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The Effect of a Preoperative Single Dose of Magnesium Sulfate *versus* Preoperative Ultrasound Guided Bilateral Transversus Abdominis Plane Block on Hemodynamics and Postoperative Analgesic Requirements in Patients Undergoing Colorectal Surgery

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Abstract

Background: The transversus abdominis plane (TAP) block is a peripheral nerve block, utilized to anesthetize the sensory nerves by local anesthetic injection in the neurovascular plane. Magnesium sulfate can prevent the induction of central sensitization from peripheral nociceptive stimuli at the spinal action site by blocking N-methyl-D-aspartate (NMDA) receptors. The aim of our study is to compare the effect of preoperative single-dose of Magnesium sulfate versus preoperative ultrasound guided bilateral transversus abdominis plane block on hemodynamics, and postoperative analgesia in patients undergoing colorectal surgical operations.

Patients and methods: This study was conducted on 40 adult patients ASA I and II scheduled for colorectal surgical operations under general anesthesia. The patients were randomly divided into two equal groups as follow:

Group I: Patients received magnesium sulfate 50 mg/kg IV as single-dose before induction of anesthesia.

Group II: Bilaterally TAP block was performed before induction of anesthesia under ultrasound guidance.

In both groups, general anesthesia was used. Measurements: HR and MABP, Intraoperative fentanyl, atracurium, and isoflurane consumption, operative time, postoperative analgesia, duration of anesthesia, and side-effects such as nausea, vomiting, and shivering.

Results: There were no significant differences between the 2 groups as regards to age, weight, duration of surgery, and the duration of anesthesia. There were no significant differences in the time of the first analgesic request in both groups. Pain score was statistically insignificant between both groups. The incidences of postoperative nausea, vomiting and shivering were more in group II than group I.

Conclusion: Preoperative administration of a single dose of magnesium sulfate (50 mg/kg) versus preoperative ultrasound guided bilateral transversus abdominis plane block in patients undergoing colorectal surgery was associated in both groups with reduction in the analgesic requirements postoperatively, with less postoperative nausea, vomiting and shivering in the magnesium sulfate group.

Keywords: Preventive analgesia; TAP block; Perioperative magnesium

Introduction

Postoperative pain after colorectal surgeries results from surgical incision in addition to intense inflammatory response as a result of surgical trauma [1-3]. Postoperative pain can be associated with physiological and psychological derangements which may adversely affect perioperative outcome and sometimes may even cause mortality. Acute perioperative pain results in poor patient satisfaction, delays mobilization and if left untreated can lead to chronic pain [4,5].

Postoperative pain after colorectal surgeries may be visceral, or somatic which become worst with movement, visceral pain takes upper hand in the first 48 h postoperatively [6].

Proper and effective plane was needed for the treatment of postoperative pain to prevent its adverse effects. Prevention of this pain has been dubbed as the "holy grail of anesthesiology" [7].

The transversus abdominis plane (TAP) block is a peripheral nerve block, utilized to anesthetize the sensory nerves supplying the anterior abdominal wall by injection of local anesthetic in the neurovascular plane between internal oblique and transversus abdominis muscle layers [8-9]. The triangle of Petit is a single entry point for performing transversus abdominis plane (TAP) block *via* description of the landmark technique to access a number of abdominal wall nerves and providing more widespread analgesia [10]. Ultrasound guided TAP block has been described, it helps us to locate the neurovascular plane between internal oblique and transversus abdominis muscle layers easily and local anesthetic was deposited with accuracy [11].

Magnesium sulfate has been used as an anticonvulsant or antiarrhythmic drug. The interference with calcium channels and N-methyl-D-aspartate (NMDA) receptors may be the mechanism of the its analgesic effect. Magnesium sulfate can prevent the induction of central sensitization from peripheral nociceptive stimuli at the spinal action site by blocking NMDA receptors in a voltage-dependent manner. Reduction of catecholamine release with decrease in sympathetic stimulation may be another mechanism which lead to decrease the stress response to the surgery. NMDA receptor antagonists like magnesium sulfate with low doses have an effect on pain threshold and could prevent pain perception [12-16]. Magnesium sulfate was used as an adjuvant agent to increase the analgesic effect of the other analgesic drugs. Magnesium sulfate was found to be effective in reducing the perioperative pain and analgesic consumption through block the somatic, autonomic and endocrinal response to painful stimulus [17,18].

