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Original Study

Effects of Bispectral Index-controlled Use of Magnesium on Propofol Consumption and Sedation Level in Patients Undergoing Colonoscopy

Kolonoskopi Uygulanan Hastalarda, Bispektral İndeks Kontrollü, Magnezyum Kullanımının Propofol Tüketimi ve Sedasyon Düzeyine Etkisi

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Ethics Committee Approval: This study approved by the Abant Izzet Baysal University Clinical Studies Ethic Committee, 25 April 2017, 2017/99.
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ABSTRACT

Objective: *The aim of this study is to investigate the effects of bispectral index-controlled use of magnesium on propofol consumption, periprocedural hemodynamic response and patient comfort.*
Material: *A total of 60 patients were enrolled in the study. In Group 1 (magnesium), a single dose 50 mg/kg magnesium sulfate diluted with 100 mL 0.9% NaCl was administered 10 minutes before the beginning of the procedure. Initially bolus dose of 0.5 mg/kg propofol was applied. The maintenance dose of propofol was 60 mcg/kg/min. During the procedure, the propofol infusion was increased by titration until the bispectral index (BIS) value of 70 was achieved. In Group 2 (saline), 100 ml 0.9% NaCl was administered 10 minutes before the beginning of the procedure. The bolus and maintenance doses of propofol, and target BIS values were the same as those in Group 1.*
Results: *When BIS values were compared between the groups, the initial BIS values in the magnesium group (Group 1) were significantly higher than those of the saline group (Group 2) ($p<0.05$). The time to reach BIS 70 was significantly shorter in the magnesium group ($p<0.05$). Propofol consumption was greater in Group 2 than in Group 1 ($p<0.05$). The time to reach BIS 70 was significantly shorter in Group 1 ($p<0.05$). No significant difference was found between the groups in terms of patient- and endoscopist-satisfaction ($p<0.05$).*
Conclusion: *The use of magnesium in addition to propofol may be an efficient and reliable option to reduce the drug consumption during colonoscopic interventions.*

Keywords: *Bispectral index, colonoscopy, magnesium*

ÖZ

Amaç: *Bu çalışmanın amacı, bispektral indeks kontrollü magnezyum kullanımının propofol tüketimi, periprosedürel hemodinamik cevap ve hasta konforu üzerine etkilerini araştırmaktır.*
Yöntem: *Çalışmaya toplam 60 hasta dahil edildi. Grup I'de (magnezyum), işlem başlamadan 10 dakika önce tek bir doz 50 mg/kg magnezyum sülfat (100 mL %0,9 NaCl ile seyreltilmiş) verildi. İşlem başlangıcında 0,5 mg/kg propofol bolusu uygulandı. Propofolün idame dozu 60 mcg/kg/dk. idi. İşlem sırasında propofol infüzyonu bispektral indeks (BIS) değeri 70 olana kadar titrasyonla arttırıldı. Grup 2 de (salin), işlem başlamadan 10 dk. önce 100 ml %0,9 NaCl uygulandı. Propofol bolus ve idame dozları ve hedef BIS değerleri Grup 1'deki ile aynıydı.*
Bulgular: *BIS değerleri gruplar arasında karşılaştırıldığında, Magnezyum grubundaki (Grup 1) ilk BIS değerleri salin grubundan (Grup 2) anlamlı derecede yüksek idi ($p<0,05$). BIS 70'e ulaşma süresi Magnezyum grubunda anlamlı derecede düşüktü (p 0,05). Propofol tüketimi Grup 2'de grup 1'den daha fazlaydı ($p<0,05$). BIS 70'e ulaşma süresi Grup 1'de anlamlı derecede düşüktü ($p<0,05$). Gruplar arasında hasta ve endoskopist memnuniyeti açısından anlamlı fark bulunmadı ($p<0,05$).*
Sonuç: *Propofole ilaveten magnezyum kullanımı kolonoskopik müdahalelerde ilaç tüketimini azaltmak için etkili ve güvenilir bir seçenek olabilir.*

