



Comparative Study between the Effect of Dexmedetomidine or Magnesium Sulphate Infusion on the Recovery Profile and Postoperative Analgesia in Patients Undergoing Laparoscopic Bariatric Surgery

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Background: The increasing incidence of morbid obesity is a crisis in national healthcare which has precipitated an increase in bariatric surgery. Bariatric surgery is an effective treatment for obesity, with a mean percentage of weight loss after 2 years of 68.2% for laparoscopic bariatric surgery.

Methods: This prospective randomized controlled study was carried out in Tanta University Hospitals in General Surgery Department on patients scheduled for elective laparoscopic bariatric surgery from July 2019 to June 2020. The study has been approved by the Institutional ethical committee at Faculty of Medicine, Tanta University with approval number (33161/05/19)

Results: There was a significant decrease in heart rate, at T2 to T9, in group II (Dexmedetomidine group) and group III (Mg sulphate group) compared to group I (Control group). There was a

significant decrease in mean arterial blood pressure, at T2 to T9, in group II and group III compared to group I. Visual analog scale for pain (VAS) was decreased significantly in group II and group III compared to group I. There was a negative increase in nausea and vomiting in group I than group II and group III. Bradycardia, hypotension and postoperative hypoxemia were insignificantly different among the three groups.

Conclusions: In patients undergoing laparoscopic bariatric surgeries, both dexmedetomidine and magnesium sulphate were safe and effective as regards early recovery profile, delayed time for the first request of analgesia and less opioid consumption.

Keywords: Dexmedetomidine; Magnesium Sulphate; Laparoscopic Bariatric.

INTRODUCTION

The increasing incidence of morbid obesity is a crisis in national healthcare which has precipitated an increase in bariatric surgery [1]. Bariatric surgery is an effective treatment for obesity, with a mean percentage of weight loss after 2 years of 68.2% for laparoscopic bariatric surgery [2].

Anesthetic management of morbidly obese patients poses a challenge to the anesthesiologist [3,4]. The incidence of obstructive sleep apnea and decreased tissue oxygenation is high in morbidly obese patients, increasing the risk of perioperative morbidity and mortality due to inadequate postoperative ventilation [5,6]. Obese patients may be sensitive to the respiratory depressant effect of opioid analgesic drugs and more likely to require postoperative ventilation to avoid hypoxic episodes [7].

It has been recommended that opioid drugs be avoided for analgesia in the morbidly obese patient because of the risk of respiratory depression [8]. This requires that alternative drugs be used in place of opioids to provide analgesia during surgery. Several drugs, including clonidine, ketamine, magnesium, lidocaine, ketorolac, and steroids have all been shown to be analgesic [9-14].

Dexmedetomidine is a highly selective α_2 -adrenergic receptor agonist; it has anxiolytic, sedative, analgesic and sympatholytic properties without significant respiratory depressant effects [15,16]. Magnesium sulphate also appears effective at improving post-operative analgesia [17]. Magnesium has an antagonistic effect at the N-methyl-D-aspartate (NMDA) receptor [18], as well as calcium-channel blocker properties [19]. Antagonism at the NMDA receptor is thought to alter the mechanism of central hypersensitivity

and to subsequently decrease analgesic requirements including opioid consumption [20].

The aim of the present study was to compare the effect of IV infusion of Dexmedetomidine or Mg sulphate on patients undergoing laparoscopic bariatric surgery. The primary outcome was the recovery profile. The secondary outcomes were time for the first request of analgesia and the incidence of post-operative complications.

2. PATIENTS AND METHODS

This study was carried out at General Surgery Department, Tanta University Hospitals after approval from Ethical Committee and obtaining informed written consent.

The study included 75 patients who were scheduled for elective laparoscopic bariatric surgery from July 2019 to June 2020. The patient was allocated according to drugs used into 3 groups (25 patients each) by using computer generated software introduced into sealed closed envelopes. The infusion agents were prepared by the aid of anesthesia resident who didn't participate in the study and has no subsequent roles in it. all infusion pumps are colored coated and labeled. Group I (Control group): The patient in this group received 50 ml of normal saline over 10 minutes followed by continuous infusion. Group II (Dexmedetomidine group): The patient in this group received loading dose of dexmedetomidine (0.5ug/kg (LBW) (Precedex, Abbot Laboratories Inc.) diluted in 50 ml saline slow intravenous over 10 minutes before induction of anesthesia followed by continuous infusion at a rate of (0.4ug/ kg (LBW)/ h) after intubation and stopped 10 minutes before the end of surgery. Group III (Mg sulphate group): The patient in this group received loading dose of mg sulphate (50mg/kg (LBW) diluted in 50 ml saline slow intravenous over 10 minutes before induction of anesthesia followed by continuous infusion at a rate of (10mg/ kg (LBW)/ h) after

intubation and stopped 10 minutes before the end of surgery.