The Hypothesis of this Study

- Preoperative administration of single dose magnesium sulfate will be effective as preincistional TAP block in reducing anesthetic requirements.
- Preoperative administration of single dose magnesium sulfate will be effective as preincistional TAP block in reducing postoperative pain score, reduce the postoperative opioid consumption and prolong the time of first analgesic request.
- Preoperative administration of single dose magnesium sulfate will be associated with less postoperative nausea, vomiting, and shivering.

The aim of our study is to compare the effect of preoperative single-dose of magnesium sulfate versus preincisional ultrasound guided bilateral transversus abdominis plane block on hemodynamics, anesthetic requirements and postoperative analgesia in patients undergoing colorectal surgical operations. Primary outcomes of our study were reduction in opioid consumption in the first 24 h postoperatively and postoperative pain scores, while the secondary outcomes were the time to fist analgesic administration; and adverse events including, nausea, vomiting, and shivering.

Patients and Methods

This randomized double blinded study was carried out in Tanta University Hospital at the surgical Department on the time period from 3/2016 to 11/2016, after approval of the hospital ethical committee and obtaining verbal and written informed consent from each patient. All patients' data were confidential with secret codes and were used for the current study only. Any unexpected risk appears during the course of the study was cleared to the patient and the ethical committee on time and the proper measures were taken to overcome these risks.

The approval code of ethical committee was 30822/3/16.

Exclusion criteria

Patients refusal to share in the study, liver disease, coagulopathy, patients on anticoagulant or thrombolytic therapy, Patients who had prior abdominal surgeries, allergy to Magnesium sulfate or local anesthetic drugs. Figure 1 shows the patients flow diagram.

Randomization

The randomization was performed using sealed numbered envelopes indicating the group of each patient. A nurse blinded to study who did not participate in patients follow up, read the number and made group assignments. All operating room personals were blind to study.

The process of inclusion in the study went on until the required number of patients was reached. Infusion pumps and syringes which used for drugs administration were identical, covered, encoded Group I, and Group II by anesthesiologist and nurse blinded to study and did not participate in the study or data collection.

Preoperative preparation

All patients underwent preoperative assessment by history taking, physical examination and laboratory investigations which include complete blood count, liver function test, renal function test, prothrombin time, INR, ECG, blood group and chest X-ray.

Premedication

All patients received 150 mg ranitidine and 10 mg of metoclopramide one hour before anesthesia.

Intraoperative management

On arrival to operating room an intravenous line was inserted. All patients preloaded with 10 ml/kg ringers solution and were attached to monitor displaying the following: ECG, HR, NIBP, $ETCO_2$ and O_2 saturation.

The patients were randomly divided into two equal groups as follows:

Group I: Patients received magnesium sulfate 50 mg/kg in 250 ml of isotonic sodium chloride solution intravenously (IV) as single-dose before induction of anesthesia and placebo TAP block was considered where the needle was inserted and 20 ml of normal saline was injected bilaterally into the transversus abdominis neuro-fascial plane.

Group II: Bilaterally TAP block was performed before induction of anesthesia under ultrasound guidance with the patient in the supine position, the ultrasound probe is placed in a transverse plane in a sterile manner between the lower costal margin and the iliac crest in the midaxillary line. Once the external oblique abdominis muscle, the internal oblique abdominis muscle, and the transversus abdominis muscles were visualized at the level of the anterior axillary line between the 12th rib and the iliac crest, the block was performed with a 20-G, 100 mm Facetted tip needle, the needle is advanced between the aponeurosis of the internal oblique abdominis muscle and the transversus abdominis muscle. Once the needle was placed in the space between the internal oblique abdominis muscle and transversus abdominis muscle, intermittent aspiration is done to exclude intravascular injection, 20 ml 0.25% levobupivacaine was deposited bilateral into the transversus abdominis neuro-fascial plane after negative aspiration. The drug was seen spreading in the TAP as a dark oval shape.

Also patients in group II received placebo 250 ml of normal saline intravenously before induction of anesthesia.

