ADMINISTRATION OF INTRAVENOUS MAGNESIUM IN PATIENTS UNDERGOING ABDOMINAL HYSTERECTOMY IS ASSOCIATED WITH REDUCED OPIOIDS CONSUMPTION IN POSTOPERATIVE PERIOD – A META-ANALYSIS

Anwar Ul Huda[1*], MBBS, FRCA, EDRA, MSc,
Tauseef Ahmed[2], FCPS, Mohammad Yasir[1],
MBBS, FCPS, EDRA

Abstract

Background: Abdominal hysterectomy can result in significant postoperative pain and morbidity which could result in delayed hospital discharge and chronic pain. Magnesium has been shown to help alleviate these problems in different surgeries. The aim of this study was to perform meta-analysis of studies evaluating the role of magnesium in the perioperative management of patients undergoing abdominal hysterectomy. The hypothesis of the review was that Magnesium is associated with significant reduction in opioids consumption, pain control and postoperative nausea and vomiting after abdominal hysterectomy.

Methods: A systematic review using Medline was conducted in accordance with the PRISMA guidelines. Randomised controlled trials studies reporting on patients receiving either intravenous magnesium or placebo during abdominal hysterectomy were considered for eligibility. Studies were appraised against the Consolidated Standards of Reporting Trials (CONSORT) checklist. A meta-analysis was performed using Review Manager 5.3.

Results: Eight randomized controlled trials were identified for inclusion (n = 330). Meta-analysis demonstrated a beneficial effect of magnesium in reducing 24 hours opioids consumption ($p = 0.002$). Pooled data analysis also showed a significant reduction in pain score at 4-6 hours postoperatively ($p = 0.006$). However, there was no advantage of magnesium with respect to postoperative nausea and vomiting ($p = 0.89$). There was no potentiation of muscle relaxant effects with use of magnesium ($p = 0.12$).

Conclusion: The use of intravenous magnesium is associated with significant reduction in 24 hours opioids consumption in patients undergoing abdominal hysterectomy. It also reduces the pain score at 4-6 hours postoperatively. It has no beneficial effect on postoperative nausea and vomiting.

Keywords: Magnesium; Abdominal hysterectomy; Pain, Nausea; Vomiting.

1 Department of Anesthesia, Security Forces Hospital, Kingdom of Saudi Arabia.
2 Department of Anesthesia, Southport and Ormskirk NHS Hospital trust, United Kingdom.
* **Corresponding author:** Anwar Ul Huda, MBBS, FRCA, EDRA, MSc. Consultant, Department of Anesthesia, Security Forces Hospital, Kingdom of Saudi Arabia. Phone: +966 502 654 719. E-mail: hudaanwar90@yahoo.com

Introduction

Abdominal hysterectomy is considered a major surgical procedure associated with a significant postoperative pain and morbidity[1] that can result in longer hospitalization, chronic pain, increased risk of venous thrombosis and lesser patients' satisfaction.[2-4]

The role of peripheral and central sensitization of dorsal horn neurons by surgical stimuli in acute pain has led to the search for novel treatments.[5] Magnesium is an important intracellular ion which helps to maintain homeostasis and plays essential role for function of enzymes, neurotransmission and cell signaling.[6] Magnesium can influence inflammatory and neuropathic pain by several different mechanisms. These include reduction in NMDA receptor activity via calcium channel blocking, a reduction in substance P synthesis, potentiation of morphine action in pre-synaptic area of dorsal horn, modulation of release and action of glutamate, substance P and calcitone gene-related peptide (CGRP) in spinal cord, reduction in Thromboxane A2 and other pro-inflammatory eicosanoids and cytokines.[7-12]

Few systematic reviews and meta-analyses[10-12] have reported the effect of perioperative magnesium administration for postoperative pain scores, analgesics consumption and adverse effect. But these studies included varieties of surgeries from all specialties. The aim of this review and meta-analysis is to investigate the effect of perioperative use of intravenous magnesium in patients undergoing abdominal hysterectomy regarding postoperative pain scores, opioids consumption and the incidence of adverse events.

Methods

A systematic review of the literature was conducted in accordance with the PRISMA guidelines using the online database Medline. The review was registered on the PROSPERO database on February 06, 2019 (Reference number CRD42019120499). Two authors performed searches independently on the February 01, 2019 and then repeated the search on the 26th of February 2019 in order to ensure accuracy. Any discrepancies were resolved through discussion between these two authors, with the senior author resolving any residual differences. The Medline search strategy used is illustrated in Table 1 and a flow diagram of the review process in Figure 1.