2.1 Inclusion Criteria

Patients aged 20-40 years with BMI 40-60 kg/m² ASA class II presented for laparoscopic bariatric surgery.

2.2 Exclusion Criteria

1. Patients refused to participate.
2. Known or suspected to have allergy to $\alpha 2$ -adrenergic agonist or sulfa drugs.
3. History of myocardial disease.
4. Clinically significant neurologic, renal, hepatic, or gastrointestinal diseases.
5. Opioid medication within 24 hours before the operation.

2.3 Statistical Analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences version 25. Shapiro-Wilks normality test and histograms were used to test the distribution of quantitative variables to select accordingly the type of statistical testing: parametric or nonparametric. Parametric variables (e.g. age) were expressed as mean and standard deviation (SD) and were compared using F test among the three groups with post hoc (LSD) test to compare each two groups. Comparison between two variables within the same group was compared by paired T test. Non- parametric variables (e.g. VAS) were expressed as median and interquartile range (IQR) and were analyzed using Kruskal-Wallis test; further analysis was performed by Mann-Whitney (U) test to compare each two groups. Comparison between two variables within the same group was compared by Wilcoxon test. Categorical variables (e.g. sex) were expressed as frequency and percentage and were statistically analyzed by Chi-square test.

P value ≤ 0.05 was considered statistically significant.

3. RESULTS

There was a significant decrease in heart rate, at T2 to T9, in group II and group III compared to group I (P1 <0.001, P2 = 0.009, <0.001, 0.002, <0.001, <0.001, <0.001, <0.001, and <0.001 respectively). There was no significant difference in in heart rate between group II and group III. Table 1.

There was a significant decrease in mean arterial blood pressure, at T2 to T9, in group II and group III compared to group I (P1 <0.001, P2 <0.001). There was no significant difference in mean arterial blood pressure between group II and group III Table 2.

VAS was significantly different among the three groups at Post-Anesthesia Care Unit (PACU), 2, 4 and 6 hours (P 0.010, <0.001, 0.018 and <0.001 respectively) and was insignificantly different among the three groups at other times of measurement as compared to PACU. At PACU, 2, 4 and 6 hours, VAS was decreased significantly in group II and group III compared to group I (P1 = 0.005, <0.001, 0.004 and <0.001 respectively, P2 = 0.029, 0.004, 0.044 and <0.001 respectively) and was insignificantly different between group II than group III. Table 3.

There was a negative increase in nausea and vomiting in group I than group II and group III (P = 0.023). Bradycardia, hypotension and postoperative hypoxemia were insignificantly different among the three groups (P = 0.069, 0.298 and 0.807 respectively). Table 4

4. DISCUSSION

The goal in anesthetic management of obese patients is to have proper anesthesia when needed, but a rapid emergence and resumption of adequate respiration and physiology very shortly after the end of the procedure. Anything done to minimize the need of postoperative opioids and minimize the risk of postoperative nausea and vomiting is very valuable. Therefore, this patient population could benefit from a drug that can produce analgesic effects without significant or long-lasting effects on respiratory function [21].

The effect of magnesium on hemodynamics due to interact in the activation of membrane Ca-ATPase and Na-K-ATPase is involved in trans membrane ion exchanges during depolarization and repolarization phases, thus acting as a cell membrane stabilizer and also as an intra cytoplasmic organelles stabilizer . This calcium inhibitory effect of Mg causes central arteriolar vasodilatation and acts against vasospasm. Another mechanism could involve the reduction of catecholamine release with sympathetic stimulation, thereby decreasing the stress response to surgery.