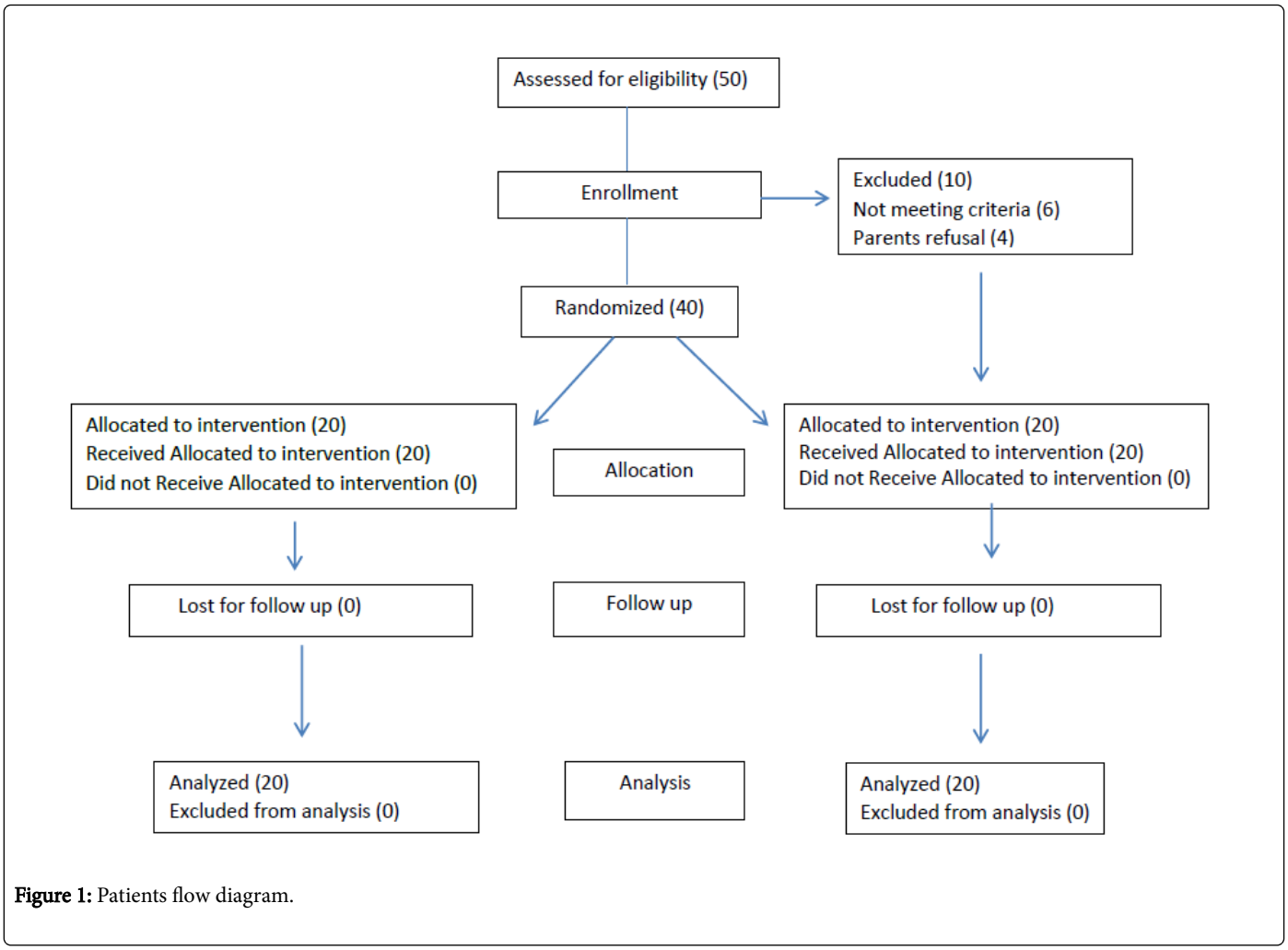

Figure 1: Patients flow diagram.

In both groups, general anesthesia was induced with intravenous injection of fentanyl 1 µg/kg, sodium thiopental 5 mg/kg, and atracurium 0.5 mg/kg. After intubation, anesthesia was maintained with 1-1.5% isoflurane in oxygen and top up doses of fentanyl and atracurium were given as needed. The tidal volume and respiratory rate were adjusted to achieve $SpO_2 \geq 95\%$ and end-tidal CO_2 between 32 and 35 mmHg. Central venous catheter was inserted through right internal jugular vein for fluids, drugs infusion and measure the central venous pressure, urinary catheter was placed for monitoring of urine output and arterial line was inserted for blood sampling and blood gas analysis.