Anahtar kelimeler: *Bispektral indeks, kolonoskopi, magnezyum*

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INTRODUCTION

Colonoscopy is one of the most commonly used methods in the diagnosis and treatment of colorectal diseases[1]. Moreover, in many cases, the procedure need to be repeated. Therefore, an effective sedation is necessary for patient comfort and ease of the procedure[2,3]. Propofol is one of the most commonly used sedative agents in endoscopic procedures[4]. It has no analgesic effect; however, it has dose-dependent sedative and amnesic effects. Propofol can be combined with different agents to reduce overuse[5]. Hypotension, respiratory depression, delayed awakening can be minimized by giving appropriate sedation doses[6]. Bispectral index (BIS) is often used to monitor depth of anesthesia and sedation. Bispectral analysis can reduce awareness during anesthesia. In addition, use of resources may be reduced as fewer drugs are required to produce amnesia. BIS values range from 0 to 100 (0, cortical silence; 100 awake, memory intact). A score between 40 and 60 is considered to indicate general anesthesia, 60 and 70 deep sedation, and 70 and 90 mild-to-moderate sedation[7].

Magnesium, one of the most common cations in the body that is necessary for many physiological processes[8]. Magnesium sulfate attenuates the hemodynamic response to tracheal intubation and significantly reduces consumption of anesthetic and analgesic drugs. Magnesium also significantly reduces BIS values[9,10].

This prospective study was designed to assess the effects of magnesium sulfate on peri-procedural hemodynamics, patient- and endoscopist- satisfaction and propofol consumption when used as an adjuvant to propofol in colonoscopy.

MATERIALS and METHODS

This study was approved by the Abant Izzet Baysal University Clinical Studies Ethics Committee on April 25, 2017, 2017/99. Written and verbal informed consent was obtained from each participant after a full explanation of the study.

After obtaining approval from the institutional clinical research ethics committee, patients aged between 40 and 75 years were enrolled in this prospective randomized controlled study. Patients were scheduled to undergo outpatient colonoscopy under balanced propofol sedation in the Department of Gastroenterological Surgery of our hospital. Sixty patients with American Society of Anesthesiologists (ASA) status II-III were included in the study. Patients who were allergic to any of the drugs that would be used in the study, those with drug dependency, severe cardiac, renal, neurological, or liver diseases, patients who had taken any sedative drug within the previous 24 hours and those who refused participation were excluded from the study. Patients were equally randomized into two groups through the closed envelope method. The patients were informed about the method of anesthesia and evaluation scales (10-unit Verbal Rating Scale (VRS), Ramsay Sedation Score, and nausea/vomiting scale). As an oral purgative, sennoside A+B calcium (XM®; solution 250 mL, Yenişehir Lab., Ankara, Turkey) was used in the pre-colonoscopy cleansing protocol. The enema containing sodium hydrogen phosphate and disodium hydrogen phosphate were administered through the rectal route (BT®; enema 210 mL, Yenişehir Lab., Ankara, Turkey). Before the procedure, the patients were taken to the preparation room and 2-3 L/min oxygen was administered via nasal cannula. Prior to the induction of anesthesia, routine monitoring procedures (electrocardiography, heart rate, blood pressure and peripheral oxygen saturation) were performed and a 20 gauge intravenous line was established. An infusion of 0.9% NaCl was administered at a rate of 5-8 ml/kg/min. BIS that uses processed electroencephalogram signals to measure the depth of sedation on a unitless scale from 0 to 100 was used to monitor the depth of anesthesia. A BIS sensor was attached to the middle and left side of the forehead and connected to a

monitor (Bispectral Index A-2000, Aspect Medical Systems, Netherlands). Baseline BIS values were recorded before, during and after each procedure and the monitor rate was set at 15 sec. The BIS value for an effective sedation was considered as 70.