Table 1. Heart rate (beats/min) among the three groups

	Group I (n = 25)		Group II (n = 25)		Group III (n = 25)		P value	P1	P2	P3
	Mean	± SD	Mean	± SD	Mean	± SD				
T0	86.28	11.19	84.60	8.87	85.60	8.19	0.821	0.534	0.801	0.711
T1	86.72	10.04	82.36	9.36	83.40	8.53	0.232	0.103	0.212	0.695
T2	87.28	11.59	74.00	9.95	79.64	8.43	<0.001*	<0.001*	0.009*	0.052
T3	90.44	10.54	79.00	8.57	80.28	8.67	<0.001*	<0.001*	<0.001*	0.628
T4	89.00	13.66	71.44	13.89	77.60	10.46	<0.001*	<0.001*	0.002*	0.092
T5	86.20	9.48	67.00	13.95	69.32	12.86	<0.001*	<0.001*	<0.001*	0.505
T6	86.16	11.11	70.88	9.17	73.28	8.28	<0.001*	<0.001*	<0.001*	0.379
T7	88.76	9.63	72.40	7.98	74.64	7.92	<0.001*	<0.001*	<0.001*	0.357
T8	90.12	11.11	70.96	8.10	74.32	8.21	<0.001*	<0.001*	<0.001*	0.203
T9	91.16	9.42	71.44	7.14	74.60	8.55	<0.001*	<0.001*	<0.001*	0.189

T0: baseline, T1: before induction, T2: before intubation, T3: after intubation, T4: skin incision, T5: after 0.5h, T6: after 1h, T7: after 1.5h, T8: after 2h, T9: end, *significant change as P value <0.05, P1: P value between group I and group II, P2: P value between group I than group III, P3: P value between group II and group III

Table 2. Mean arterial blood pressure (mmHg) among the three groups

	Group I (n = 25)		Group II (n = 25)		Group III (n = 25)		P value	P1	P2	P3
	Mean	± SD	Mean	± SD	Mean	± SD				
T0	91.88	11.61	89.96	9.72	90.96	8.42	0.795	0.500	0.746	0.725
T1	92.60	9.35	88.80	8.63	89.60	8.68	0.287	0.135	0.237	0.751
T2	92.96	12.65	79.40	8.13	81.08	9.38	<0.001*	<0.001*	<0.001*	0.564
T3	95.88	10.94	83.08	8.62	84.96	9.61	<0.001*	<0.001*	<0.001*	0.498
T4	94.60	12.28	79.72	9.88	81.96	12.15	<0.001*	<0.001*	<0.001*	0.493
T5	90.64	12.13	73.40	9.44	76.04	11.09	<0.001*	<0.001*	<0.001*	0.397
T6	92.12	11.95	77.12	9.66	79.16	8.02	<0.001*	<0.001*	<0.001*	0.473
T7	94.68	9.94	78.48	7.74	79.64	8.34	<0.001*	<0.001*	<0.001*	0.640
T8	95.32	9.83	76.88	8.81	79.12	9.14	<0.001*	<0.001*	<0.001*	0.396
T9	97.68	9.93	77.44	7.87	79.88	8.33	<0.001*	<0.001*	<0.001*	0.328

T0: baseline, T1: before induction, T2: before intubation, T3: after intubation, T4: skin incision, T5: after 0.5h, T6: after 1h, T7: after 1.5h, T8: after 2h, T9: end, *significant change as P value <0.05, P1: P value between group I and group II, P2: P value between group I than group III, P3: P value between group II and group III

Table 3. Visual analogue scale (VAS) among the three groups

		PACU	2h	4h	6h	8h	10h	12h	18h	24h
		Group I (n = 25)	Median	2	3	4	4	4	4	3
	Range	3-5	3-4	3-5	2-4	2-5	3-5	2-4	3-5	3-5
Group II (n = 25)	Median	1	1	2	1	3	3	3	3	3
	Range	1-2	1-2	1-4	1-2	2-4	3-4	2-4	3-5	2-4
Group III (n = 25)	Median	1	2	2	1	4	3	4	4	3
	Range	2-4	2-4	2-5	2-3	2-5	3-5	2-5	3-4	2-4
P value		0.010*	<0.001*	0.018*	<0.001*	0.207	0.338	0.743	0.930	0.148
P1		0.005*	<0.001*	0.004*	<0.001*	0.297	0.196	0.665	0.864	0.062
P2		0.029*	0.004*	0.044*	<0.001*	0.393	0.214	0.637	0.841	0.148
P3		0.375	0.447	0.478	0.720	0.090	0.880	0.483	0.702	0.740

Table 4. Complications in the three groups

	Group I (n = 25)	Group II (n = 25)	Group III (n = 25)	P value
Nausea and vomiting	9 (36%)	2 (8%)	3 (12%)	0.023*
Bradycardia	1 (4%)	7 (28%)	4 (16%)	0.069
Hypotension	2 (8%)	6 (24%)	5 (20%)	0.298
Postoperative hypoxemia	2 (8%)	1 (4%)	2 (8%)	0.807