During skin closure, intravenous (IV) infusion of diclofenac sodium (75 mg diluted in 100 ml of normal saline), and 1 gm of paracetamol were given intravenously combined with infiltration of wound with 20 ml of bupivacaine 0.5% in both groups. At the end of surgery metoclopramide 0.15 mg/kg and dexamethasone 0.15 mg/kg were administered for prophylaxis of postoperative nausea and vomiting (PONV). Ondansetron 0.1 mg/kg was administered for treatment of PONV. After completion of surgery, inhalational anesthesia was stopped and muscle relaxant was reversed with atropine and neostagmine and the patient allowed to breathe spontaneously. The ETT was removed when the patients fulfilled the criteria of extubation (spontaneous eye opening, purposeful movement, intact reflex) and the patients were transferred to postanesthesia care unit for further follow up.

The pain intensity was assessed by a person who was blind to study by using Numeric Rating Scale (NRS) with 10 cm length (starting from 0, no pain, to 10, worst pain) at 2 h, 4 h, 6 h, 8 h, 12 h, 18 h, and 24 h after recovery. If Numeric Rating Scale (NRS) value more than 4, pethedine 0.5 mg/kg was given intravenously and can be repeated every 3 h till the NRS less than 4. The time to first dose of analgesia and total 24 h of pethedine consumption postoperatively recorded in all patients.

Measurements

- Demographic data.
- HR and MABP as base line and every 5 min till end of surgery.
- Intraoperative fentanyl, atracurium, and isoflurane consumption was recorded
- Operative time was measured from skin incision to skin closure.
- The duration of anesthesia.
- Postoperative Numeric Rating Scale (NRS).
- Time to first analgesic request.
- Total 24 h pethedine consumption.
- Side-effects such as nausea, vomiting, and shivering were noted.

Shivering scale

- Grade 0-no sign of shivering
- Grade 1-vasoconstriction, cyonosis and piloerection
- Grade 2-visible tremor only in one muscle group
- Grade 3-visible tremor in more than one muscle group
- Grade 4-intense shivering, tremor of the head and arms and piloerection

Patients were discharged postoperatively when they had no or mild pain (NRS<3), and had no bleeding and or nausea or vomiting.

Statistical analysis

The sample size was calculated using the following assumption: the reduction in opioid consumption in the first 24 h postoperatively was the main response variable. Power analysis identified 20 patients per group, required to detect 20% reduction in postoperative opioid consumption between both groups with a power 80% and a significant level of 0.05.

Comparison of demographic data, time of surgery was done by Student's t-test. Two way analysis of variance with correction for repeated measurements was used for heart rate and blood pressure comparison. Pain score was analyzed with Mann-Whitney-U test nonparametric measurements (expressed as median (range).

Results

This study was carried out on 40 adult patients divided into two groups, 20 patients in each group. There were no statistically significant differences as regards to age, weight, duration of surgery, and the duration of anesthesia between both groups (Table 1).

Characters	Group I=Magnesium sulfate group (n=20)	Group II = Transversus Abdominis Plane Block group (n=20)
Age (years)	48 ± 5	52 ± 7
Weight (kg)	68 ± 8	72 ± 7
Duration of surgery (min)	160 ± 35	155 ± 32
Duration of anesthesia (min)	168 ± 5	165 ± 6
Male/Female	15/5	16/4
Time to first analgesic request (h)	4 ± 2	4 ± 1
Data are expressed as mean ± SD (standard deviation), n= Numbers of the patients. No statistically significant differences between the 2 groups		

Table 1: Demographic data, duration of surgery, duration of anesthesia and time to first analgesia.

There were no statistically significant differences in the baseline heart rates and mean arterial blood pressure in the patients in both groups. The HR and MABP were increased significantly in group II 5min, 10min, and 30 min after intubation and while it maintained stable in group I (Tables 2 and 3).

HR	Group I = Magnesium sulfate group (n=20)	Group II = Transversus Abdominis Plane Block group (n=20)
Base line	82 ± 4	84 ± 5
T1	88 ± 7	98 ± 5*
T2	86 ± 5	100 ± 7*
T3	88 ± 7	96 ± 6*
T4	80 ± 6	82 ± 8
T5	82 ± 7	84 ± 9
T6	84 ± 6	82 ± 8
At end of operation	86 ± 7	84 ± 9
Data are expressed as mean ± SD, n= Numbers of the patients, T1=5 min after induction, T2=10 min after induction, T3=30 min after induction, T4=60 min after induction, T5=90 min after induction, T6=120 min after induction. *P<0.05 denotes statistically significance between the 2 groups(the heart rate was increased significantly in transversus abdominis plane block group compared to magnesium sulfate group).		

