Egyptian Journal of Anaesthesia 33 (2017) 357–363

HOSTED BY

Contents lists available at ScienceDirect

Egyptian Journal of Anaesthesia

journal homepage: www.sciencedirect.com

Research article

Evaluation of analgesia by epidural magnesium sulphate versus fentanyl as adjuvant to levobupivacaine in geriatric spine surgeries. Randomized controlled study

Tarek Radwan, Mohamed Awad, Rania Fahmy *, Mohamed El Emady, Mohamed Arafa

Intensive Care Medicine and Pain Management, Faculty of Medicine, Cairo University, Kasr Al Ainy St., Cairo 11562, Egypt

1. Introduction

Aging is known to result in diminished functional reserve across organ systems which when combined with age related diseases limit the patient's ability to tolerate perioperative stress. Inadequate intra and postoperative analgesia add to the increased risk of respiratory, cardiovascular and cognitive complications encountered in geriatric population making perioperative care challenging [1].

Epidural anesthesia has been considered as an effective treatment of operative pain as it blunts endocrinal, autonomic and somatic responses which may be highly beneficial in perioperative care of elderly population [2].

A number of opioid and non opioid adjuvants have been introduced over the years to improve neuraxial analgesia, nevertheless researchers continue aiming at finding superior adjuvants with less side effects. Adjuvants include Opioids, GABA agonists, adrenergic agonists, NMDA antagonists, COX-inhibitors and Ach-esterase inhibitor [3,4].

Levobupivacaine, the pure S(−) enantiomer of racemic bupivacaine was found to be a safer substitute to bupivacaine in epidural anesthesia. It is less cardiotoxic and neurotoxic in comparison to bupivacaine with the advantage of a better ratio of sensory to motor blockade [5].

Opioids like fentanyl as adjuvants to epidural anesthesia result in superior analgesia though there is an increased risk of pruritus, urinary retention, nausea, vomiting and respiratory depression [6].

Magnesium, a divalent cation, posses antinociceptive action through noncompetitive blockade of the NMDA receptor resulting in calcium antagonism. It has been used in different doses as adjuvant and by several routes as intravenous, epidural and intrathecal [7].

We hypothesized that adding magnesium sulphate to epidural levobupivacaine provides better pain control and prolongs analgesia than using levobupivacaine alone, moreover it isn't inferior if not superior to the combination of epidural levobupivacaine and fentanyl in elderly patients undergoing lumbar spine surgeries.

The current study aims at assessment of the efficiency of magnesium sulphate as an analgesic adjuvant to levobupivacaine in elderly patients undergoing lumbar spine surgeries and whether its analgesic effect is superior to either levobupivacaine alone or the combination of levobupivacaine and fentanyl.

2. Materials and methods

After obtaining informed written consents and approval of the ethical committee of the anesthesia department; 66 patients scheduled for single level lumbar spine discectomy and laminectomy in neurosurgical theatre were blindly randomized into three groups and subjected to a comparative study. Randomization was achieved using computer software (research randomizer.org) concealment of numbers was guaranteed using closed envelopes.

2.1. Patients selection

2.1.1. Inclusion criteria

Patients were above 65 years old, both males and females, ASA physical status I and II with optimized blood pressure not exceeding 140/90 and well controlled diabetes as evidenced by HbA1c < 7%, no cognitive dysfunctions, no abnormalities in hepatic or renal functions and ±20% of mean ideal body weight for age (BMI index for elderly is optimum between 23 and 29.9 kg/m^2) [8]. All patients were operated upon while assuming the prone position.

2.1.2. Exclusion criteria

Patients suffering from scoliosis or kyphosis, having hematological disease, bleeding or coagulation abnormalities, as well as patients with history of adverse reaction to any of the study medication, chronic pain syndrome, communication difficulties preventing reliable assessment, accidental dural puncture, failure of epidural block and surgical procedures taking more than three hours were excluded from the study.

Peer review under responsibility of Egyptian Society of Anesthesiologists.

* Corresponding author.

E-mail addresses: dtradwan@yahoo.com (T. Radwan), walidawad2003@yahoo.com (M. Awad), ransam98@gmail.com (R. Fahmy), mohamed.farid@hotmail.com (M. El Emady), dr.3arafa1@gmail.com (M. Arafa).

http://dx.doi.org/10.1016/j.egja.2017.07.003

2.2. Preoperative preparation

Before the operation, visual analogue scale (VAS) for pain was the chosen method for assessment of pain and all patients were instructed how to respond to the scale.

In the preparation room, after cannulation with an 18 gauge venous cannula, all patients were given 10 ml/kg Ringer's acetate solution as a preload.

Patients were monitored with non-invasive blood pressure, pulse oximetry and ECG. Capnogram was added after induction of anesthesia.