Fig. 1
Flow diagram of Medline review process

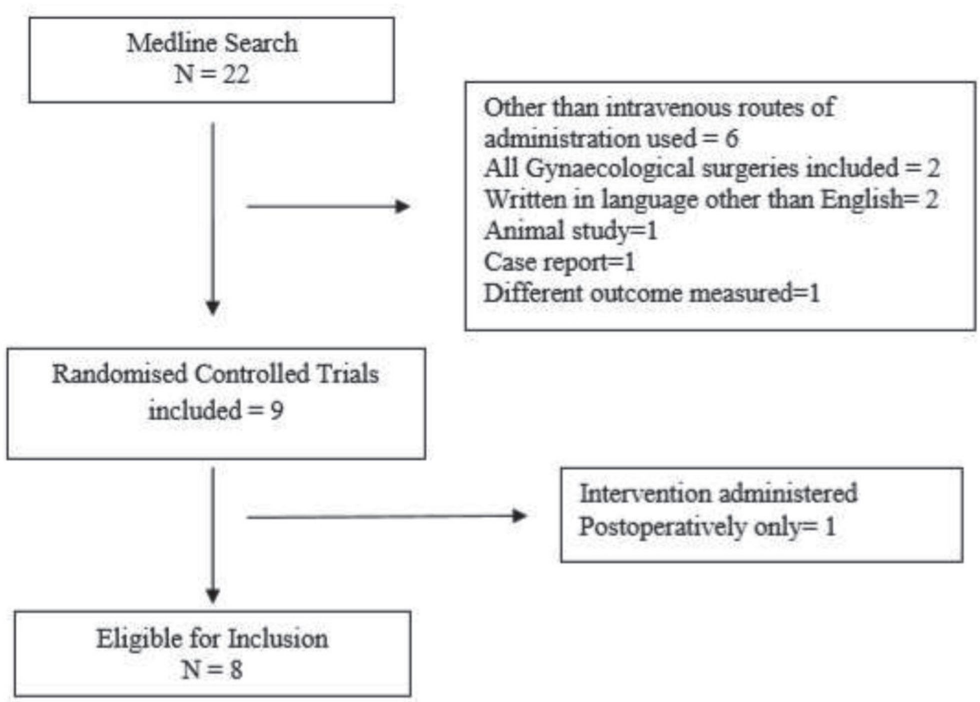


Table 1
Search strategy for Medline

Search Term	Number of studies
Magnesium (#1)	10,5919
Magnesium sulfate (#2)	9,751
#1 or #2	10,5919
Hysterectomy (#3)	46,104
Pain (#4)	8,397
#1 AND #2 AND #3 AND #4	22

We included randomized controlled clinical trials, which were published in the English language, and presented them in Table 2. The study must have evaluated the efficacy of intravenous magnesium for postoperative pain relief in patients undergoing abdominal hysterectomy. Any regimen of intravenous magnesium administration was acceptable providing dosing was clearly defined in study methodology and the study included a control group that had been randomized to receive placebo treatment. To be eligible the study must have reported one of the two primary outcome measures, defined as either pain scores in the early post-operative period or reduction in post-operative opioid consumption. The early post-operative period was defined as the first 24 hours after the surgical procedure. Secondary outcome measures

Table 2
Concise details of included studies

Study	Population	Intervention (s)	Comparator	Outcome	Results
Haryalchi et al. [15] N = 40	ASA I&II Elective TAH	15 mg/kg magnesium as infusion pre-op GA Mean age 48.30 years	Placebo pre-op GA Mean age 50.70	VNRS Opioid consumption Beta endorphins level postop Side effects	VNRS in intervention group was significantly lower than placebo at 6 and 12 hours postop ($p = 0.0001$) Opioid consumption was significantly lower at 24 hours in intervention group ($p = 0.0001$) Beta endorphins level was significantly lower in intervention group ($p = 0.04$)
Jarahzadeh et al (16) N = 60	ASA I&II 35-65 years Abdominal hysterectomy	50 mg/kg magnesium sulfate post induction Mean age 52 years	Placebo post induction Mean age 51 years	VAS score Opioid consumption Side effects	VAS score in magnesium group was significantly lower than placebo group at immediately after surgery and 1, 2, 6 and 12 hours postoperatively ($p <0.05$). Opioid consumption was significantly lower than placebo group at immediately after surgery and 1, 2, 6 and 12 hours postoperatively ($p <0.05$).
Kahraman et al (17) N = 40	ASA I&II 18-65 years Abdominal hysterectomy	Spinal Anaesthesia 65 mg/kg magnesium sulfate during operation Mean age 43 years	Spinal Anaesthesia Placebo Mean age 41 years	VAS score Duration of sensorial block Plasma and CSF magnesium concentration	VAS scores were lower in magnesium group than those in placebo group at 2 and 4 hours after surgery ($p <0.001$) Regression of sensorial block was longer in magnesium group than placebo group ($p <0.01$)

