RESEARCH ARTICLE / ARAŞTIRMA MAKALESİ

DOI: 10.4274/atfm.galenos.2022.99422
Ankara Üniversitesi Tıp Fakültesi Mecmuası 2022;75(2):309-314

SURGICAL SCIENCES / CERRAHİ TIP BİLİMLERİ

Does the Addition of Magnesium Sulfate to Continuous Femoral Block in Knee Arthroplasty Decrease Postoperative Analgesic Requirements?

Diz Artroplastisinde Sürekli Femoral Bloğa Magnezyum Sülfat Eklenmesi Postoperatif Analjezik İhtiyacını Azaltır mı?

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Abstract

Objectives: We aimed to determine the effect of magnesium infusion added to continuous femoral nerve block on postoperative opioid consumption and pain scores in total knee arthroplasty.

Materials and Methods: Sixty-five American Society of Anesthesiologists I-II patients who were between 18 and 65 years of age, scheduled to undergo elective unilateral knee arthroplasty, were recruited and randomized into groups LM and L. All patients were given 30 mL 0.5% levobupivacaine and 1 mL 1:200.000 adrenaline through a femoral catheter. Arthroplasty was performed under spinal anesthesia using 10 mg hyperbaric bupivacaine. Patients in group LM (n=30) were given 40 mg $MgSO_4$ in normal saline as intravenous infusion over 20 minutes intraoperatively and 12 mg $MgSO_4$ in 240 mL 10 mL/h normal saline over 24 hours postoperatively. Patients in group L (n=30) were given 100 mL normal saline over 20 minutes intraoperatively and 240 mL normal saline 10 mL/h over 24 hours postoperatively. All patients were given 0.125% 10 mL/h levobupivacaine via the femoral catheter and morphine intravenous patient controlled anesthesia for 24 hours postoperatively in addition to acetaminophen 4x1 g and lornoxicam 2x8 mg. Hemodynamic parameters, opioid consumption and pain at rest and movement were recorded at 1, 2, 4, 6, 12, 24, 36 and 48th postoperative hours.

Results: The patients in group LM had significantly lower resting visual analogue score (VAS) and verbal pain rating score (VPRS) scores at the postoperative 4, 6, 12 and 24th hours. VAS and VPRS scores during movement were significantly lower in group LM at postoperative 12 and 24th hours. Total opioid consumption was 11.6±4.6 mg in group L and 9.8±4.3 mg in group LM (p=0.032).

Conclusion: Multimodal analgesia is necessary when the effects of postoperative pain on morbidity and mortality following total knee arthroplasties are considered and magnesium added to continuous femoral nerve block, intravenous morphine PCA, lornoxicam and acetaminophen provides effective pain control as a part of multimodal analgesia.

Key Words: Arthroplasty, Magnesium Sulphate, Continuous Femoral Nerve Block, Postoperative Pain

Öz

Amaç: Total diz artroplastisi sonrasında sürekli femoral sinir bloğuna eklenen magnezyum infüzyonunun postoperatif opioid tüketimi ve ağrı skorları üzerine etkilerini incelenmesi amaçlanmıştır.

Gereç ve Yöntem: Etik onay ve yazılı onam alınmasının ardından Amerikan Anesteziyologlar Derneği I-II, 18-65 yaş arası elektif unilateral diz artroplastisi planlanan toplam 65 hasta çalışmaya dahil edildi ve grup L ve grup LM olmak üzere iki gruba randomize edildi. Tüm hastalara femoral kateterden 30 mL %0,5 levobupivakain ve 1 mL 1:200.000 adrenalin verilmesini takiben 10 mg hiperbarik bupivakain ile spinal anestezi altında artroplasti operasyonu gerçekleştirildi. Grup LM'deki hastalara (n=30) intraoperatif dönemde 20 dakika içinde 40 mg/kg $MgSO_4$ 100 mL %0,9 salin intravenöz infüzyon olarak verildi. Postoperatif dönemde bu hastalara 12 mg $MgSO_4$ 240 mL salin içinde 10 mL/sa hızında infüzyon olarak verildi.

