Intra Peritoneal Instillation of Bupivacaine or Bupivacaine plus Magnesium Sulphate or Bupivacaine plus Dexamethasone on Post-Operative Pain after Laparoscopic Cholecystectomy: A Randomized Controlled Study

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ABSTRACT

Background: Laparoscopic cholecystectomy as opposed to open cholecystectomy is currently the most accepted surgical technique for cholelithiasis. Intraperitoneal administration of some drugs can be effective for pain relief after laparoscopic surgery. Intraperitoneal instillation of local anesthetics and opioids is gaining popularity for better pain relief.

Objectives: To compare the effect of adding dexamethasone or magnesium sulphate to bupivacaine on quality and duration of analgesia after intra-peritoneal instillation after laparoscopic cholecystectomy.

Patients and methods: Our prospective study was conducted on sixty patients with ASA physical status I or II. Their ages ranged between 18-60 years scheduled for laparoscopic cholecystectomy under general anesthesia in Menoufia University Hospitals. Patients were randomly divided into three groups, 20 patients each. Patients in group B (bupivacaine group): received 25 ml 0.25% bupivacaine. Group M (Magnesium sulphate group) received 20 ml 0.25% bupivacaine and 5 ml (500 mg) magnesium sulphate. Group D (Dexamethasone group) received 20 ml 0.25% bupivacaine and 2 ml (8mg) dexamethasone completed to 25 ml with 3 ml normal saline.

Results: First time of analgesia was significantly longer among magnesium group than dexamethasone group and bupivacaine group ($p < 0.05$). Nalbuphine consumption in 24 hrs, was higher among bupivacaine group followed by dexamethasone group then magnesium group ($p < 0.05$). Also, VAS score was significantly higher in bupivacaine group at 4 hour than other groups and, at 6-hour it was higher in dexamethasone group and bupivacaine group with no significant difference but highly significantly more than magnesium. In magnesium group VAS score was low over 24 hours.

Conclusion: Our study found that magnesium sulphate is a good additive than dexamethasone when combined with bupivacaine in intra-peritoneal instillation as it prolonged the duration of analgesia and reduced postoperative pain scores and nalbuphine consumption after laparoscopic cholecystectomy.

Keywords: Laparoscopic cholecystectomy, Intra-peritoneal instillation, Bupivacaine, Magnesium sulphate, Dexamethasone.

INTRODUCTION

Laparoscopic cholecystectomy as opposed to open cholecystectomy is currently the most accepted surgical technique for cholelithiasis [(1)]. Laparoscopic procedures have many advantages over open procedures such as lesser hemorrhage, better cosmetic results, lesser post-operative pain, and shorter recovery time, leading to shorter hospital stay and less expenditure [(2)].

There is a significant difference in the quality of pain related to laparoscopic surgery as compared to laparotomy. The pain after laparotomy is mostly parietal whereas it is more of visceral pain following laparoscopic cholecystectomy [(3)]. Characteristically, the pain following laparoscopic cholecystectomy is highly variable in intensity and duration and is largely unpredictable [(4)]. Pain results from stretching of the intra-abdominal cavity [(5)], peritoneal inflammation, and diaphragmatic irritation caused by residual carbon-dioxide in the peritoneal cavity [(6)]. Many methods have been proposed to relieve post-operative pain following laparoscopic cholecystectomy [(7)]. Intra-peritoneal administration of some drugs can be effective for pain relief after laparoscopic surgery. Intra-peritoneal instillation of local anesthetics and opioids is gaining popularity for better pain relief [(8)].

The local anesthetic agents provide anti-nociception by affecting nerve membrane-associated proteins and by inhibiting the release and action of prostaglandins, which stimulate the nociceptors and cause inflammation [(9)]. Absorption from a large peritoneal surface may be the mechanism of analgesia [(10)]. Magnesium inhibits calcium entry into the cell through a noncompetitive blockade of the N-methyl-d aspartate (NMDA) receptor [(11)]. Magnesium is also a physiological calcium antagonist at different voltage-gated channels [(12)]. Administration of magnesium sulfate ($MgSO_4$) through different routes has been used in anesthetic practice for decreasing perioperative pain. $MgSO_4$ also has been used to attenuate the adverse hemodynamic changes associated with pneumoperitoneum and improve the quality of recovery [(13)].