Wilder-Smith et al (18) N = 24	ASA I&II 20-75 years Hysterectomy	200 mg magnesium Laevulinate as IV bolus followed by infusion as 200 mg/hour GA Mean age 48 years	Placebo GA Mean age 45.7 years	Pain score Opioid consumption Side effects	Pain score was lower in magnesium group than control group at 3 hours postoperatively (p = 0.04) Cumulative morphine consumption was similar in two groups except at first hour (p = 0.04)
Ko et al (19) N = 60	ASA I&II Total abdominal hysterectomy	50 mg/kg magnesium sulfate as bolus dose post induction followed by 15 mg/kg infusion GA Mean age 44.2 years	Placebo GA Mean age 42.9 years	VAS score Epidural analgesics consumption CSF magnesium concentration Side effects	VAS scores at rest and during forced expiration were similar and less than 4 in both groups (p >0.05). Cumulative postoperative epidural analgesic consumption were similar in both groups.
Taheri et al (20) N = 40	ASA I&II Total abdominal hysterectomy	50 mg/kg magnesium sulfate as single dose GA Mean age 50.45 years	Placebo Mean age 51.85 years	NRS score Opioids consumption Side effects	NRS score decreased in magnesium group at 6, 12 and 24 hours postoperatively significantly (p <0.05). Pethidine consumption was significantly lower in magnesium group than placebo group over 24 hours (p = 0.0001)
Tramer et al (21) N = 42	ASA I&II Abdominal hysterectomy	GA 3 g MgSO4 bolus followed by 0.5 g/hour during 20 hours Mean age 49 years	Placebo Mean age 47 years	VAS score at rest and during peak flow Discomfort Morphine consumption Side effects	VAS scores at rest and during peak flow were similar in both groups throughout study Morphine consumption was significantly lower in magnesium group during first 48 hours (p <0.03) and most pronounced during first 6 hours (p <0.004) Magnesium group experienced less discomfort during 1st and 2nd postoperative days
Kara et al (22) N = 24	ASA I&II Adults aged 26-65 years Abdominal hysterectomy	GA 30 mg/kg MgSO4 bolus followed by 500 mg/hour for 20 hours Mean age 43.33	Placebo Mean age 42.83 years	VAS score Morphine consumption Side effects	At 30 minutes and 18 hours postoperatively, VAS scores at rest and during sitting and coughing were higher in control group (p <0.05). At rest of times, VAS scores were similar. Cumulative morphine consumption were significantly lower at 30 minutes and 18 hours postoperatively (p <0.05)

included the incidence of nausea and vomiting within 24 hours of surgery and muscle relaxant potentiation. Only primary research was considered for review with any abstracts, comments, review articles and technique articles excluded. The clinical studies were appraised independently by two authors with respect to the Consolidated Standards of Reporting Trials (CONSORT) checklist.[13] Potential bias of studies was evaluated using the Cochrane Collaboration's tool for assessing risk of bias in randomised trials.[14] A meta-analysis of the included trials was performed. Data for pain assessment, opioids consumption and post-operative nausea and vomiting was pooled for 1st 24 hours after the surgical procedure dependent on the last reported time point in each study. Muscle relaxant potentiation was pooled at early postoperative period and was reported as being either present or not. For continuous data, the standardized mean difference was used to describe the size of the treatment effect, and, for dichotomous data, relative risks were used. A random effects model was used for all analyses. The level of significance was set at p-value <0.05. All statistical analyses were performed with Review Manager 5.3. Heterogeneity was measured and expressed as I^2.

Results

Pain Scores

Haryalchi and colleagues[15] found that intravenous magnesium infusion at 15 mg/kg/hr intraoperatively during TAH improved postoperative pain scores significantly at 6 and 12 hours postoperatively. They reported pain scores (VNRS) as 6.30 ± 0.73 in intervention group vs 9.80 ± 0.62 in control group at 6 hours while 6.30 ± 0.98 in intervention group vs 7.75 ± 1.121 in control group at 12 hours. There was no significant difference in VNRS score between groups at 24 hours. Jarahzadeh and colleagues[16] in their study used 50 mg/kg intravenous magnesium sulfate or placebo post induction depending on the group and found out that mean pain scores were significantly lower at all measured times between 0-12 hours postoperatively (p-value <0.05).