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Received/Geliş Tarihi: 08.01.2022 **Accepted/Kabul Tarihi:** 23.02.2022

Grup L'deki hastalara (n=30) ise intraoperatif dönemde 20 dakika içinde 100 mL salin postoperatif dönemde ise 240 mL salin intravenöz olarak verildi. Tüm hastalara postoperatif femoral kateterden %0,125 10 mL/sa levobupivakain ve morfin hasta kontrollü analjezi (HKA) 24 saat boyunca devam edildi. Tüm hastalara ek analjezik olarak asetaminofen 4x1 g ve lornoksikam 2x8 mg uygulandı. Hemodinamik parametreler, istirahat ve hareket sırasında ağrı skorları ile opioid tüketimi 1, 2, 4, 6, 12, 24, 36. ve 48. saatlerde kaydedildi.

Bulgular: Grup LM'deki hastalarda postoperatif 4, 6, 12 ve 24. saatlerde daha düşük istirahat vizüel analog skor (VAS) ve sözel ağrı skoru (VPRS) skorları izlendi. Hareket sırasındaki VAS ve VPRS skorları da grup LM'deki hastalarda 12 ve 24. saatlerde anlamlı düşüktü. Toplam opioid tüketimi grup L'de 11,6±4,6 mg iken grup LM'de 9,8±4,3 mg idi (p=0,032).

Sonuç: Total diz artroplastisi sonrasında postoperatif ağrının morbidite ve mortalite üzerine etkileri düşünüldüğünde multimodal analjezi gereklidir ve sürekli femoral sinir bloğu, intravenöz morfin HKA, lornoksikam ve asetaminofene eklenen magnezyum, multimodal analjezinin bir parçası olarak etkin ağrı kontrolü sağlamaktadır.

Anahtar Kelimeler: Artroplasti, Magnezyum Sülfat, Sürekli Femoral Sinir Bloğu, Postoperatif Ağrı

Introduction

Early mobilization and rehabilitation are very important for effective pain control following total knee arthroplasty. Multimodal analgesic approach is based on the utilization of drugs with different mechanisms of action and is associated with a better analgesic effect and lower side effect profile (1). Peripheral nerve blocks as a part of this approach decreases postoperative pain scores and systemic response while providing effective analgesia with less adverse effects compared to neuraxial techniques (2-4).

Magnesium sulfate is a physiological calcium channel blocker and antagonizes the N-methyl d-aspartate (NMDA) receptors (5). The changes in intracellular calcium levels can affect the excitability of the dorsal horn cells which play an important role in the perception pain. NMDA receptors are found in the peripheral visceral and somatic nociceptors which are responsible from the transmission of nociceptive stimuli and the central nervous system where central sensitization occurs. NMDA receptors are reported to enhance analgesic effect by blocking or delaying the acute tolerance to opioids (6).

The number of studies investigating magnesium infusion as part of multimodal analgesia in total knee arthroplasty operations is limited (7). The primary aim of this study is to evaluate the effect of magnesium infusion added to continuous femoral nerve block on postoperative opioid consumption following total knee arthroplasty.

Materials and Methods

Following ethics committee approval (Ankara University Faculty of Medicine Ethics Committee, no: 26-516, date: 14.03.2011), written informed consent was obtained from 65 patients who were randomized into two groups using closed envelope method. Group LM consisted of 30 patients who were given intravenous magnesium infusion in the intraoperative and postoperative period while group L consisted of 30 patients who were given normal saline in the same volume and rate in the intraoperative and perioperative period. The study was conducted with adherence to the Declaration of Helsinki. Patients between 18 and 65 years of age, American Society of Anesthesiologists I-II, female and male, scheduled to undergo elective unilateral total knee arthroplasty were included in the study. Exclusion criteria were patient refusal, emergency surgery, history of inguinal surgery on the operation side, known allergy to study drugs, severe systemic disease, history peripheral neuropathy and coagulation disorders.

Following ECG, non-invasive blood pressure and peripheral oxygen saturation monitoring, femoral nerve block was applied in all patients. Local anesthesia was achieved by 2 mL 2% prilocaine after sterile draping. Point of entry was determined as 1 cm lateral of the femoral artery pulse and 2 cm inferior to the inguinal ligament. Thirty milliliters of 0.5% levobupivacaine with 1 mL 1:200.000 adrenalin was slowly injected perineurally after eliciting femoral nerve motor response (dancing patella) with 0.5 mA using a peripheral nerve stimulator. A multiorifice catheter was threaded for 5 cm through the needle. Sensory block was evaluated on the anterior aspect of the thigh 15 minutes after the application of local anesthetic.