Steroid injection produces a degree of vasoconstriction, so one theory suggests that the drug acts by reducing local anesthetic absorption. Another theory tells that dexamethasone potentiates the activity of inhibitory potassium channels on nociceptive C-

Received:4 /5 /2021
Accepted:30 /6 /2021

fibers (via glucocorticoid receptors), thereby decreasing their activity [14].

AIM OF THE WORK

The primary outcome to determine the first time to request analgesia after intra-peritoneal instillation of bupivacaine or bupivacaine plus magnesium sulphate or bupivacaine plus dexamethasone on post-operative pain after laparoscopic cholecystectomy, and to assess post-operative pain with VAS score, analgesic consumption, incidence of complications and to measure hemodynamic changes.

PATIENTS AND METHODS

60 healthy patients of ASA I & II scheduled for laparoscopic cholecystectomy of both sexes were enrolled in this study and were randomly divided into three equal groups (20 patients each) to receive bupivacaine (group B), bupivacaine plus $MgSO_4$ (group M), and bupivacaine plus Dexamethasone (group D). They were aged between 18 and 60 years.

Exclusion criteria: Patients with disturbed conscious level, hemodynamic instability, impaired renal or hepatic function, allergy to any of the drugs used in the study, acute cholecystitis, patients with severe cardiac, respiratory, and neurological diseases, those in whom procedure was converted to open cholecystectomy and in whom abdominal drain was put.

Randomization of patients was made by computer-generated program into three equal parallel groups (20 patients each). Group B received 25 ml 0.25% bupivacaine. Group M received 20 ml 0.25% bupivacaine and 5 ml (500 mg) magnesium sulphate. Group D (20 patients) received 20 ml 0.25% bupivacaine and 2 ml (8 mg) dexamethasone completed to 25 ml with 3 ml normal saline**.**

Pre-operative detailed history, general physical examination and relevant systemic examination of all the patients was done following all standard protocols and precautions. Routine investigations such as CBC, urine analysis, liver function tests, serum electrolytes, random blood sugar, and electrocardiogram were performed and analyzed in detail prior to procedure following all standard precautions and protocols required. Before operation, the patients were instructed to use a 10 cm visual analogue score (VAS) (endpoints labeled 'no pain' and 'worst possible pain'). Incisional pain was defined as superficial pain in the abdominal wall, or wound pain. Intra-abdominal pain was defined as deep, dull, and difficult to localize pain inside the abdomen, or resembling biliary colic. Shoulder pain was defined as pain in the shoulder.

On arrival at operation room (OR), routine intraoperative monitoring (ECG, noninvasive blood pressure, pulse oximetry, and capnography were established. General anesthesia was induced with intravenous fentanyl (1-2 μg/kg), propofol (2.0 mg/kg) and atracurium (0.5 mg/kg), then orotracheal intubation. Patients were maintained with 50% O_2 and 50% air, 0.5-1 vol% isoflurane 1 MAC, and 0.1 mg/kg atracurium time scheduled for maintenance of muscle relaxation. Minute ventilation was adjusted to keep end-tidal PCO_2 at 35-45 mmHg. After anesthesia induction, pneumoperitoneum was created by insufflation of CO_2 to maintain intra-abdominal pressure between 12 and 15 mmHg through the surgical procedure.

At the end of the surgery, residual neuromuscular blockade was reversed with neostigmine 0.05 mg/kg and atropine 0.01 mg/kg intravenously after return of protective reflexes. Studied drugs were prepared by an anesthesiologist not involved in the study. Anesthesiologist who observed the patient and surgeon was unaware of the study group until the end of the study. At the end of the surgery, the study solution was given intraperitoneally before removal of trocar in Trendelenberg's position, into the hepatodiaphragmatic space, on gall bladder bed and near and above hepatoduodenal ligament. After completion of the surgical procedure patients were transferred to the postanesthetic care unit (PACU). After achieving an Aldrete score of 9 or higher, patients were discharged from the PACU to an intermediate care unit for 24 h.