2.3. Placement of epidural needle

Placement of epidural catheter was achieved in sitting position two levels above the level of surgery using the loss of resistance technique.

A 20 gauge multi-orifice epidural catheter was then inserted 4 cm into the epidural space in a cephalic direction. 3 ml lidocaine 2% added to 1:200,000 epinephrine (0005 mg/ml) was injected through the catheter to exclude both subarachnoid and intravascular placement respectively.

2.4. Activating the epidural

Five minutes later; patients were randomized to one of three groups; group A received 14 ml levobupivacaine 0.5% + 1 ml saline, group B received 14 ml levobupivacaine 0.5% + 50 mg magnesium sulphate in 1 ml saline and group C received 14 ml levobupivacaine 0.5% + 50 microgram fentanyl. Infusions were prepared by a clinical pharmacist not included in data collection and the attending anesthetist was blinded to the type of solution injected.

Sensory block was assessed by using analgesia to pin prick. Motor blockade was evaluated by using modified Bromage scale (0: no motor block; 1: inability to raise extended legs; 2: inability to flex knees; 3: inability to flex ankle joints) [9].

2.5. Induction and maintenance of general anesthesia

After establishment of motor and sensory blockade, anesthesia was induced using 2 mg/kg propofol, 1.5 μg/kg fentanyl, intubation was facilitated by atracurium 0.5 mg/kg to provide muscular relaxation.

Afterwards, atracurium was infused at a rate of 0.5 mg/kg/h to maintain muscle relaxation, while isoflurane between (1–1.5%) endtidal was used to maintain hypnosis.

Patients were operated upon while assuming the prone position which was checked and secured avoiding eye & nose compression, nerve stretching, kinking of the tube & respiratory embarrassment.

Subsequently continuous epidural infusion was initiated: Group A received levobupivacaine 0.125%, group B received levobupivacaine 0.125% + 2 mg/ml magnesium sulphate and group c received levobupivacaine 0.125% + 4 μg/ml fentanyl. Drugs were prepared in 20 cc syringe and the rate of infusion in each group was 5 ml/h.

2.6. Recovery

Atracurium infusion stopped at the start of closure of the deep fascia; after resuming the supine position, all anesthetics were discontinued and epidural infusion was stopped. After tracheal extubation and removal of epidural catheter patients were transferred to the recovery room where all hemodynamic parameters were monitored.

One gram of iv paracetamol was given to the patients when VAS > 3 and every 8 h thereafter. A second rescue analgesic in the form of 50 mg iv meperidine was given to patients if VAS remained > 3 one hour after iv paracetamol.

2.7. Data collected

1. Peri and intraoperative hemodynamics in the form of HR (heart rate) and MAP (mean arterial pressure): baseline, 20 min after epidural activation, every 15 min after start of the surgery and till skin closure, once reaching recovery room and every hour for six hours.
2. Time taken to achieve complete sensory and motor block.
3. Post-operative assessment of pain every hour for six hours using the Visual Analogue Scale where 0 = no pain and 10 = worst possible pain [10].
4. Number of patients requiring iv paracetamol in each group.
5. Number of patients requiring iv meperidine in each group.
6. Post operative assessment of sedation using modified Ramsay scale (Grade 1: Patient is anxious and agitated or restless, 2: Patient is co-operative, oriented, and tranquil, 3: Patient responds to commands only, 4: Patient exhibits brisk response to light glabellar tap or loud auditory stimulus, 5: Patient exhibits a sluggish response to light glabellar tap or loud auditory stimulus, 6: Patient exhibits no response). Assessment was done every 30 min for three hours [11].
7. Number of patients suffering from postoperative nausea, vomiting, itching and urine retention.

2.8. Study outcomes

2.8.1. Primary outcome

MAP six hours after recovery between groups.

2.8.2. Secondary outcomes

Peri and intraoperative hemodynamics, onset of sensory and motor blocks, VAS for six hours postoperative, the incidence of patients requiring postoperative analgesia in each group throughout the six hours after recovery, Ramsay sedation score for three hours postoperative and the incidence of patients suffering from side effects such as nausea, vomiting, itching and urine retention.

2.9. Sample size

Power calculation revealed that 66 patients, equally distributed into three groups (22 per group) will be needed in order to have 80% power to detect a large effect size ($f = 0.4$) regarding the primary outcome, which was MAP six hours after recovery between groups and assuming $\alpha = 0.05$. Sample size calculation was done using G*Power 3 for Windows.

2.10. Statistical analysis

Data were coded and entered using the statistical package SPSS (Statistical Package for the Social Science) version 23. Ordinal data was analyzed using Friedman test and Kruskal-Wallis test within the same group and in between the three different groups respectively. Nominal data was analyzed between the different groups using Chi-squared or Fisher's exact test. Parametric data was analyzed using repeated measure ANOVA within each group and using one way ANOVA between the three different groups. A P value < 0.05 was considered statistically significant.