Kahraman and colleagues[17] used intravenous magnesium sulfate at 65 mg/kg during operation under spinal and the result showed that pain score (VAS) were significantly lower in intervention group (2 ± 1 and 2 ± 1) compared to control group (6 ± 2 and 5 ± 2) at 2 and 4 hours respectively (p-value <0.001) although there was no difference in pain scores at 8 and 12 hours postoperatively.

Wilder-Smith and colleagues[18] used intravenous magnesium laevulinate 200 mg (8.2 mmol) or placebo as slow bolus pre-induction followed by continuous infusion of placebo or magnesium at 200 mg/hour for 5 hours. At 3 hours postoperatively, patients in magnesium group experienced more pain as compared to control group, although there was no significant difference in pain score between two groups at all other times.

Ko and colleagues[19] used 50 mg/kg intravenous MgSO4 as bolus dose followed by a continuous infusion of 15 mg/kg/hour for 6 hours in magnesium group while control group received isotonic saline only. A patient controlled epidural infusion was used for postoperative pain in both groups and the results showed that visual analogue pain scores at rest and during forced expiration were similar and less than 4 in both groups during time of each examination until 72 hours.

Taheri and colleagues[20] in their study administered 50 mg/kg of intravenous magnesium sulfate in normal saline or just normal saline as control. They reported that pain scores decreased in magnesium group at 6, 12 and 24 hours after surgery significantly (p value<0.05) but there was no significant difference at emergence time.

Tramer and colleagues[21] used 20% magnesium sulphate or normal saline 15 ml intravenously before start of surgery and then followed by 2.5 ml/hour for next 20 hours. They reported that from 18-48 hours, discomfort was significantly less in magnesium treated patients compared to patients in control group. Although, pain values (VAS score) at rest and during peak flow were similar in both groups throughout the study period.

Kara and colleagues[22] in their study used a bolus of 30 mg/kg of intravenous magnesium sulfate or normal saline before start of surgery and then 0.5 g/hour infusion for next 20 hours. They reported that pain values at rest and during sitting and coughing were significantly higher in control group as compared to magnesium group at 30 minutes and 18 hours postoperatively (p-value <0.05). There was no significant difference in pain scores between two groups at other times.

Pooled meta-analysis of included studies showed significant difference in pain score between magnesium group and control group only at 4-6 hours postoperatively (p = 0.006) as shown in figure 2. There was no significant difference between two groups at other times including 0-2 hours, 12 hours and 24 hours postoperatively.

Opioids consumption

Haryalchi and colleagues[15] reported that pethidine consumption was significantly lower as 10±18.92 mg in intervention group vs 68 ± 17.42 mg in control group in first 24 hours postoperatively (p-value 0.0001). Jarahzadeh and colleagues[16] in their study reported that mean morphine consumption at different time intervals were significantly lower in magnesium group up to 12 hours postoperatively (p <0.05). Wilder-Smith and colleagues[18] in their study did not find any significant difference in cumulative morphine consumption at different time intervals except for the first hour postoperatively (magnesium 9.3 mg vs placebo 12.8 mg). Ko and colleagues[19] reported that cumulative postoperative epidural analgesic doses via PCEA were similar in both groups at different time intervals. Taheri and colleagues[20] in their study demonstrated that 24 hours Pethidine consumption was 16.75 mg in magnesium group vs 68 mg in control group and it was found to be statistically significant (p <0.05).

Tramer and colleagues[21] reported that cumulative mean morphine consumption after 48 hours were 65 mg in magnesium group and 91 mg in control group (p <0.03). Also, morphine consumption during four different time intervals revealed that patients in magnesium group consumed significantly (p <0.04) less morphine than those in control group during 1st 6 hours postoperatively but not thereafter. Kara and colleagues[22] reported that postoperative morphine consumption at 24 hours postoperatively was significantly lesser in magnesium group vs control group (35.55 vs 43.43 mg).

Pooled analysis of studies demonstrated that intravenous Magnesium sulfate use reduced the postoperative opioids requirements significantly in patients undergoing abdominal hysterectomy (p = 0.002) by 25.05% as shown in figure 3. We used 1:10 ratio of efficacy for the doses of pethidine vs Morphine as Haryalchi and colleagues[15] and Taheri and colleagues[20] used Pethidine in postoperative period.