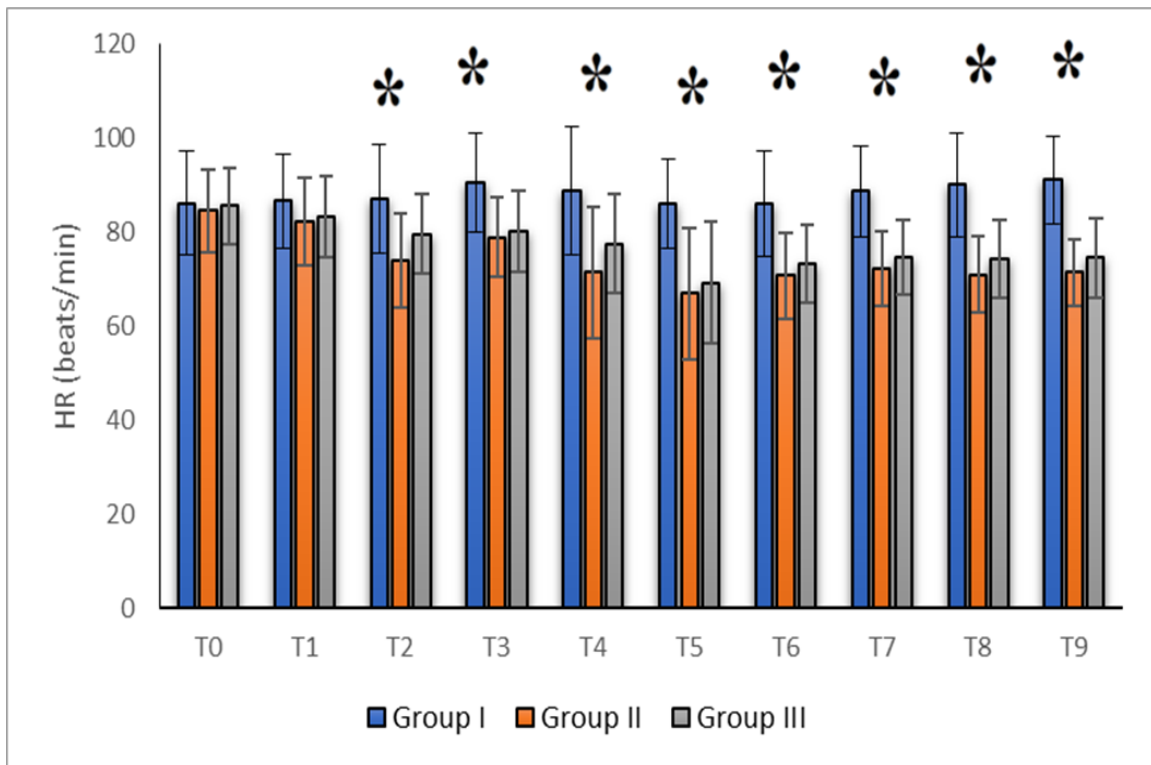


Fig. 1. Heart rate among the three groups
*denotes a significant change among the three groups