3. Results

While 72 patients qualified for the study only 66 completed the study and were randomized among the three groups. Dropouts

were as follows: 3 refused to participate in the study, 2 were excluded due to accidental dural puncture and 1 was excluded due to failure of epidural block.

There were no statistically significant differences in demographic data between the three groups as regards patients' age and sex.

When considering haemodynamics:

- There was no statistically significant difference in Heart rate (HR) between the three groups in baseline readings, as well as 20 min after activation of epidural.
  After induction of general anesthesia, statistically significant differences were observed between the three groups at the following times, at skin incision and every 15 min for two and half hours afterwards, where HR was less in both groups B and C than group A, e.g.: at skin incision (group A 69.45 ± 5.27, group B 61.09 ± 5.49, group C 60.82 ± 6.23, P < 0.001); at 150 min after skin incision (group A 69.40 ± 3.78, group B 56.00 ± 2.65, group C 60.50 ± 13.44, P 0.045).
  Postoperatively after discontinuing the drugs, statistically significant differences were still observed between the three groups in all readings (p < 0.05) where HR was lower in groups B and C than group A (Fig. 1).
- There was no statistically significant difference in mean arterial pressure (MAP) between the three groups in baseline readings however after activation of the epidural statistically significant differences were observed, at 20 min, at skin incision, at 15 and 30 min surgical time where MAP in group C was slightly higher than groups A and B, e.g.: at skin incision (group A 80.41 ± 6.27, group B 82.95 ± 4.89, group C 86.41 ± 5.53, P 0.003), afterwards MAP became comparable between the three groups throughout the operation and till recovery of the patients.
  Postoperatively statistically significant differences were observed between the three groups at the fifth and sixth hours where MAP was lower in groups B and C than group A, at the fifth hour (group A 85.05 ± 3.79, group B 74.36 ± 2.95, group C 75.77 ± 3.22, P value < 0.001), and at the sixth hour (group A 91.95 ± 3.11, group B 75.59 ± 2.82, group C 76.23 ± 3.15, P value < 0.001) (Fig. 2).

As regards sensory and motor blocks there were statistically significant differences between the three groups (p < 0.001), both were faster in group B in comparison to groups A and C as shown in Table 1.

Pain assessment using VAS showed no statistically significant difference between the three groups in the first and second hours postoperative.

Starting from the third hour statistical significant differences were observed between the three groups (p value < 0.05), VAS was higher in group A than in groups B and C though none of the patients required analgesia.

In the fifth and sixth postoperative hours VAS was significantly higher in group A than in groups B and C, VAS in fifth hour (group A 3.86 ± 1.08, group B 2.36 ± 0.49, group C 2.64 ± 0.73, P value < 0.001), VAS in sixth hour (group A 5.27 ± 1.28, group B 3.09 ± 0.43, group C 3.18 ± 0.66, P value < 0.001) (Fig. 3). Moreover, 20 (90.91%) patients in Group A required analgesia in the form of 1 g iv paracetamol in comparison to 1 (4.55%) patient in group B and 2 (9.09%) patients in group C, this finding was statistically significant and the p value was < 0.00001. Besides, 10 (45.45%) of the 20 patients in group A required a second rescue analgesic in the form of 50 mg iv meperidine in comparison to none in group B and 1 (4.55%) in group C, this finding was statistically significant and the p value was 0.00008 (Fig. 4).

Assessment of post operative sedation was done for all patients 30 min after extubation and every 30 min for three hours using Ramsay sedation score and no statistically significant differences were detected between the three groups in all readings (Fig. 5).

Though there were no statistically significant differences between groups as regards nausea, vomiting, itching and urine retention, two patient suffered from post operative nausea and vomiting in both groups A and C and two patients suffered from