Nausea and Vomiting

Haryalchi and colleagues[15] found that none of the patients in either group had nausea or vomiting in postoperative period. Kahraman and colleagues[17] reported that there was only one patient with nausea and vomiting in each of the magnesium and control groups. Tramer and colleagues[21] reported that 10 patients out of 21 in control group and 6 patients out of 21 in magnesium group had postoperative nausea and it was not found to be statistically significant. Ko and colleagues[19] reported that 2 out of 29 patients in control group and 6 out of 29 patients in magnesium group complained of nausea during 24 hours postoperatively

Fig. 2

Pain at 4-6 hours

	Magnesium group			Control group				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Haryalchi 2017	6.3	0.73	20	9.8	0.62	20	12.8%	-5.07 [-6.39, -3.74]
Jarahzadeh 2016	5.53	1.43	30	7.03	0.76	30	14.9%	-1.29 [-1.85, -0.73]
Kahraman 2014	2	1	19	5	2	19	14.4%	-1.86 [-2.63, -1.08]
Ko 2001	3.1	1.1	29	3	1.5	29	15.0%	0.08 [-0.44, 0.59]
Taheri 2015	6.45	1.05	20	9.8	0.62	20	13.6%	-3.81 [-4.88, -2.73]
Tramer 1996	3.9	0.9165	21	3.7	1.3748	21	14.8%	0.17 [-0.44, 0.77]
Wilder-Smith 1997	1	0.5	13	1	0.9	11	14.4%	0.00 [-0.80, 0.80]
Total (95% CI)			**152**			**150**	**100.0%**	**-1.59 [-2.73, -0.45]**

Heterogeneity: $Tau^2 = 2.19$; $Chi^2 = 104.45$, df = 6 ($P < 0.00001$); $I^2 = 94\%$
Test for overall effect: Z = 2.73 (P = 0.006)

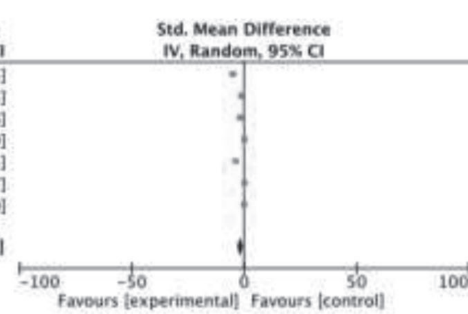
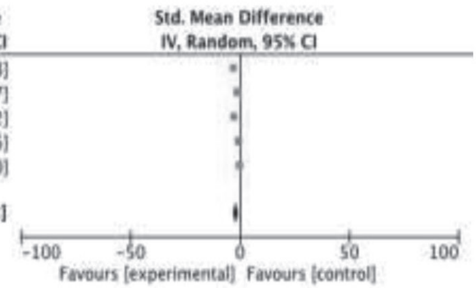


Fig. 3

Opioids consumption for 24 hours postoperatively

Study or Subgroup	Magnesium group Mean	SD	Total	Control group Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
Haryalchi 2017	1	1.89	20	6.8	1.74	20	19.3%	-3.13 [-4.08, -2.18]
Kara 2002	35.55	0.48	12	43.43	7.2	12	19.5%	-1.49 [-2.41, -0.57]
Taheri 2015	1.675	1.823	20	6.8	1.742	20	19.7%	-2.82 [-3.72, -1.92]
Tramer 1996	42	17.872	21	60	26.1207	21	21.2%	-0.79 [-1.42, -0.16]
Wilder-Smith 1997	42	11	13	46	14	11	20.2%	-0.31 [-1.12, 0.50]
Total (95% CI)			**86**			**84**	**100.0%**	**-1.68 [-2.74, -0.62]**

Heterogeneity: Tau² = 1.27; Chi² = 32.71, df = 4 (P < 0.00001); I² = 88%
Test for overall effect: Z = 3.11 (P = 0.002)



and 1 in each group vomited. Taheri and colleagues[20] in their study did not have any patient who experienced nausea or vomiting in 24 hours postoperatively in either group. Wilder-Smith and colleagues[18] reported 7 patients in control group vs 9 patients in magnesium group to have postoperative nausea/vomiting. Pooled analysis of data from all studies did not demonstrate any statistically significant difference in incidence of postoperative nausea and vomiting in magnesium vs control group ($p = 0.89$) as shown in figure 4.

Muscle relaxant potentiation

Kara and colleagues[22] reported that use of intraoperative vecuronium doses was similar between magnesium vs control group. Ko and colleagues[19] reported intraoperative mean vecuronium doses were 0.11 mg/kg in control group vs 0.08 mg/kg in magnesium group and this difference was found to be statistically significant ($p<0.05$). Tramer and colleagues[21] did not find any statistically different intraoperative vecuronium doses between two groups. Pooled analysis of the studies demonstrated that the doses of muscle relaxants intraoperatively were lower in magnesium group although this did not show any statistically significance ($p = 0.12$).