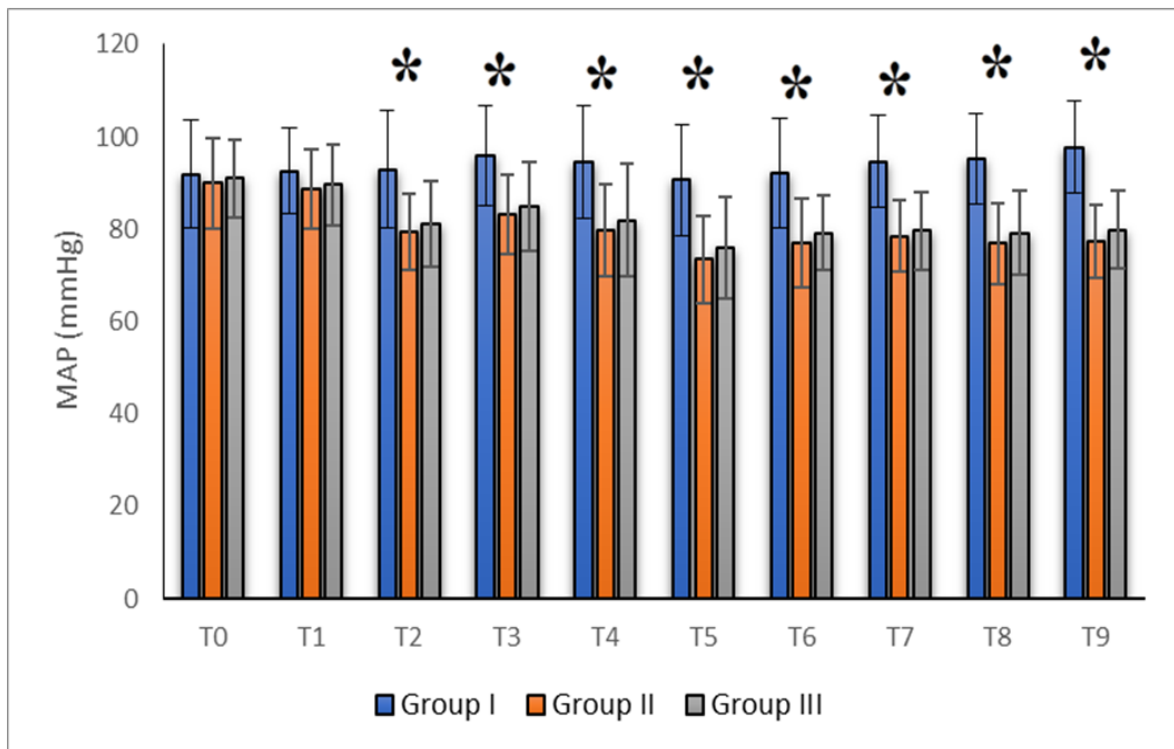


Fig. 2. Mean arterial blood pressure among the three groups
*denotes a significant change among the three groups