Ten milligrams of hyperbaric bupivacaine were given intrathecally through the L4-5 vertebral interspace using a 25G Quincke spinal needle in the lateral decubitus position with the operated side placed inferiorly in all patients. The patients were held in this position until the sensory block reached T10 level.

After obtaining the desired sensory block level, the patients in group LM were given 40 mg/kg $MgSO_4$ in 100 mL 0.9% sodium chloride as intravenous infusion which was completed in 20 minutes. The patients in group L were given the same amount of normal saline in the same amount of time. Once the bolus infusion was over, the patients in group LM were given 12g $MgSO_4$ in 240 mL (10 mL/h) normal saline as intravenous infusion while the patients in group L were given only normal saline (10 mL/h for 24 hours).

Levobupivacaine (0.125%, 10 mL/h) infusion was started through the femoral nerve catheter after the end of motor block in all patients which was continued for 24 hours postoperatively.

Additionally, all patients were given intravenous morphine patient controlled analgesia (PCA) with a concentration of 0.1 mg/dL, 10 mL bolus, lock-out time 60 minutes and 4 hours limit 40 mL which was continued for 48 hours postoperatively. Acetaminophen 4x1 g and lornoxicam 2x8 mg was given to all patients throughout the postoperative period.

The patients were evaluated for mean arterial pressure (MAP), heart rate, visual analogue score (VAS, 0-10), verbal pain rating score (VPRS, 0-5) and Ramsay sedation score (1: anxious and agitated or restless or both 6: no response to stimulus) at 1, 2, 4, 6, 12,24, 36 and 48th hours by an anesthesiologist blinded to the study. Additionally, side effects (nausea, vomiting, pruritus, hypotension, flushing, double vision), additional analgesic requirements and motor block (Bromage score 1: freely moves foot and leg, 4: cannot move feet or leg) (8). Range of motion (ROM) was defined as maximum passive ROM the patient could tolerate and was measured at 12, 24 and 48th hours postoperatively. Quadriceps muscle strength was evaluated using manual muscle test (MMT). Timed Up and Go test (TUG) (Time necessary for the patient to, in seconds, stand up from a standard arm chair, walk a distance of 3, turn, walk back to the chair, and sit down) was used to evaluate mobilization. Patient satisfaction was measured using a 5-point Likert scale (1: Completely satisfied, 5: Completely dissatisfied) at the end of 48 hours.

Statistical Analysis

SPSS for Windows 26.0 was used for statistical analyses. Power analysis showed that 24 patients in each group was necessary in order to detect a 30% decrease in opioid consumption with 80% power. A total of 65 patients were recruited into the study in order to compensate for possible losses. Quantitative variables were evaluated with average, standard deviation, median and minimum-maximum values while qualitative variables were evaluated using numbers and percentages. T-test or Mann-Whitney U test was used to check for differences between quantitative variables and normal distribution of variables. Chi-squared test was used to check for differences between qualitative variables. Differences concerning VAS, VPRS and ROM were evaluated using Mann-Whitney test and intragroup changes were evaluated using Friedman test. Level of statistical significance was set at p=0.05.

Results

Two patients in group L and three patients in group LM were excluded from the data analysis due to catheter dislocation and the study was concluded with 60 patients in total. There were no statistically significant differences concerning demographic variables, femoral block time, block onset time and total surgery duration (Table 1).

The groups were similar concerning mean arterial pressure and heart rate measured in the intraoperative and postoperative period.

The patients in group LM had significantly lower resting VAS and VPRS scores at the postoperative 4, 6, 12 and 24th hours (Figure 1).

Similarly, VAS and VPRS scores during movement were significantly lower in group LM at postoperative 12 and 24th hours (Figure 2).

The number of PCA demands were significantly lower at all measurement times and the number of deliveries were significantly lower at the postoperative 12, 24 and 48th hours in group LM compared to group L (Figure 3). Total opioid consumption was 11.6±4.6 mg in group L and 9.8±4.3 mg in group LM (p=0.032).

Side effect profiles were similar between two groups. Mild sedation was observed in 3 patients in group LM and 1 patient in Group L. No patients complained from flushing, diplopia or headaches. Two patients in group L and five patients group LM complained from nausea (p=0.424) while no patients vomited. Groups were similar concerning MMT and TUG test results (p=0.181 for TUG test and p=0.214 for MMT). While only two patients in group L were completely satisfied, 15 patients in group LM reported complete satisfaction (p<0.001). There were no findings associated with catheter infection in any patients.