Heterogeneity

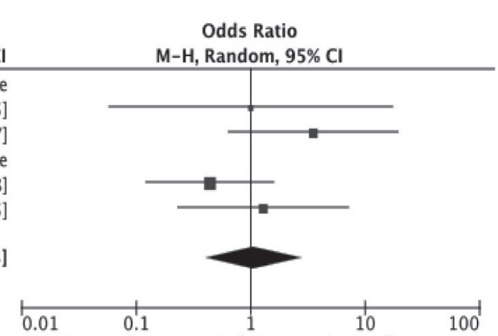
I^2 was used to assess heterogeneity between studies, specifically the extent of variation among the effects observed (between study variance). For postoperative pain score, I^2 was high, 95% for 0-2 hours, 94% for 4-6 hours and 92% for 12 hours although I^2 pain score at 24 hours was 78%. Heterogeneity for opioids consumption at 24 hours was also significant high with I^2 value of 88%. I^2 value for postoperative nausea and vomiting was low as 21% showing mild heterogeneity. While I^2 for muscle relaxation potentiation with the use of intravenous magnesium was also high as 87%. There could be different reasons for this like use of difference doses and timing of magnesium sulphate and use of different pain score as two of the studies used VNRS as pain scale. But at the same time, caution

Fig. 4

Postoperative nausea and vomiting

Study or Subgroup	Magnesium group Events	Total	Control group Events	Total	Weight	Odds Ratio M-H, Random, 95% CI
Haryalchi 2017	0	20	0	20		Not estimable
Kahraman 2014	1	19	1	19	10.5%	1.00 [0.06, 17.25]
Ko 2001	6	29	2	29	25.5%	3.52 [0.65, 19.17]
Taheri 2015	0	20	0	20		Not estimable
Tramer 1996	6	21	10	21	38.5%	0.44 [0.12, 1.58]
Wilder-Smith 1997	9	13	7	11	25.4%	1.29 [0.23, 7.05]
Total (95% CI)		**122**		**120**	**100.0%**	**1.07 [0.41, 2.83]**
Total events	22		20			

Heterogeneity: Tau² = 0.21; Chi² = 3.80, df = 3 (P = 0.28); I² = 21%
Test for overall effect: Z = 0.14 (P = 0.89)



should be applied in interpreting these values because it is well recognised that in small meta-analyses the number of studies included is often inadequate to accurately estimate heterogeneity.

Discussion

We found out in our review that use of intravenous magnesium intraoperatively reduced opioids consumption in first 24 hours postoperative period. A review article comprising of animal and human trials concluded that magnesium is useful for reducing postoperative pain by enhanced opioid analgesic effects.[23] Similarly, another meta-analysis of 20 RCTs[24] demonstrated that systemic perioperative magnesium might be useful for postoperative pain and opioid use. They reported that magnesium reduced postoperative opioids consumption by a large effect at lower limit of 99% confidence interval, -10.52 (-13.50 to -7.54) mg of intravenous morphine equivalents. Lysakowski and colleagues[25] in a systematic review of 14 RCTs although did not find any reduction in analgesics consumption with use of Magnesium.

Our meta-analysis of all included studies showed the beneficial effect of magnesium in reducing pain score at 4-6 postoperatively only. Although among the included studies, Kahraman and colleagues[17] found magnesium to be effective in reducing postoperative pain at 2 and 4 hours and Kara and colleagues[22] found better control with the use of magnesium at 30 minutes and then at 18 hours. While Lysakowski and colleagues[25] in a systematic review of 14 RCTs did not find any advantage of using Magnesium sulphate on postoperative pain scores.

Guo and colleagues[26] in their meta-analysis comprising of 27 RCTs involving 1504 patients having different surgeries showed that in urogenital surgeries, systemic magnesium induced a significantly increased postoperative analgesia indicated by both decrease in postoperative pain score as -1.94 (95% CI, -2.64 to -1.24; P<0.01) and analgesic consumption. De Oliveira and colleagues[24] showed that use of perioperative magnesium reduces postoperative pain and opioid consumption and hence should be considered as a strategy to alleviate postoperative pain.

Another review by Albrecht and colleagues[27] reported that postoperative morphine consumption was reduced by 12.7% in magnesium group after gynaecology surgery while in our meta-analysis morphine consumption at 24 hours was reduced by 25.05%. Peng and colleagues[28] demonstrated that perioperative systemic magnesium use results in reduced cumulative analgesic requirement and also a longer time to first analgesic request in some trials. However, its effect on postoperative pain intensity still remains controversial.