All patients stayed in PACU for 2 h after the end of surgery. The intensity of post-operative pain was recorded for all the patients using VAS score at 0.5, 1, 2, 4, 6, 12 and 24 h after surgery and over all VAS score (mean of all VAS scores), (VAS score 0 - no pain, VAS score 10 - worst possible pain). Patients who reported VAS ≥ 3 were given nalbuphine (4 mg) intravenously as rescue analgesia. Patients were also be observed for post-operative nausea and vomiting. Patients who suffered nausea or vomiting were given ondansetron 4 mg IV. Time to the first request of analgesia (considering the extubation as time 0), VAS score, total dose of analgesia, adverse or side effects and hemodynamic changes over 24 h postoperatively were noted.

Sample size calculation, based on the results of pervious study **Maharjan *et al.*** [15], the mean difference for time of 1st analgesic (hours) between the magnesium sulphate group and bupivacaine group was 2.47 hrs. The sample size was calculated at power 90% and CI 95% and it was 20 subjects per group. With a withdrawal/ non-evaluable subject rate of 10% a total 22 per group subjects were recruited. An equal number was recruited for bupivacaine plus dexamethasone as there was no study combined the three groups together.

Ethical approval:

An approval of the study was obtained from Menoufia University academic and ethical committee. Every patient signed an informed written consent for acceptance of the operation. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Statistical analysis

The collected data were coded, processed and analyzed using the SPSS (Statistical Package for Social Sciences) version 22 for Windows® (IBM SPSS Inc, Chicago, IL, USA). Data were tested for normal distribution using the Shapiro Walk test. Qualitative data were represented as frequencies and relative percentages. Chi square test (χ^2) to calculate difference between two or more groups of qualitative variables. Quantitative data were expressed as mean ± SD (Standard deviation). Independent samples t-test was used to compare between two independent groups of normally distributed variables (parametric data). P value ≤ 0.05 was considered significant.

RESULTS

Demographic data of patients (age, sex and ASA classification) were comparable between both groups (table 1).

As regards first time of analgesia, it was significantly longer among magnesium group than other groups [(211.75 ± 60.0 min for bupivacaine group, 293.50 ± 79.32 min for dexamethasone group and 525.75 ± 145.5min for magnesium group, p < 0.05)]. Nalbuphine consumption in 24 hrs was significantly higher among bupivacaine (marcaine) group, followed by dexamethasone group than magnesium group, (p < 0.05) (table 2).

As regards postoperative visual analogue scale, at 0.5, 1 and 2 hours VAS was comparable between both groups but the difference was non-significant. At 4-hours, VAS showed higher values in marcaine group than magnesium and dexamethasone groups and the difference between them was significant (P < 0.001). At 6-hour postoperative, VAS showed significantly higher values in marcaine group than magnesium group (P < 0.05). Also, lower in marcaine than dexamethasone but the difference was non-significant (P = 0.056). At 12 and 24 hours, VAS showed significantly higher values in marcaine group than the other groups (P < 0.05) (table 3).

Intraoperative MAP was comparable between studied groups as shown in table (4). As regards heart rate, it was non-significant between the studied groups at 0.5, 1 and 2 hours postoperative (P > 0.05). At 4-hour postoperative, heart rate showed higher values in marcaine group than other groups but the difference was non-significant (P < 0.001). At 6-hour postoperative, heart rate showed significantly higher values in marcaine group than magnesium group (P = 0.005). Also, heart rate showed lower values in marcaine than dexamethasone but the difference was non-significant (P = 0.064). At 12 and 24 hours, VAS showed higher values in marcaine group than in the other groups (P < 0.001) (table 5).