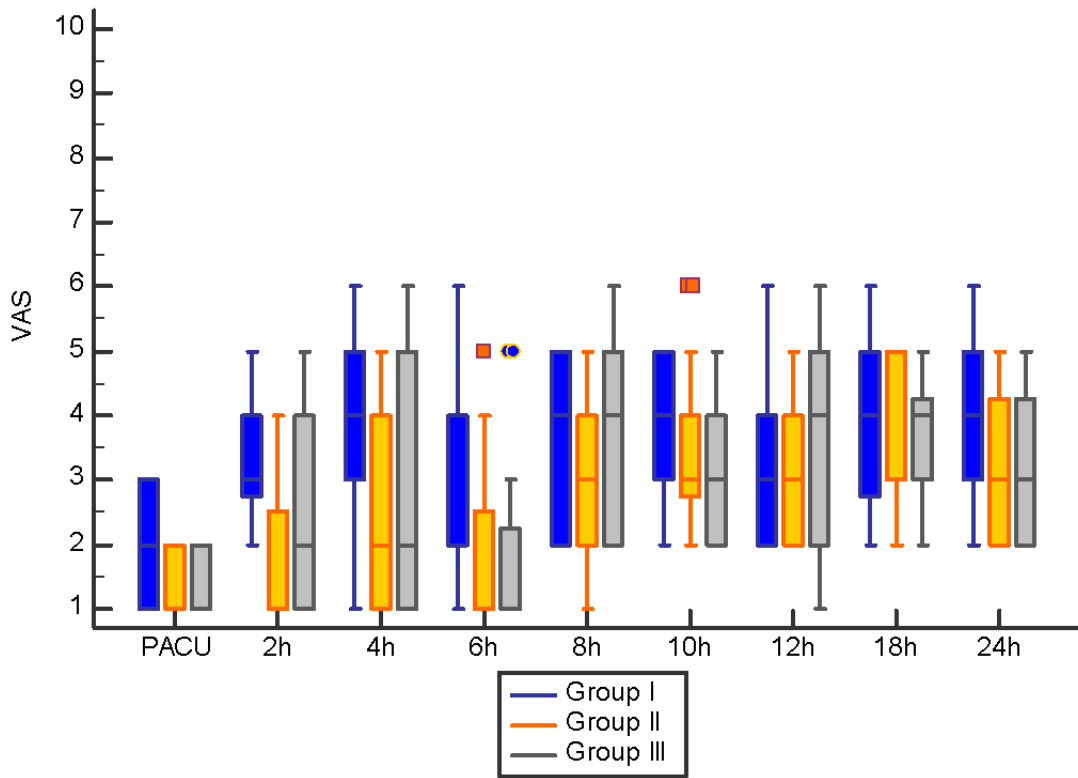


Fig. 3. Visual analogue scale (VAS) among the three groups

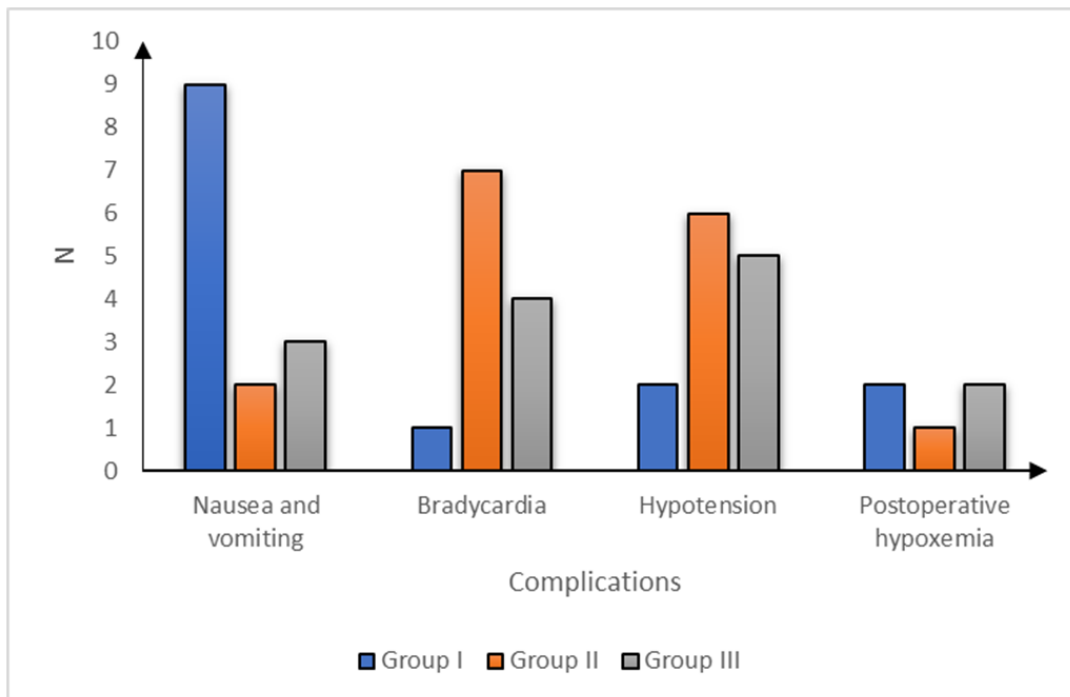


Fig. 4. Complications in the three groups

In agreement with the present study, Bakhamees et al. [22] in their study on eighty adult patients scheduled for elective laparoscopic Roux-en-Y gastric bypass surgery evaluated the effect of

dexmedetomidine versus placebo on hemodynamic profile. They found that heart rate and mean arterial blood pressure were decreased in dexmedetomidine group when compared with placebo.

Moreover, Tufanogullari et al. [23] evaluated the effect of Dexmedetomidine on morbidly obese patients where they were randomly assigned to 1 of 4 treatment groups: Dexmedetomidine infusion rates of 0.2, 0.4, 0.8 ug / kg / h IV group and control group who received a saline infusion during surgery. patients assigned to the control group required more frequent use of antihypertensive rescue medication and the high dose Dexmedetomidine group required greater use of cardiovascular medication to treat hypertensive episodes during surgery.

Also, a study by Jee et al. [24] the reported that after administration of a bolus of 50 mg/kg of magnesium sulphate before pneumoperitoneum in patients undergoing laparoscopic cholecystectomy, systolic and diastolic arterial blood pressures were significantly higher in the control group than in the magnesium group at 10 min, and 30 min post pneumoperitoneum

In controversy to this study, Kiran et al. [25] the patients undergoing inguinal surgery were randomized to receive either magnesium sulphate 50 mg/kg in 250 ml of saline solution IV (*Group I*) or same volume of saline (*Group II*). They found that Comparison of hemodynamic parameters during study medication and intraoperative period between *group I* and *group II* at different time intervals was statistically insignificant.

Against the current study, Salman et al. [26] In this study 60patients 20-40years old ASA I-II patients undergoing gynecologic laparoscopic surgery were randomized into 2 groups .The remifentanyl group (group R) and dexmedetomidine group (group D) received a bolus of 1 ug/kg over 10minutes, followed by 0.2 ug/kg/minute preoperative infusion of remifentanyl ,and 0.4 ug/kg/hour of dexmedetomidine. This study demonstrated that dexmedetomidine infusion causes similar hemodynamics compared to remifentanyl in ambulatory laparoscopic surgeries..