Murphy and colleagues[29] in a meta-analysis showed that perioperative magnesium administration was not associated with reduced postoperative nausea or vomiting (RR = 0.76, 95% CI: 0.52-1.09, p value = 0.14) as also was the case in our meta-analysis. On the other hand, Peng and colleagues[28] demonstrated that $MgSO_4$ significantly decreased the adverse events of vomiting (5.1% vs 16.5%; Relative risk 0.32) and nausea (6.2% vs 16.5%; Relative risk 0.38).

Our meta-analysis demonstrated that magnesium group required about 4.5% lesser doses of neuromuscular blockage intraoperatively as compared to control group although this was not found to be significant. Rodriguez-Rubio and colleagues[30] in their meta-analysis found that magnesium sulfate significantly reduces the requirement of neuromuscular blockers (p <0.001).

There are differences with regard to the methods by which magnesium was administered in a number of studies. Because the number of RCTs in which epidural and intra-articular pathways were utilized is limited, only intravenous magnesium was included in this meta-analysis.

One of the limitations was that studies used different strategies for doses and duration of magnesium bolus and infusion. Kahraman and colleagues[17] used magnesium sulphate 65 mg/kg infusion in 250 ml 5% dextrose at 3.5 ml/min rate during operation, while Wilder-Smith and colleagues[18] used 200 mg Magnesium Laevulinate as IV bolus five minutes before induction of anaesthesia followed by continuous infusion at 200 mg/hours for 5 hours. Kara and colleagues[22] used IV MgSO4 30 mg/kg as bolus and then 500 ml/hour by infusion for postoperatively as well for 20 hours. Haryalchi and colleagues[15] used lower dose IV MgSO4 of 15 mg/kg/hour in 100 ml isotonic saline without a bolus. In the study by Tramer and colleagues[21], the patients in intervention group received 15 ml 20% MgSO4 as bolus followed by 2.5 ml/hour of continuous infusion for 20 hours while Ko and colleagues1[9] used 50 mg/kg MgSO4 as bolus and then 15 mg/kg/hour for 6 hours. So, all studies used IV Magnesium bolus and infusion except Haryalchi and colleagues[15] which only used IV infusion.

As long as pain scores are concerned, most of the studies used visual analogue scale (VAS) apart from two. Haryalchi and colleagues[15] used verbal numeric rating scale (VNRS) and Wilder-Smith and colleagues[18] used intensity rate scale (0-4). None of the studies included in this meta-analysis mentioned about the use of non-opioids analgesics in postoperative period except Wilder-Smith and colleagues[18] used NSAIDs as rescue analgesics.

Conclusion

Magnesium is associated with reduction in opioids consumption in first 24 hours after abdominal hysterectomy. It also reduces pain score at 4-6 hours postoperatively although it does not confer any advantage to postoperative nausea and vomiting.

Financial disclosures: None.

Conflicts of interest: All authors declare that there are no conflicts of interest