The groups were determined as follows; Group 1 (magnesium sulfate group): magnesium sulfate (Magnezyum Sulfat 15% Onfarma 10 ml 10 amp, Ankara, Turkey) + propofol (Propofol Lipuro 1%, B. Braun Irengun, Istanbul, Turkey), Group 2 (Saline group): 100 ml 0.9% NaCl + Propofol. In Group 1, 50 mg/kg magnesium sulfate diluted with 100 mL 0.9% NaCl solution was administered 10 minutes before the beginning of the procedure. At the beginning of the procedure a bolus dose of 0.5 mg/kg propofol was used. The maintenance dose of propofol was 60 mcg/kg/min. During the procedure, the propofol infusion was increased by titration until the BIS value of 70 was achieved. In Group 2, 100 ml 0.9% NaCl solution was administered (without magnesium) 10 minutes before the beginning of the procedure. The bolus and maintenance doses of propofol, and target BIS values were same with those in Group 1. Systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), heart rate (HR), peripheral oxygen saturation (SpO_2), and BIS values were measured and recorded at 0., 5., 10., 15., 20. and 30. minutes before and during the intervention. Systolic blood pressure less than 90 mmHg or a decrease in systolic pressure greater than 20% of baseline values, which was measured before the intervention was considered as hypotension. In the event of hypotension, intravenous fluid was administered and 5 mg ephedrine hydrochloride (Ephedrine 0.05 g/ml, Osel, Istanbul, Turkey) was given, if no response was obtained to resuscitation with IV fluid administration. A heart rate below 50 bpm was considered as bradycardia and IV atropine sulfate 0.5 mg (Atropine sulfate injection Galen, Istanbul,Turkey) was given for the treatment of bradycardia. Oxygen (4 L/min) was delivered via face mask if SpO_2 was below 95%. If respiratory depression (SPO_2 less than 85% for longer than 60 seconds) occurred, the patients were treated with delivery of additional oxygen, and maneuvers as head extension and chin lift. If desaturation continued, mask ventilation was performed. Side effects such as hypotension, hypertension, tachycardia, bradycardia, desaturation, nausea, vomiting, pruritus, anesthesia and complications of the colonoscopic procedure were recorded during and after the intervention. Four-point nausea vomiting scale was used to assess nausea and vomiting. The pain rating was evaluated using a verbal rating scale [VRS- Very bad (0), Bad (1), Good (2), Very good (3)] at 30 min, 60 min and 2 h after the procedure. Grade of sedation was evaluated by Ramsay sedation scale after the intervention. Evaluation of patient-, and endoscopist- satisfaction [Very bad (0), Bad (1), Good (2), Very good (3)] was performed after the intervention. The total drug doses used in both groups were calculated and recorded after the procedure.

Statistical analysis

Statistical Package for Social Science (SPSS 23.0) program was used for statistical analysis. The descriptive variables; age, height, weight, heart rate (HR), mean arterial pressure (MAP), duration of intervention were expressed as mean ± standard deviation. The Kolmogorov-Smirnov test was used to determine whether variables were normally distributed. Independent-Samples T-test was used to analyze normally distributed variables between groups. Analysis of variance (ANOVA) for repeated measures was used to compare BIS scores, MAP and HR values at pre-procedural, 1^{st}, 5^{th} and 10^{th} minutes of propofol administration. Chi-square and Fisher's exact test were used for the analysis of categorical variables. A p value less than 0.05 ($p<0.05$) was accepted as the cut-off value for statistical significance.

RESULTS

Sixty patients who were scheduled for elective colonoscopy were enrolled in the study. There

was no significant difference in terms of demographic characteristics and duration of intervention between the two groups (p<0.05, Table 1).

Table 1. The demographic characteristics of patients, time to reach BIS 70, propofol and magnesium consumption.

	Group I (Magnesium)	Group II (Saline)	p value
Age	58.2 (±11)	58.5 (±11)	0.908
Gender (M/F)	13/17	18/12	0.301
Weight (kg)	74.5 (±77)	70.8(±10)	0.124
Duration of intervention (min)	12.7 (±4.7)	12.9 (±4.8)	0.873
Reaching BIS 70 (sec)	155 (±70)	245 (±118)	0.010
Propofol (mg)	75.9 (±24)	98.1 (±56)	0.019
Magnesium (mg) (per patient)	105.9 (±3.53)		

The values were presented as mean (±standard deviation)

Hypotension was not observed in groups. In Group 1, when the pre-procedural MAP value was compared with the 10th minute MAP value a significant decrease was found (p<0.05). In Group 2, MAP values at 1st and 5th minute were found to be significantly decreased compared to pre-procedural values (p<0.05, Figure 1). When the MAP values were compared, values at 10th minute were significantly lower in Group 1 (p<0.05).