Table (1): Comparison between the studied groups according to demographic characteristics

Variables	Marcaine (n=20)		Magnesium (n=20)		Dexamethasone (n=20)		Test of sig	P value	Post hoc test
Age Mean ± SD Range	44.65±9.38 28-59		43.60±8.41 27-57		44.15±8.12 27-58		F=0.07	0.929	P1: 0.703 P2: 0.856 P3: 0.841
	N	**%**	**N**	**%**	**N**	**%**			
Gender Male Female	5 15	25 75	6 14	30 70	7 13	35 65	**χ2**=0.47	0.788	-
ASA I II	11 9	55 45	13 7	65 35	12 8	60 40	**χ2**=0.41	0.812	-

ASA: American Society of Anesthesiologists, **SD:** stander deviation, **F:** ANOVA test **X2 test:** Chi-square test, *: significant **P1:** comparison Marcaine vs. Magnesium, **P2:** comparison Marcaine vs. Dexamethasone, **P3:** comparison Magnesium vs. Dexamethasone.

Table (2): Comparison between the studied groups according to first time of analgesia and nalbuphine consumption

Variables	Marcaine (n=20) Mean ± SD	Magnesium (n=20) Mean ± SD	Dexamethasone (n=20) Mean ± SD	Test of sig	P value	Post hoc test
First time of analgesia	211.75 ± 60.05	525.75 ± 145.55	293.50 ± 79.32	F = 51.22	< 0.001*	P1,3: <0.001* P2: 0.014*
Nalbuphine consumption in 24 hrs.	10.80 ± 5.52	3.80 ± 4.58	7.60 ± 3.87	F = 11.08	< 0.001*	P1: <0.001* P2: 0.036* P3: 0.014*

SD: stander deviation, **F:** ANOVA test, *: significant, **P1:** comparison Marcaine vs. Magnesium, **P2:** comparison Marcaine vs. Dexamethasone, **P3:** comparison Magnesium vs. Dexamethasone

Table (3): Comparison between the studied groups according to VAS score

VAS score	Marcaine (N=20) Mean ± SD	Magnesium (N=20) Mean ± SD	Dexamethasone (N=20) Mean ± SD	F	P value	Post hoc test
0.5 h	0.75±0.28	0.5±0.22	0.58±0.06	1.495	0.067	P1: 0.077 P2: 0.083 P3: 0.15
1 h	1.3±0.58	0.5±0.22	0.65±0.75	1.431	0.068	P1: 0.067 P2: 0.072 P3:250
2 h	1.50±1.00	0.6±0.41	0.78±0.85	1.829	0.55	P1: 0.053 P2: 0.490 P3:062
4 h	4.60±1.05	0.63±0.42	0.80±1.39	47.005	<0.001**	P1,2: <0.001* P3: 0.350
6 h	2.11±1.60	0.65±0.69	2.35±1.53	65.989	<0.001**	P1,3: <0.001* P2: 0.056
12 h	5.90±0.72	1.00±0.72	4.20±1.64	99.389	<0.001**	P1,3: <0.001* P2: 0.037*
24 h	6.50±0.69	1.55±0.69	5.00±1.12	175.076	<0.001**	P1,3: <0.001* P2: 0.024*

VAS: visual analogue scale, **SD:** stander deviation, **F:** ANOVA test, *: significant, **P1:** comparison Marcaine vs. Magnesium, **P2:** comparison Marcaine vs. Dexamethasone, **P3:** comparison Magnesium vs. Dexamethasone

Table (4): Comparison between the studied groups according to (Mean Arterial Pressure)

Variables		Marcaine (n=20) Mean ± SD	Magnesium (n=20) Mean ± SD	Dexamethasone (n=20) Mean ± SD	F	P value	Post hoc test
MAP	**0.5 h**	85.65±5.66	85.55±7.07	84.40±6.34	0.237	0.790	P1: 0.961 P2: 0.538 P3: 0.571
	1 h	84.05±5.66	84.85±6.88	83.90±6.26	0.132	0.877	P1: 0.689 P2: 0.940 P3: 0.635
	2 h	85.35±6.67	84.75±7.04	84.55±6.22	0.078	0.925	P1: 0.776 P2: 0.705 P3: 0.925
	4 h	86.65±5.76	85.60±6.77	85.45±5.92	0.225	0.799	P1: 0.592 P2: 0.541 P3: 0.939
	6 h	87.65±4.75	85.90±6.63	86.40±5.82	0.485	0.618	P1: 0.343 P2: 0.497 P3: 0.786
	12 h	90.00±5.38	86.05±6.88	88.15±5.63	2.170	0.123	P1: 0.042 P2: 0.334 P3: 0.273
	24 h	91.10±4.86	86.20±7.01	89.80±5.51	2.043	0.094	P1: 0.540 P2: 0.486 P3: 0.057