Discussion

The effect of adding intravenous magnesium infusion to continuous femoral nerve block on postoperative opioid consumption following total knee arthroplasty was investigated in a randomized prospective manner and this technique has provided effective pain control and decreased opioid consumption.

Table 1: Demographic data, block characteristics and duration of surgery

	Group L (n=30)	Group LM (n=30)	p-value
Age (years)	71.1±5.4	71.0±5.3	0.905
Weight (kg)	76.8±4.6	78.8±4.4	0.091
Height (cm)	168.1±4.9	168.6±5.8	0.718
Sex (F/M)	26/4	26/4	1.000
ASA (I/II)	16/14	14/16	0.796
Duration of block (min.)	7.1±1.4	7.0±1.5	0.850
Block onset time (min.)	13.3±2.0	13.8±2.0	0.297
Duration of surgery (min.)	81.0±6.8	79.5±5.9	0.328

F: Female, M: Male, ASA: American Society of Anesthesiologists classification, min.: Minute

Studies on pain after total knee arthroplasty reveal that both central and peripheral mechanisms are involved (9). Multimodal analgesia techniques have gained acceptance since monotherapy is not sufficient on its own.

Preemptive analgesia, neuraxial anesthesia, peripheral nerve blocks, PCA, local wound infiltration and combined use of opioid and non-opioid drugs can be listed as multimodal analgesia techniques (10). The ultimate endpoint of this technique is to

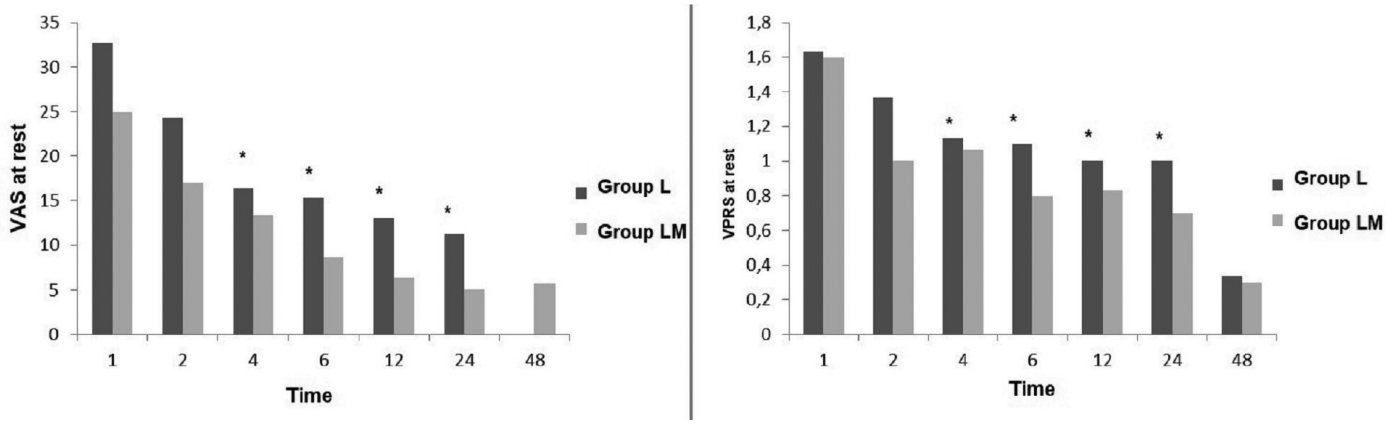

Figure 1: VAS and VPRS scores at rest

Visual analogue score (VAS) and verbal pain rating score (VPRS) scores at rest, *signifies statistically significant difference (4, 6, 12, 24th hour p-values for VAS at rest are 0.003, 0.001, 0.001, and 0.001 respectively; p-values for VPRS at rest are 0.012, 0.017, 0.023 and 0.037 respectively)