As regard to anesthetic requirements, dexmedetomidine and magnesium sulphate decreased the total intraoperative fentanyl dose, intraoperative cis-atracurium dose and isoflurane consumption as compared to control group .

It could be explained that α_2 -adrenergic mechanisms are involved in the modulation of nociception at the level of spinal noradrenergic systems. There is clear evidence that α_2 -adrenoceptors are located on the dorsal horn neurons of the spinal cord and might release endogenous opiate compounds. Thus, the α_2 -adrenoceptor agonists may offer interesting new possibilities in the treatment of pain and may help to reduce intraoperative opioids requirements [27]

It is well known that magnesium sulphate inhibits acetylcholine release at motor nerve terminals, thus potentiating the effect of neuromuscular blocking agents. [28] Although magnesium has mild sedative effects and this help to decrease intraoperative anesthetic requirements.

Also, Albrecht et al. [29] in the first systematic review of the literature and meta-analysis to assess the analgesic effect of perioperative intravenous magnesium administration, suggested that peri-operative magnesium can provide a clinically important reduction in opioid consumption.

Also, Levaux et al. [30] in their prospective, randomized study, demonstrated a significant decrease in opioid consumption in patients who received 50 mg/kg magnesium sulphate during the pre-operative periods.

Moreover, Le Guen et al. [31] in their study on 66 patients where they compared between dexmedetomidine or comparable volumes of saline as a placebo to determine the extent to which dexmedetomidine reduced the requirement of propofol and remifentanyl. They found that patients given dexmedetomidine required significantly less propofol and remifentanyl for anesthetic induction.

In addition, Bakhamees et al. [32] Eighty adult patients scheduled for elective laparoscopic Roux-en-Y gastric bypass surgery were randomly assigned to one of two study groups; Group D (40 patients) received dexmedetomidine (0.8- μ g/kg bolus, 0,4 μ g \cdot kg $^{-1}$ \cdot h $^{-1}$) and Group P (40 patients) received normal saline (placebo) in the same volume and rate. Intraoperative and postoperative mean blood pressure and heart rate were recorded. The total amount of intraoperative fentanyl and propofol required to maintain anesthesia were measured. ReThey found that the intraoperative infusion of

dexmedetomidine decreased the total amount of propofol and fentanyl required to maintain anesthesia.

Also, Ryu et al. [33] According to this study, eighty-four patients undergoing elective laparoscopic gastrectomy were randomized to receive iso-tonic saline (group C) or magnesium sulfate (group M, loading dose with 50 mg/kg over 10 min and then 15 mg/kg/h by continuous infusion) to maintain the moderate neuromuscular blockade using rocuronium. Two experienced surgeons scored the quality of surgical space condition using a 5-point surgical rating scale (SRS). The secondary outcomes included recovery profiles, postoperative pain and adverse events. They concluded that Intraoperative administration of magnesium sulfate improved the quality of surgical space conditions and decreased neuromuscular blocking agent requirement.

As regard the recovery profile, dexmedetomidine and magnesium sulphate significantly decreased the time to spontaneous eye opening, the time of orientation and the time to tracheal extubation as compared control group. This may be explained by the decrease in fentanyl and isoflurane consumption.

Also, Ryu et al. [33] showed that there were no differences between iso-tonic saline (group C) and magnesium sulfate (group M) according to recovery profile in patients undergoing laparoscopic gastrectomy.

As regards to the postoperative analgesia, dexmedetomidine and magnesium sulphate prolonged the time to first analgesic request and decreased the consumption of morphine as rescue analgesia significantly in comparison to the control group.

The initial request for analgesia was significantly delayed in patients who delivered dexmedetomidine, the most obvious explanation for prolonged analgesia, as suggested by Arain et al. [34] that dexmedetomidine has a half-life of approximately 2 hours and thus remained pharmacologically active well after the infusion was terminated at the end of anesthesia.

Also, Albrecht et al. [29] found that cumulative intravenous morphine consumption was reduced by an average of 24.4% in favor of the magnesium group.

