetic resonance imaging.

## INTRODUCTION

Spontaneous spinal epidural hematoma (SSEH) is a uncommon condition, the cause of bleeding is still unknown. SSEH is typically characterized by sudden onset of back or neck pain and rapid development of an epidural mass leading to compression (8). Although spontaneous recovery can occur (3, 5, 9, 10, 12), urgent surgery is usually required for decompression (2, 7, 8).

Our purpose is to report a case of SSEH in 20 years old man with complete neurological recovery after immediate surgical intervention, and to discuss the diagnosis and management of SSEH.

## **CASE REPORT**

## **History and Physical Examination:**

A 20-year-old man was admitted to the Department of Neurosurgery of Gülhane Medical School with a 2 day history of back pain, urinary retention and weakness of both arm and legs. The patient noted rapid increase of his symptoms in the last three hours. There was no history of spinal trauma, hypertension metabolic or hematological disorders and he was not taking anticoaqulant. On neurological examination, he was found to have severe paraparesis, bilateral sensory disturbance of all modalities below the C7 level.

Blood presure was 130/80 mm. Hg., laboratory values, including haemostasis and blood coagulation time were all within normal limits.

# **Radiological Examination:**

T1 and T2 weighted magnetic resonance images (MRI) revealed an epidural hematoma extending from C7 to Th2, localized in the dorsal spinal epidural space (Figure 1).

#### **Operation:**

The patient was operated on soon after the diagnosis had been confirmed by MRI. Laminectomyy was performed from C7 through Th2. A partially organized blood clot extending from C7 to Th2 and epidural clot was totaly removed. During surgery no vascular abnormality was observed and dural pulsation was evident at the end of the procedure.

## Postoperative Course:

The postoperative course was uneventful rapid motor and sensory improvement was achieved and the patient was able to walk by himself 7 days after the operation. An MRI of the spine was performed 3 weeks after the operation which was reported normal (figure 2).

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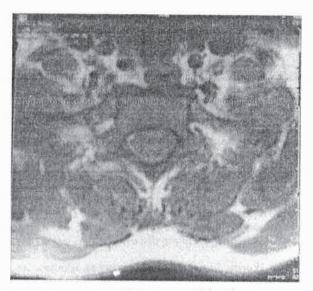


Figure 1: (a) The MR images obtained at the first examination. Sagittal view T1-weighted sequence reveal mass lesion in posterior epidural space at C6-Th2. (b) Axial T1-weighted image at the C7 level shows the hematoma in the posterior part of the spinal canal and spinal cord compression.

## **DISCUSSION**

SSEH are rarely seen in clinical practice and generally occur in adults males and are most frequently located in the lower cervical or thoracolumbar regions (2, 8).

The mechanism of the bleeding is unknown, venous bleeding within the valveless epidural venous plexus or arterial bleeding are speculative explanations (6).

In our case, there was no identifiable cause of the hematoma. Previously myelography and computerized tomography were the diagnostic methods for SSEH with myelography an extradural defect could be seen, but no information about the nature of the lesion was revealed (1, 8, 11). More recently, high-resolution computerized tomography scan allowed a more precise localization and even a better definition of the suspected nature of the lesion.



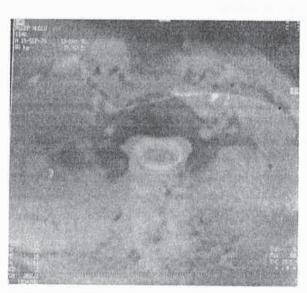


Figure 2: (a) Postoperative T1-weighted sagittal and FL2D15 axial scans (b) showing disappearance of spinal cord compression.

MRI is the best examination for diagnosis and follow-up sagittal sections disclose a mass located in posterior epidural space. It is clearly outlined with tapering superior and inferior margins. The duramater is visualised as curvilinear low signal, separating the hematoma from the cord. The hematoma is isointense or slightly hyperintense on T1-weighted images and heterogeneous on T2-weighted images within 24 hours of onset later, hematoma gives high signal on both T1 and T2-weighted sequences (1, 4).

In conclusion, SSEH is a rare neurosurgical entity. Surgery is the only treatment for most spontaneous SSEH cases. Conservative management is justified only limited cases, when neurological signs are mild or absent and no progression occurs. MRI should be the choice of assesment in acute compressive syndromes of the spinal cord.

- 1. Avrahami, E., Tadmor, R., Ram, Z., Feibel, M., Itzhak, Y.: MR demonstration of spontaneous acute epidural hematoma of the thoracic spine. Neuroradiology, 31: 89-92, 1989.
- 2. Beatty, R.M., Winston, K.R.: Spontaneous cervical epidural hematoma. J. Neurosurg, 61: 143-8, 1984.
- Bernsen, PLJA., Haan, J., Vielvoye, G.J.: Spinal epidural hematoma visualised by magnetic resonance imaging. Neuroradiology, 30: 280-3, 1988.
- Boukobza, M., Guichard, J.P., Boissonet, M., George, B., Merland, J.J.: Spinal epidural hematoma; Report of 11 cases and review of the literature. Neuroradiology, 36; 456-9, 1994.
- 5. Brawn, LA., Bergual UEG., Davies-Jones GAB.: Spontaneous spinal epidural hematoma with spontaneous resolution. Postgrad Med, 62: 885-7, 1986.
- Calliauw, L., Dhara, M., Martens, F., Vannerem, L.: Spinal epidural hematoma without lesion of the spine. Clin Neurol Neurosurg, 90: 131-6, 1988.

- 7. Cooper, D.W.: Spontaneous spinal epidural hematoma; Case report. J. Neurosurg, 10: 1059-63, 1960.
- 8. Foo, D., Rossier, A.B.: Preoperative neurological status in predicting surgical outcome of spinal epidural hematomas. Surg Neurol, 15: 389-401, 1981.
- Harik, S.I., Rakhle, M.E., Reis, D.J.: Spontaneously remitting spinal epidural hematoma in a patient on anticoagulants. N Eng.Med., 284: 1355-7, 1971.
- Hernandez, D., Vinuela, F., Feasby, T.E.: Recurent paraplegia with total recorvery from spontaneous epidural hematoma. Ann. Neurol, 11: 623-4, 1982.
- Nagel, M.A., Taff, I.P., Cantos, E.L., Patel, M.P. Maytal, J., Berman, D.: Spontaneous spinal epidural hematoma in a 7 year old girl, Diagnostic value of magnetic resonance imaging. Clin Neurol Neurosurg, 91: 157-60, 1989.
- Saito, S., Katsube, H., Kobayashi, Y.: Spinal epidural hematoma with spontaneous recovery demonstrated by magnetic resonance imaging. Spine, 19: 483-6, 1994.

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