Table 2: Heart rate (beats/minute) changes in both groups.

There were no statistically significant differences in the time of the first analgesic request in both groups (Table 1). There were no statistically significant differences between both groups as regards to fentanyl, atracurium and isoflurane requirement during anesthesia (Table 4).

MABP	Group I = Magnesium sulfate group (n=20)	Group II = Trans versus Abdominis Plane Block group (n=20)
Base line	85 ± 9	84 ± 8
T1	80 ± 7	96 ± 8*
T2	84 ± 8	100 ± 10*
T3	86 ± 7	96 ± 8*
T4	86 ± 8	88 ± 7
T5	80 ± 9	86 ± 9
T6	82 ± 8	90 ± 7
At end of operation	85 ± 9	88 ± 8
Data are expressed as mean ± SD, n= Numbers of the patients, T1=5 min after induction, T2=10 min after induction, T3=30 min after induction, T4=60 min after induction, T5=90 min after induction, T6=120 min after induction. *P<0.05 denotes statistically significance between the 2 groups (the mean arterial blood pressure was increased significantly in transversus abdominis plane block group compared to magnesium sulfate group).		

Table 3: Mean Arterial Blood Pressure (mmHg) changes in both groups.

Pain score was statistically insignificant between both groups at 2 h, 4 h, 6 h, 8 h, 12 h, 18 h, and 24 h postoperatively (Table 5).

Variables	Group I = Magnesium sulfate group (n=20)	Group II= Transversus Abdominis Plane Block group (n=20)
Intraoperative Fentanyl (µg/kg)	2 ± 0.6	2 ± 0.5
Atracurium (mg/kg)	0.6 ± 0.03	0.6 ± 0.04
*Dial set of isoflurane (%)	1	1
24 h Pethidine consumption (mg)	55 ± 17	56 ± 16
Data are expressed as mean ± SD, n= Numbers of the patients, *Data are expressed as (%). No statistically significant differences between the 2 groups.		

Table 4: Fentanyl, Atracurium, Isoflurane and 24 h Pethidine consumption in both groups.

Variables	Group I = Magnesium sulfate group (n=20)	Group II = Transversus Abdominis Plane Block group (n=20)
2h	2	2
4 h	3	4
6h	3	2
8 h	4	3
12 h	3	3
18h	5	4
24 h	2	2
Data are expressed as median, n=Numbers of the patients. No statistically significant differences between the 2 groups.		

Table 5: Postoperative Numeric Rating Scale in both groups.

There were no statistically significant differences between both groups as regards to 24 h pethedine consumption (Table 5). The incidences of postoperative nausea, vomiting and shivering were more in group II than group I (Table 6).

Characters	Group I = Magnesium sulfate group (n=20)	Group II = Trans versus Abdominis Plane Block group (n=20)
Nausea and Vomiting	2 (10%)	4 (20%)*
Shivering	1 (5%)	6 (30%)*
Data are expressed as number (%), n=Numbers of the patients. *P<0.05 denotes statistical significance between the 2 groups. The incidences of postoperative nausea, vomiting and shivering were significantly higher in transversus abdominis plane block group compared to magnesium sulfate group.		

Table 6: The incidence of postoperative adverse events.

Discussion

Our study demonstrated that, preoperative administration of single dose of magnesium sulfate 50 mg/kg or performing preoperative ultrasound guided bilateral TAP block was associated with stable hemodynamic, the time of first analgesic request was prolonged, and postoperative analgesic consumption was reduced in patients undergoing colorectal surgery.

However, Magnesium sulfate administration preoperatively was associated with les postoperative nausea, vomiting and shivering.

Preemptive analgesia is a method in which the intervention was given before start of noxious stimulus so, prevents the central sensitization caused by tissue damage and inflammatory mediators which associated with decreased intraoperative and postoperative analgesic consumption and reduce the change of acute postoperative pain to chronic one. But there were conflicting results about the efficacy of preemptive analgesia in reducing the severity, and chronicity of acute postoperative pain and this could explained by the fact that, there are many factors affecting the postoperative pain as the presence of preoperative pain, genetic factors, painful intraoperative stimulations as retraction, skin incision, cutting viscera, muscle or tendon cutting and postoperative release of inflammatory mediators [19,20].