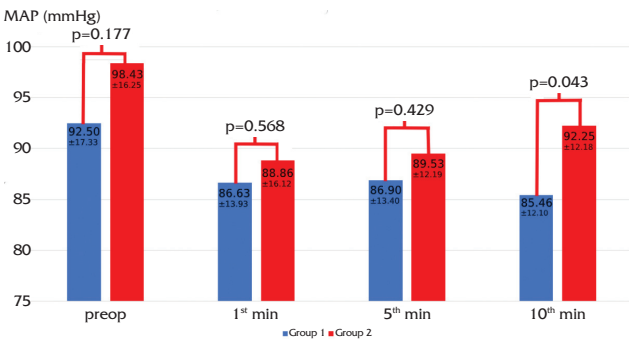

Figure 1. Comparison of the mean arterial pressure values between the groups MAP; Mean arterial pressure.

In both groups, the values of HR were compared with the pre-procedural values, and a significant decrease was observed at the 1st, 5th and 10th minutes of the procedure (p<0.05, Figure 2).

The dose of magnesium was 105.9 mg per patient in Group 1. The mean amount of propofol consumption was 75.9±24 mg in Group 1 and 98.1±56 mg in Group 2. There was a significant difference between the two groups in terms of propofol consumption (p<0.05, Table 1).

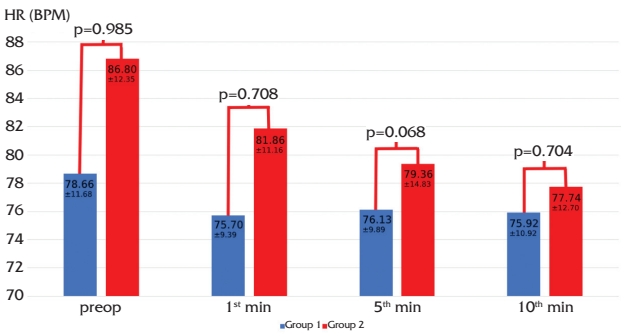

Figure 2. Comparison of the mean heart rate values between the groups HR; Heart rate, BPM; Beats per minute.

When BIS values were compared between the groups, the baseline BIS values in the Mg2+ group were significantly higher than that of the saline group (p<0.05; Table 2, Fig 3). Nevertheless, the time to reach BIS 70 was significantly shorter in the Mg2+ group (p<0.05) (Table 2).

Table 2. Comparison of BIS values in the Magnesium and Saline groups.

	BIS preop (mean±SD)	BIS 1st min (mean±SD)	BIS 5th min (mean±SD)	BIS 10th min (mean±SD)
Group 1 (magnesium)	98.2±2.05	75.3±6.72	68.7±6.80	66.6±6.80
Group 2 (saline)	87.5±11.6	73.8±9.91	66.9±4.85	67.2±4.60
Total	93.0±9.82	74.6±8.39	67.8±5.94	66.9±5.78

The values were presented as mean (±standard deviation)

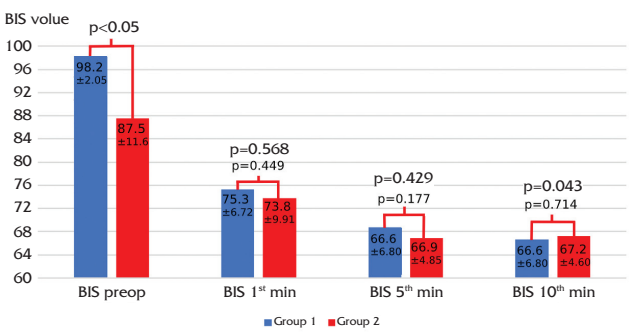

Figure 3. Comparison of the mean bispectral index values between the groups BIS; Bispectral index.

The BIS values at 1st, 5th and 10th min were significantly lower than the pre-procedural value in both groups ($p<0.05$) (Figure 3).

There was no significant difference between groups in terms of VRS scores, patient -, and endoscopist-satisfaction ($p<0.05$). Desaturation, nausea and vomiting were not observed in any of the groups.