MAP: mean arterial pressure, **SD:** stander deviation, **F:** ANOVA test**,** *: significant, **P1:** comparison Marcaine vs. Magnesium, **P2:** comparison Marcaine vs. Dexamethasone, **P3:** comparison Magnesium vs. Dexamethasone

Table (5): Comparison between the studied groups according to heart rate (HR)

Variables		Marcaine (n=20) Mean ± SD	Magnesium (n=20) Mean ± SD	Dexamethasone (n=20) Mean ± SD	F	P value	Post hoc test
HR	**0.5 h**	67.80±4.57	67.80±3.12	69.90±3.37	2.099	0.132	P1: 1.00 P2: 0.081 P3: 0.081
	1 h	69.05±4.19	68.15±2.62	70.65±3.82	2.470	0.094	P1: 0.433 P2: 0.166 P3: 0.320
	2 h	70.20±4.59	68.05±2.37	70.85±4.53	1.720	0.485	P1: 0.140 P2: 0.981 P3: 0.120
	4 h	76.45±4.38	68.30±2.97	71.20±5.06	9.644	<0.001*	P1:<0.001* P2:0.042* P3:0.073
	6 h	73.40±4.17	68.50±2.44	75.15±5.45	19.887	<0.001*	P1: 0.005* P2: 0.064 **P3:** <0.001*
	12 h	80.50±3.90	69.20±2.65	78.20±5.63	39.649	<0.001*	P1,3: <0.001* P2: 0.092
	24 h	83.20 ± 4.02	68.90 ± 2.69	80.75 ± 4.97	72.888	< 0.001*	P1,3: <0.001* P2: 0.058

HR: heart rate, **SD:** stander deviation **F:** ANOVA test**, *:** significant **P1:** comparison Marcaine vs. Magnesium, **P2:** comparison Marcaine vs. Dexamethasone **P3:** comparison Magnesium vs. Dexamethasone

DISCUSSION

Different techniques have been implemented to decrease postoperative pain following laparoscopic cholecystectomy. Intra-peritoneal instillation of bupivacaine with or without adjuvants is one of popular modalities used to prevent post-operative pain. Various drugs are used in combination with local anesthetics to help reduce onset of effect, prolong the duration of action and to increase the chance of successful blockade. Toward these ends, a number of studies have been conducted with varying results [(16)]**.** Many adjuvants like epinephrine, clonidine, opioids, ketamine and midazolam were combined with local anesthetics to prolong the duration of analgesia. However, the glucocorticoid (dexamethasone) has been shown to be effective in a small number of preclinical and clinical studies [(17)]**.** Magnesium (Mg), the fourth most abundant cation in the body and the second most abundant intracellular cation, considered as a physiological blocker of N-Methyl-D-aspartate (NMDA) receptors. Magnesium (Mg) has anti nociceptive effects due to its antagonistic effect of NMDA receptors [(18)]**.**

Our study aimed to compare dexamethasone versus magnesium sulphate as additive to bupivacaine in intraperitoneal instillation on pain management after laparoscopic cholecystectomy. Sixty patients with ASA physical status I- II, aged from 18-60 years were included in the study and randomly divided into 3 groups, twenty patients for each group. Group B [bupivacaine (marcaine) group as control group], group M (bupivacaine plus magnesium) and group D (bupivacaine plus dexamethasone). Our primary outcome measure was duration of analgesia starting from local anesthetic injection till the first call for analgesia, which was longer in Mg group. Secondary measures were post-operative hemodynamics, postoperative VAS, postoperative nalbuphine consumption in the first 24 hours and postoperative complications. Age, ASA status and gender were comparable between both groups. As regards duration of analgesia, it was prolonged in dexamethasone group than bupivacaine group and in magnesium group than other two groups. As regards first call for analgesia, it was at 211.75 ± 60.0 min for bupivacaine group, 293.50 ± 79.32 min for dexamethasone group and 525.75 ± 145.5 min for magnesium group. Postoperative nalbuphine consumption was significantly lower in magnesium group. All patients in control group and nearly in dexamethasone group received nalbuphine as analgesic in postoperative 24 hours while half of patients only needed nalbuphine in magnesium group.