References

1. Azari L, Santoso JT, Osborne SE. Optimal pain management in total abdominal hysterectomy. Obstet Gynecol Surv. 2013;68(3):215-27.
2. Imani F, Rahimzadeh P. Gabapentinoids: gabapentin and pregabalin for postoperative pain management. Anesth Pain Med. 2012;2(2):52-3.
3. Pandey D, Sehgal K, Saxena A, Hebbar S, Nambiar J, Bhat RG. An audit of indications, complications, and justification of hysterectomies at a teaching hospital in India. Int J Reprod Med. 2014;2014:279273.
4. Rawal N, Berggren L. Organization of acute pain services: a low-cost model. Pain. 1994;57(1):117-23.
5. Scholz J, Woolf CJ. Can we conquer pain? Nat Neurosci. 2002;5 Suppl:1062-7.
6. Fawcett WJ, Haxby EJ, Male DA. Magnesium: physiology and pharmacology. Br J Anaesth. 1999;83(2):302-20.
7. Esperanza Recio-Pinto, Castillo C. Peripheral N-methyl-D-aspartate receptors as possible targets for chronic pain treatment. Techniques in Regional Anesthesia and Pain Management. 2010;14(2):48-58.
8. Fisher K, Coderre TJ, Hagen NA. Targeting the N-methyl-D-aspartate receptor for chronic pain management. Preclinical animal studies, recent clinical experience and future research directions. J Pain Symptom Manage. 2000;20(5):358-73.
9. Hewitt DJ. The use of NMDA-receptor antagonists in the treatment of chronic pain. Clin J Pain. 2000;16(2 Suppl):S73-9.
10. De Kock MF, Lavand'homme PM. The clinical role of NMDA receptor antagonists for the treatment of postoperative pain. Best Pract Res Clin Anaesthesiol. 2007;21(1):85-98.
11. Petrenko AB, Yamakura T, Baba H, Shimoji K. The role of N-methyl-D-aspartate (NMDA) receptors in pain: a review. Anesth Analg. 2003;97(4):1108-16.
12. Nechifor M. Magnesium involvement in pain. Magnes Res. 2011;24(4):220-2.
13. Schulz KF, Altman DG, Moher D, Group C. CONSORT 2010 statement: updated guidelines for reporting parallel group randomised trials. BMJ. 2010;340:c332
14. Higgins JP, Altman DG, Gotzsche PC, Juni P, Moher D, Oxman AD, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ. 2011;343:d5928.
15. Haryalchi K, Abedinzade M, Khanaki K, Mansour Ghanaie M, Mohammad Zadeh F. Whether preventive low dose magnesium sulphate infusion has an influence on postoperative pain perception and the level of serum beta-endorphin throughout the total abdominal hysterectomy. Rev Esp Anestesiol Reanim. 2017;64(7):384-90.
16. Jarahzadeh MH, Harati ST, Babaeizadeh H, Yasaei E, Bashar FR. The effect of intravenous magnesium sulfate infusion on reduction of pain after abdominal hysterectomy under general anesthesia: a double-blind, randomized clinical trial. Electron Physician. 2016;8(7):2602-6.
17. Kahraman F, Eroglu A. The effect of intravenous magnesium sulfate infusion on sensory spinal block and postoperative pain score in abdominal hysterectomy. Biomed Res Int. 2014;2014:236024.
18. Wilder-Smith CH, Knopfli R, Wilder-Smith OH. Perioperative magnesium infusion and postoperative pain. Acta Anaesthesiol Scand. 1997;41(8):1023-7.
19. Ko SH, Lim HR, Kim DC, Han YJ, Choe H, Song HS. Magnesium sulfate does not reduce postoperative analgesic requirements. Anesthesiology. 2001;95(3):640-6.
20. Taheri A, Haryalchi K, Mansour Ghanaie M, Habibi Arejan N. Effect of low-dose (single-dose) magnesium sulfate on postoperative analgesia in hysterectomy patients receiving balanced general anesthesia. Anesthesiol Res Pract. 2015;2015:306145.
21. Tramer MR, Schneider J, Marti RA, Rifat K. Role of magnesium sulfate in postoperative analgesia. Anesthesiology. 1996;84(2):340-7
22. Kara H, Sahin N, Ulusan V, Aydogdu T. Magnesium infusion reduces perioperative pain. Eur J Anaesthesiol. 2002;19(1):52-6.
23. Bujalska-Zadrozny M, Tatarkiewicz J, Kulik K, Filip M, Naruszewicz M. Magnesium enhances opioid-induced analgesia-What we have learnt in the past decades? Eur J Pharm Sci. 2017;99:113-27.
24. De Oliveira GS, Jr., Castro-Alves LJ, Khan JH, McCarthy RJ. Perioperative systemic magnesium to minimize postoperative pain: a meta-analysis of randomized controlled trials. Anesthesiology. 2013;119(1):178-90.
25. Lysakowski C, Dumont L, Czarnetzki C, Tramer MR. Magnesium as an adjuvant to postoperative analgesia: a systematic review of randomized trials. Anesth Analg. 2007;104(6):1532-9, table of contents.
26. Guo BL, Lin Y, Hu W, Zhen CX, Bao-Cheng Z, Wu HH, et al. Effects of Systemic Magnesium on Post-operative Analgesia: Is the Current Evidence Strong Enough? Pain Physician. 2015;18(5):405-18.
27. Albrecht E, Kirkham KR, Liu SS, Brull R. Peri-operative intravenous administration of magnesium sulphate and postoperative pain: a meta-analysis. Anaesthesia. 2013;68(1):79-90.
28. Peng YN, Sung FC, Huang ML, Lin CL, Kao CH. The use of intravenous magnesium sulfate on postoperative analgesia in orthopedic surgery: A systematic review of randomized controlled trials. Medicine (Baltimore). 2018;97(50):e13583.
29. Murphy JD, Paskaradevan J, Eisler LL, Ouanes JP, Tomas VA, Freck EA, et al. Analgesic efficacy of continuous intravenous magnesium infusion as an adjuvant to morphine for postoperative analgesia: a systematic review and meta-analysis. Middle East J Anaesthesiol. 2013;22(1):11-20.
30. Rodriguez-Rubio L, Nava E, Del Pozo JSG, Jordan J. Influence of the perioperative administration of magnesium sulfate on the total dose of anesthetics during general anesthesia. A systematic review and meta-analysis. J Clin Anesth. 2017;39:129-38.