In agreement with our study, Kizilcik et al. [35] In this study eighty patients undergoing sleeve

gastrectomy. Patients were randomly assigned to one of two equal groups (magnesium sulfate group [group M] versus normal saline one [group C]). Two syringes of magnesium sulfate which contain 30 and 20 mg/kg in 50 ml of isotonic saline solutions were prepared by the pharmacy department and given to the investigator blinded to the study groups. The magnesium group received 30 mg/kg of iv (intravenous) bolus dose of magnesium sulfate 30 min before the induction of general anesthesia, whereas patients in control group received only 50 ml of isotonic saline solution at the same period. It was found that Perioperative use of magnesium sulfate reduced postoperative pain and opioid consumption in obese patients undergoing sleeve gastrectomy operations.

Moreover, Shamim et al. [36] in this study 60 patients were systematically randomized into two groups of 30 each. Patients were kept NPO 8 hours prior and given Tablet Alprazolam 0.25mg and Omeprazole 20 mg at bed time day before surgery and morning of surgery. Group1 received magnesium sulphate 50 mg/kg in 250 ml of isotonic 0.9%N.S intravenously over 15 to 20 minutes in the preoperative room and Group II ,Same volume of isotonic 0.9%N.S iv. over 15 to 20 minutes ,before shifting the patient immediately afterwards to the operation room. They concluded that magnesium sulphate produce adequate postoperative pain relief associated with laparoscopic cholecystectomy.

In addition, Hofer et al. [37] conducted their study to describe the anesthetic management of a patient with extreme obesity undergoing bariatric surgery whose intraoperative narcotic management was entirely substituted with dexmedetomidine. The narcotic sparing effects of dexmedetomidine were evident both intraoperatively (low isoflurane requirements) and postoperatively (lower total dose of self-administered PCA morphine).

However against the current study, McQueen-Shadfar et al. [38] assessed the impact of intraoperative dexmedetomidine infusion on postoperative analgesia in women undergoing major open and laparoscopic gynecologic surgery under general anesthesia. a total of 580 women included in the analysis, (293 open surgery (103 dexmedetomidine, 190 controls) and 287 laparoscopic surgery (101 dexmedetomidine, 186 controls). In women undergoing laparoscopic surgery, there was no opioid sparing effect intraoperatively or in PACU.

This study used dexmedetomidine in a different method from our study as they used infusion rate in the range of 0.2- 0.7 mic/kg/hr without bolus dose and was started 19 min after induction of anesthesia and stopped 23 min before end of surgery.

In controversy to this study Bhatia et al. [39] found that administration of magnesium 50 mg/kg in the pre-operative and 15 mg/ kg/h in the per-operative periods to patients undergoing open cholecystectomy did not significantly decrease the requirement of morphine during the first 24 h of the post-operative period. Also, they found that the cumulative intra- and post-operative need for morphine was similar in the magnesium and the control groups.

As regards VAS at PACU, VAS was decreased significantly in dexmedetomidine and magnesium sulphate groups compared to control group.

The present study was also supported by Jeon et al. [40] who found that Cumulative analgesic consumption and pain scores were also lower during the entire postoperative period.

According to adverse events, there was no statistically significant difference in adverse events between dexmedetomidine and magnesium groups. The incidence of post operative nausea and vomiting was higher in control group than other 2 groups .It could be explained by higher consumption of opioids in control group.

In agreement with our study, Salman et al. [41] compared dexmedetomidine with remifentanyl in desflurane based ambulatory gynecologic laparoscopic surgery, in respect to its effects on orientation, discharge time, nausea-vomiting and postoperative analgesic need on sixty patients allocated to either the remifentanyl group and dexmedetomidine group, they reported that postoperative nausea, vomiting, and analgesic requirements were less in dexmedetomidine group compared to remifentanyl in ambulatory laparoscopic surgeries. It may be an alternative to remifentanyl in ambulatory anesthesia.

CONCLUSIONS

The current study recommends using dexmedetomidine and magnesium infusions in bariatric surgery. Further studies are recommended to evaluate the effect of Dexmedetomidine infusion in dose of 0.2 mic/

kg/hr instead of 0.5 mic/kg/hr to avoid incidence of hypotension and bradycardia. Also, further studies using dexmedetomidine and magnesium with maintenance dose without loading one are recommended.

CONSENT

This study was carried out at General Surgery Department, Tanta University Hospitals after approval from Ethical Committee and obtaining informed written consent.

ETHICAL APPROVAL

The study has been approved by the Institutional ethical committee at Faculty of Medicine, Tanta University with approval number (33161/05/19)

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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