As regards VAS score we found that it was significantly higher in bupivacaine group at 4 hours than in dexamethasone and magnesium groups and most of patients called for analgesia. At 6-hours we found that it was higher in dexa group and bupivacaine group with non-significant difference but highly significantly more

than magnesium and most of patients required analgesia. In magnesium group, VAS score was low over 24 hours. Supporting our results are the results of **Shelly *et al.*** [19] where their study was conducted on sixty-five women belonging to American Society of Anesthesiologists physical status 1 or 2, aged between 35 and 70 years, scheduled for total abdominal hysterectomy under subarachnoid block. Patients in group B (n = 32) received 18 mL 0.25% bupivacaine (45 mg) with 2 ml normal saline (NS), whereas those in group B & M (n = 33) received 18 mL 0.25% bupivacaine (45 mg) with 1.5 mL (150 mg) $MgSO_4$ and 0.5 mL NS in the ultrasound (USG)-guided TAP block performed on each side after the completion of the surgery under SAB. They reported that addition of $MgSO_4$ to bupivacaine in a dose of 150 mg led to lower VAS pain scores, prolongation of analgesia and less requirement of rescue analgesia. **Mahrajan** [15] in a study on 60 patients of (ASA) physical status I and II of 18-65 years undergoing laparoscopic surgery in the abdomen were randomly divided into two groups of 30 each to be administered one of the following intraperitoneal instillations: "bupivacaine group" received 30 ml of 0.25% bupivacaine not exceeding the dose 2.0 mg/kg and "magnesium sulphate group" 0.25% bupivacaine 30 ml along with 50 mg/kg of magnesium sulphate. They found that the combined instillation of bupivacaine and magnesium sulphate into the peritoneal cavity at the end of laparoscopic surgery rendered patients to be better in pain control and less consumption of analgesics in first 24 hours compared to sole bupivacaine group.