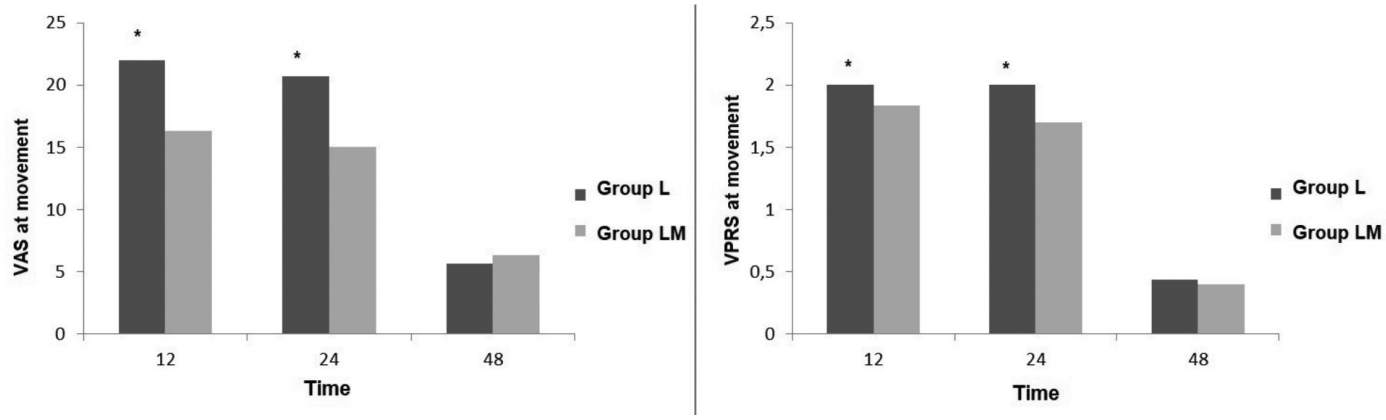

Figure 2: VAS and VPRS scores during movement

Visual Analogue Score (VAS) and verbal pain rating score (VPRS) scores during movement, *signifies statistically significant difference (12 and 24th hour p-values for VAS at movement are 0.001 and 0.001 respectively; p-values for VPRS at movement are 0.032 and 0.023 respectively)

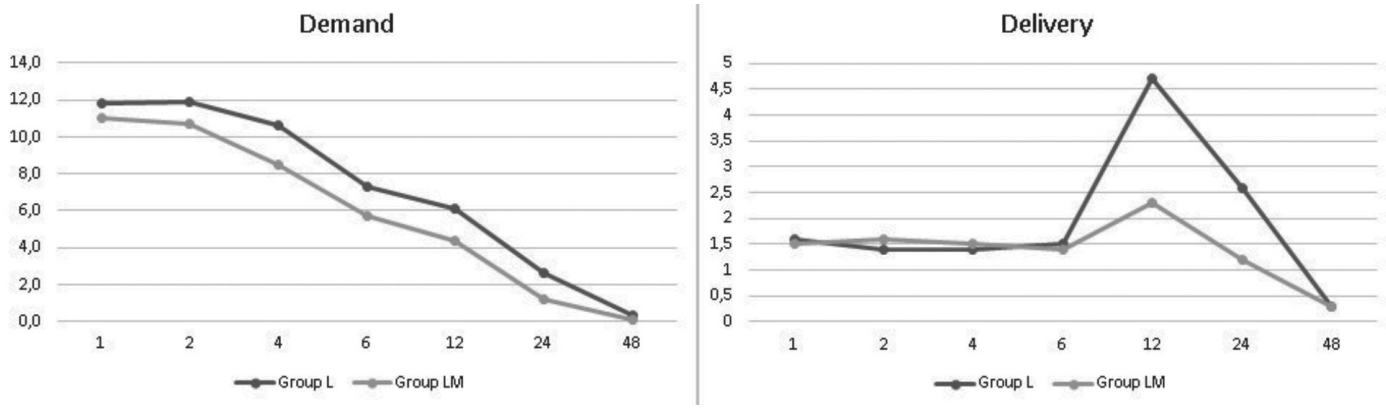

Figure 3: Demand and delivery values

Intravenous patient controlled analgesia demand and delivery values. P-values for demand at 1, 2, 4, 6, 12, 24 and 48th hours are 0.042, 0.003, 0.001, 0.001, 0.004, 0.001 and 0.010 respectively. P-values for delivery at 12, 24 and 48 h hours are 0.001, 0.001 and 0.010 respectively

provide maximal analgesic effect while minimizing adverse effects via combination of more than one type of analgesic. In this study; continuous femoral nerve block, NSAIDs, paracetamol and intravenous magnesium infusion in addition to morphine which was used as a rescue analgesic. Our results reveal that intravenous magnesium reduces opioid consumption.