DISCUSSION

In the current study, we investigated the effect of magnesium sulfate as an adjuvant for sedation with propofol in colonoscopic procedures. When magnesium sulfate was given before the procedure, the BIS value rapidly decreased to sedation level and the amount of propofol consumption was significantly reduced.

Colonoscopic interventions under sedation have increased in recent years. Many drugs are being used alone (midazolam, diazepam, propofol, ketamine, droperidol, fentanyl, remifentanil) or in combination[11,12]. No consensus has been reached for the optimal drug combination for endoscopy. One of the most commonly used anesthetic agents is propofol.

Many studies have shown that propofol is safe and effective[13,14]. It has also been demonstrated that it shortens the induction period and increases satisfaction of endoscopists and patients[15]. However, it can lead to suppression of protective reflexes, especially in elderly patients, and significant depression in respiratory and cardiac parameters[16-18].

It is possible to reduce the consumption and adverse side effects of a medication by combining with an adjuvant medication. The use of appropriate individual doses of propofol may improve health outcomes, reduce unnecessary costs and overuse of anesthesia which can be achieved by monitoring sedation levels[19]. Bispectral index (BIS) monitoring is an objective and reliable way to observe sedation levels. BIS is obtained from the electroencephalogram (EEG). Some hypnotic drugs such as ketamine and opioids are not suitable for BIS monitoring. BIS does not predict the physical response to hemodynamic stimulation and recovery time of the patient's consciousness[7,20].

The awareness of anesthesia can be reduced by monitoring depth of sedation with bispectral analysis. It can also decrease use of resources since fewer medications are used to provide amnesia. Moreover, it also provides easy recovery from anesthesia. The BIS value is obtained 15-30 seconds earlier than the EEG data. Anesthetic concentration in the brain, level of analgesia and surgical stimulation may affect intraoperative BIS values. BIS values reflect the cerebral metabolic rate generated by hypnotic agents. Neurologic diseases, encephalopathy, cerebral ischemia, hypothermia, genetically determined low-voltage conditions, EMG and sedation can impact BIS values[21]. In the literature, it has been found that many drugs were used in combination with propofol in colonoscopy. However, the use of magnesium as an adjuvant has not been reported in previously published studies.

Studies have shown that perioperative magnesium may reduce the need for anesthetic use, the time required for BIS to reach 60, and intraoperative analgesic consumption[9,10,22-24]. Amer et al.[10] reported that the use of magnesium in the pediatric general anesthesia may lead to significantly lower BIS values and reduction of time to reach values below BIS 60. Likewise, Olgun et al.[25] found that perioperative use of magnesium sulfate reduces the consumption of propofol, desflurane and postoperative morphine requirement. Seyhan et al.[26] have shown that a single dose of magnesium sulfate (40 mg/kg) reduces intraoperative propofol consumption by 13.5%. In the present study, we also found that the use of magnesium sulfate before colonoscopy reduced propofol consumption.

In a study investigating the effects of magnesium sulfate and clonidine on hemodynamic parameters and postoperative recovery, Altan et al.[9] found that consumption of propofol, magnesium sulfate and clonidine significantly reduced propofol consumption and time to reach BIS 60 in both magnesium and clonidine groups. They reported that the need for fentanyl in the Mg2+ group was not associated with any cardiovascular or hemodynamic side effect but the duration of extubation was longer and the recovery was slower. They also noted that the use of BIS may be a valuable tool for guiding the administration of propofol and BIS monitoring may reduce the propofol consumption. In the present study, we also found reduced propofol consumption in the Mg2+ group. Although the initial BIS values were significantly higher in the Mg2+ group, the time to reach BIS 70 was significantly shorter. Since the groups were randomized, the observed difference may be due to the initial effect of Mg2+, which is used in the treatment of cerebral vasospasm. It has been shown that Mg2+ is well tolerated in humans. However, if serum concentrations are too high, it can lead to hypotension, bradycardia and later to more poorer outcomes[8,26]. In the current study, no side effects were observed.

CONCLUSION

The addition of magnesium sulfate to propofol was determined to be a safety measure ameliorating respiratory and hemodynamic complications during colonoscopy carried out under BIS monitoring. The addition of magnesium to propofol may be an alternative to the use of propofol alone for sedation in colonoscopic interventions in order to reduce the drug consumption.

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