Al-Refaey *et al.* [20] mentioned in their study, on ninety patients of ASA I and II who were planned for transversus abdominis plane block after laparoscopic cholecystectomy. They were divided into three groups: Control group, bupivacaine group and bupivacaine plus magnesium group. They reported that Adding $MgSO_4$ as an adjuvant to bupivacaine in TAP block during anesthesia for laparoscopic cholecystectomy improved postoperative analgesia in the form of increased duration, decreased analgesic requirements and PONV. **Haghighi *et al.*** [21] in a randomized double blind study about the effect of magnesium sulfate on sensory and `motor axillary plexus blockade. They concluded that addition of magnesium sulfate to lidocaine increased the duration of motor and sensory axillary block in the upper extremities during surgeries when compared to the use of lidocaine alone. **Also, Abd-Elsalam *et al.*** [22] concluded in a randomized, double-blinded clinical trial included 60 women undergoing total abdominal hysterectomy who were divided into 2 groups (30 patients per group). Group I received a TAP block with 20 ml per side of 0.25% bupivacaine plus 2 ml magnesium sulphate 10% (200 mg). Group II received a TAP block with 20 ml per side of 0.25% bupivacaine. They found that the mean total morphine consumption over the first 24 hours postoperatively was significantly lower in group I (7.63 ± 2.93 mg) than in group II (16.20 ± 3.24 mg) ($P < 0.001$). Another study done by **Dogru *et al.*** [23] on adding magnesium to levobupivacaine for axillary brachial plexus block in AV fistula surgery. They found that motor and sensory block onset times were statistically decreased in group with magnesium sulphate. **Bondok and Abd El-Hady** [24] studied the effect of intra-articular magnesium in knee arthroscopy, and showed that magnesium resulted in a significant decrease in the postoperative VAS in the first 24 h, which became less significant thereafter. In addition, there was significant decrease in the dose of postoperative rescue analgesia with a longer delay in the need for that analgesia, concluding that intra-articular magnesium could be a useful alternative for postoperative analgesia. **Starvani *et al.*** [25] found that intraperitoneal injection of hydrocortisone in combination with bupivacaine before gas insufflation in laparoscopic cholecystectomy can reduce postoperative pain better than bupivacaine alone. **Paramaswamy *et al.*** [26] conducted a study on 120 patients with isolated hand and forearm injuries who were divided into three equal groups. Ultrasound guided axillary brachial plexus block was performed in patients in group C with 30 mL of 0.375% bupivacaine plus 2 mL of normal saline, group D with 30 mL of 0.375% bupivacaine plus 8 mg dexamethasone and group K with 30 mL of 0.375% bupivacaine plus 30 mg ketorolac. They found that dexamethasone and ketorolac as adjuvant to bupivacaine in axillary plexus blocks significantly prolonged analgesia and duration of motor and sensory block. These effects were more enhanced with dexamethasone than ketorolac. Additionally, **Naghipour *et al.*** [27] conducted a study on seventy two adult patients scheduled for elective abdominal or thoracic surgery under epidural anesthesia. They were randomly allocated into two groups to receive either bupivacaine (0.5%) - fentanyl (50 μg) and dexamethasone (8 mg) in lumbar or thoracic epidural anesthesia or bupivacaine-fentanyl and normal saline via epidural catheter. This study revealed that dexamethasone added to bupivacaine-fentanyl solution in epidural analgesia prolonged the duration of analgesia in abdominal or thoracic surgery.

Regarding effect of magnesium over dexamethasone, **Gaballah *et al.*** [28] conducted a trial on patients who were included to undergo laparoscopic unilateral ovarian cystectomy to assess the efficacy of intraperitoneal different combinations for postoperative pain relief. they found that intraperitoneal bupivacaine-magnesium combination provides better analgesia and reduces postoperative morphine consumption than bupivacaine-hydrocortisone or magnesium-hydrocortisone combinations. Against our result, **Mahgoub** [29] compared the duration of postoperative analgesia after adding either magnesium sulfate or dexamethasone to levobupivacaine for performing supraclavicular brachial plexus block for upper-limb surgeries. They found that no significant differences were observed between group D (dexamethasone was

added to levobupivacaine) and group M (which was given magnesium sulfate along with levobupivacaine) with respect to blood pressure and heart rate. Also, **Hamed *et al.* [30]** stated in their study that when dexamethasone and magnesium sulfate were added to bupivacaine in ultrasound guided supraclavicular plexus block, both of them proved to prolong the duration of block and the analgesia time, both of them fasten the sensory block onset time, but dexamethasone was significantly more effective in prolonging the analgesia duration and the block duration. Dexamethasone shortens the motor block onset time while magnesium does not enhance the motor block onset time.

As regards postoperative complications, no significant differences were observed between the groups, nearly same number of patients among groups experienced nausea or vomiting.

As regards hemodynamics, MAP measurements were comparable between the groups and there was no significant difference. HR was comparable among groups with no difference at 0.5, 1 and 2 hours. At 4- hours, there was higher in marcaine group than in the other two groups. At 6-hours, it was higher in dexamethasone and marcaine groups than in magnesium group but the difference between them was non-significant. Finally, there was a lack in the studies that previously used dexamethasone and magnesium as adjuvant to local anesthetics in intraperitoneal injection but our results correlated with studies where dexamethasone or magnesium was used separately or in other peripheral nerve blocks.

CONCLUSION

Magnesium sulphate is a good additive than dexamethasone when combined with bupivacaine in intraperitoneal instillation after laparoscopic cholecystectomy as it prolonged the duration of analgesia and reduced postoperative pain scores and nalbuphine consumption.

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