Magnesium has been applied in different doses via different routes in studies investigating its analgesic efficiency. Magnesium as an adjuvant to bupivacaine in femoral nerve block following anterior cruciate ligament repair has prolonged sensory and motor block duration while decreasing postoperative analgesic requirements (11,12). Similar to our study, intravenous magnesium application has decreased analgesic requirements in various surgical procedures (7,13). However, the number of studies where magnesium is used as postoperative infusion is limited. Specifically, there is no study where magnesium is applied as intraoperative bolus followed by infusion for 24 hours.

As far as studies where systemic magnesium is used are concerned, Hwang et al. (14) have used intraoperative intravenous magnesium in addition to spinal anesthesia in hip and lower extremity trauma surgery and have stated that 50 mg/kg magnesium infusion in 15 minutes following spinal anesthesia decreases opioid consumption. Dabbagh et al. (15) have reported that intraoperative 8 mg/kg/h intravenous magnesium infusion given until the end of surgery in lower extremity trauma surgery lowers pain scores and decreases opioid requirements in the first 24 hours postoperatively. On the contrary, Frassanito et al. (6) have not found any significant effect of an intravenous 40 mg/kg/h magnesium infusion followed by 10 mg/kg/h infusion on postoperative pain management and analgesic consumption and have stated that intrathecal morphine and multimodal analgesia could have suppressed any possible analgesic effect magnesium. Similar to dosage regime used by Tramer et al. (16), we observed that intraoperative 40 mg/kg slow bolus of magnesium followed by an infusion of 500 mg/h for 24 hours in addition to spinal anesthesia and continuous femoral nerve block decreased opioid consumption and lower pain scores without causing any side effects.

Femoral nerve block has been widely accepted as the gold standard for pain management following total knee arthroplasty. This technique not only provides excellent pain management but also contributes to less opioid consumption, lower incidence of nausea and vomiting, shorter length of hospital stay, and long term functional recovery (9). In a study which included 510 patients, Fowler (17) have compared epidural analgesia and femoral nerve block and stated that femoral nerve block provided equivalent pain control to epidural analgesia while causing less adverse effects. In a metaanalysis which evaluated 7 studies with 525 patients, Li et al. (18) have compared continuous and single shot femoral nerve block and found that continuous femoral nerve block provided a more effective pain control. On the other hand, femoral nerve block has been associated with an increased risk of neurological and vascular injury (19) in addition to limited knee extension with risk of postoperative falls due to loss of quadriceps muscle strength (20). In our study, continuous femoral block did not cause loss of quadriceps strength or falls after mobilization at 24th hour. The fact that femoral nerve block did not cause any serious side effects in our study can be explained by the lower dose of levobupivacaine without any boluses.

Study Limitations

The relatively small sample size can be considered as a limitation of our study. Although the lack of measurement of serum magnesium levels before and after the infusion can be seen as a limitation, the dose of magnesium used in our study is far less than 4 g loading and 1-2 g/h infusion which is used in the treatment of preeclampsia (21). Additionally, studies where magnesium dose is similar to ours have reported that post-infusion magnesium levels had risen to 1.4-1.8 times of pre-infusion levels and have not reported any side effects (22).

Conclusion

In conclusion, this randomized prospective controlled study has shown that multimodal analgesia is necessary when the effects of postoperative pain on morbidity and mortality following total knee arthroplasties are considered and magnesium provides effective pain control as a part of multimodal analgesia. The differences in magnesium administration techniques and doses show that new studies on this subject are necessary.

Ethics

Ethics Committee Approval: Study approval was obtained from Ankara University Faculty of Medicine Ethics Committee (project no: 26-516 and date: 14.03.2011).

Informed Consent: Written informed consent was obtained from 65 patients.

Peer-reviewed: Externally peer-reviewed.

Authorship Contributions

Concept: B.K.K., P.E., Z.K.B., A.H.S., Design: B.K.K., P.E., Z.K.B., A.H.S., Data Collection or Processing: B.K.K., P.E., Z.K.B., A.H.S., Analysis or Interpretation: B.K.K., P.E., Z.K.B., A.H.S., Literature Search: B.K.K., P.E., Z.K.B., A.H.S., Writing: B.K.K., P.E., Z.K.B., A.H.S.

Conflict of Interest: The authors declare no conflicts of interest.

Financial Disclosure: The authors declare that they have not received any financial support to perform this study.

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