Preventive analgesia is appropriate term which utilize preemptive analgesia and multimodal techniques, began before operation and continued in the operative and postoperative time, it combines multiple analgesics regimen which reduce the dose of each drugs, reduce or eliminate the unwanted side effects, enhance recovery and reduce the hospital stay and associated with early discharge from hospital, increased duration of action of analgesic drugs to decrease long-term pain sensitivity at the peripheral and central levels [21-23].

Magnesium sulfate was considered the fourth most common cation in the body and plays an important role in many physiologic processes [24].

Our study demonstrated that, the preoperative administration of single dose magnesium sulfate was associated with prolonged time to first analgesic request and decreased the pethedine consumption postoperatively with less incidences of postoperative nausea, vomiting and shivering.

Our study was in line with Seyhan et al. [25] they concluded that, preoperative magnesium sulfate infusion was associated with reduced the 24 h postoperative morphine consumption in patients undergoing gynecologic surgery.

Additionally Gupta et al. [26] reported that, preoperative administration of magnesium sulfate in patients undergoing spinal surgeries was associated with stable hemodynamics.

Moreover, Taheri et al. [27] concluded that preoperative infusion of 50 mg/kg magnesium sulfate 15 min before surgery significantly decrease the postoperative pain and opioid consumption in patients undergoing total abdominal hysterectomy under general anesthesia without any adverse effects.

Also Ryu et al. [28] reported that, preoperative magnesium sulfate 50 mg/kg was associated with significant decrease in the postoperative pain and decrease postoperative opioid consumption.

Asadollah et al. [29] found that, preoperative and continuous infusion of magnesium sulfate was associated with significant decrease in pain score postoperatively with reduced the need to opioid analgesia in patients undergoing lower abdominal laparotomy.

Postoperative shivering was associated with undesirable effects as it increases plasma catecholamine concentrations threefold, increase

oxygen consumption and requirements which may precipitate myocardial ischemia in cardiac patients and also associated with less patient's satisfaction, increase hospital cost, and were remembered as bad event and worst aspects of surgery [30].

Prevention of postoperative shivering is considered one of the most important functions of magnesium sulfate [31]. Administration of magnesium sulfate decreases the incidence of shivering by up to 70-90% [28,32].

Our study in agreement with previous studies [28,33] they concluded that intraoperative magnesium sulfate infusion was associated with less incidences of PONV and less postoperative shivering.

The main cause of postoperative pain after colorectal surgeries was the abdominal wall incision. Injection of local anesthetics into the transversus abdominis plane will result in block the nerves of the anterior abdominal wall before they pierce the musculature to innervate the abdomen wall [4].

The transverse abdominis plane (TAP) block is a peripheral nerve block which was used to block the nerves supplying the anterior abdominal wall (T6 to L1). It reduces the severity and chronicity of perioperative pain, reduces the opioid consumption in the postoperative period and reduces the side effects of opioids as sedation and postoperative nausea and vomiting [34,35].

In our study, pre-incisional ultrasound guided bilateral transversus abdominis plane block was associated with significant improved in postoperative pain score, reduced postoperative analgesic consumption, and increased in the time to first analgesic request with no reported complications.

This in agreements with Amr et al. [36] they concluded that a pre-incisional TAP was reported to be safe procedure, decrease acute postoperative pain, reduce the analgesic requirements, prolong the time to first analgesic administration with no recorded side effects.

Also, Belavy et al. [37] reported that TAP block reduced opioid consumption after cesarean section when used as a part of multimodal analgesic therapy.

Moreover, Peteren et al. [38] demonstrated that there is a clinically significant reductions of post-operative opioid requirements and pain, as well as some effects on opioid-related side effects (sedation and post-operative nausea and vomiting) in patients received TAP block.

In controversy to our study Costello et al. [39] concluded that, TAP block did not improve the quality of postoperative pain after cesarean section delivery.

Also Ghisi et al. [40] found that, TAP block did not reduce morphine consumption during the first postoperative 24 h after elective total laparoscopic hysterectomy.

The limitations of our study include the following: no control group, we did not measure the depth of anesthesia, the sample size may be small and postoperative magnesium sulfate and calcium levels were not measured.

Conclusion

Preoperative administration of a single dose of magnesium sulfate (50 mg/kg) versus preoperative ultrasound guided bilateral transversus abdominis plane block in patients undergoing colorectal surgery was associated in both groups with reduction in the analgesic requirements postoperatively, with less postoperative nausea, vomiting and shivering in the magnesium group.

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