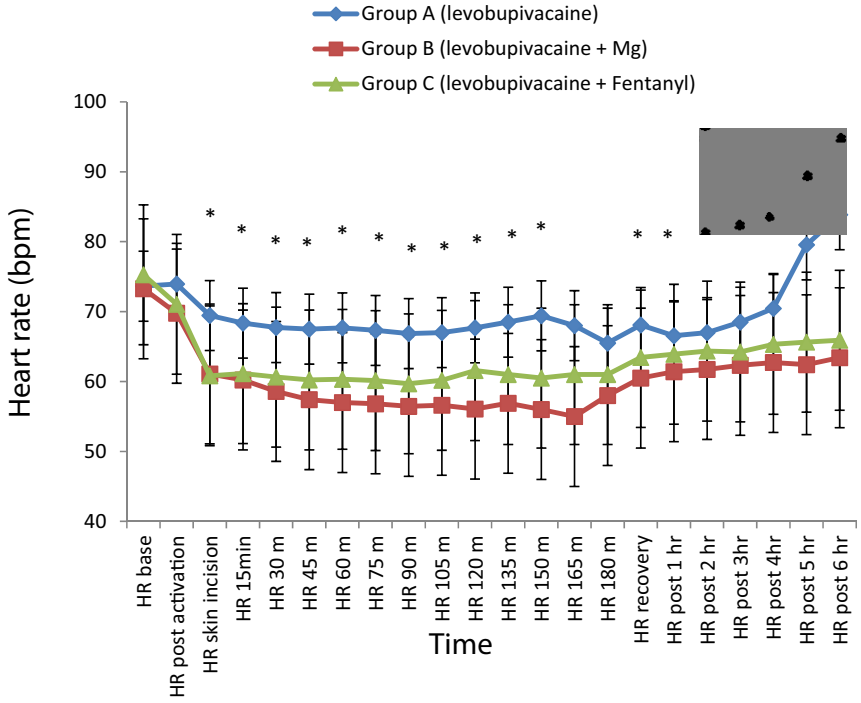

Fig. 1. Comparison between the three groups as regards HR. * denotes statistically significant difference between the 3 groups (p-value < 0.05).

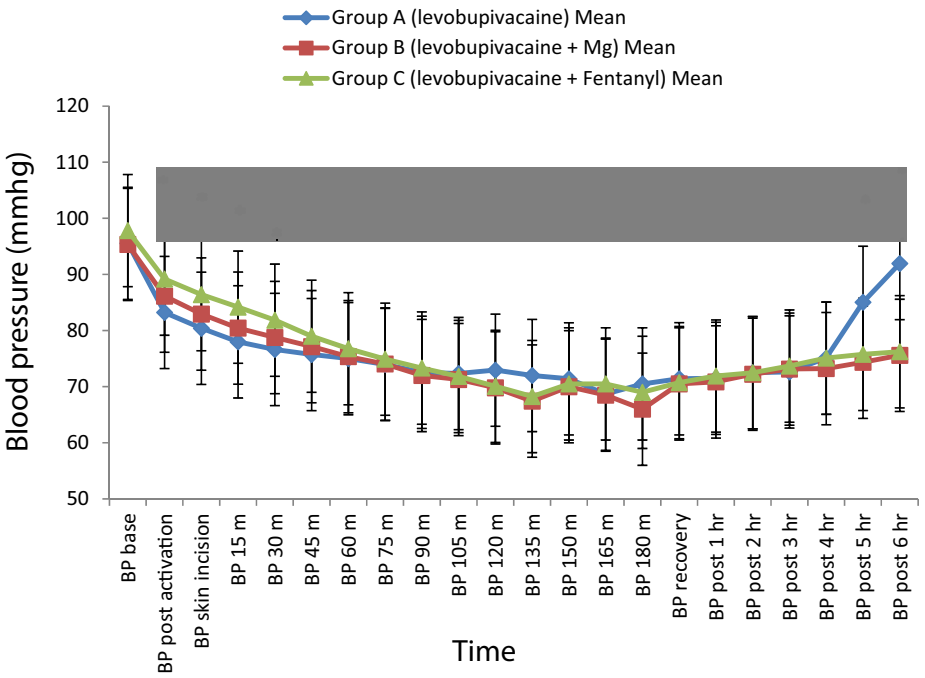

Fig. 2. Comparison between the three groups as regards mean arterial blood pressure. * denotes statistically significant difference between the 3 groups (p-value < 0.05).

Table 1
Motor and sensory block.

	Group A (levobupivacaine)	Group B (levobupivacaine + Mg**)	Group C (levobupivacaine + Fentanyl)	P value
Motor block (min)	19.27 ± 1.67	13.18 ± 1.33*	19.32 ± 1.70	<0.001*
Sensory block (min)	17.32 ± 1.39	11.09 ± 0.92*	17.32 ± 1.36	<0.001*

Data are expressed as mean ± SD.
* Denotes statistically significant difference between the 3 groups (p-value < 0.05).

itching in group C, while no one suffered from urine retention in the three groups (Fig. 6).

4. Discussion

Several studies suggest that inadequate analgesia in the elderly contributes to prolonged hospital stay, increased complications, frequent readmissions and poor patient outcomes [12].

The present study was designed in elderly patients undergoing single level lumbar discectomy and laminectomy surgery under general anesthesia to assess the analgesic effect of the co administered epidural magnesium sulphate added to levobupivacaine when compared to either fentanyl added to levobupivacaine or levobupivacaine alone.

The study showed that hemodynamic variables were mostly better in the 2 groups receiving magnesium and fentanyl as adjuvants to levobupivacaine in comparison to the group receiving just levobupivacaine specially as regards the heart rate. Moreover, in the postoperative period, MAP was significantly lower at fifth and sixth hours in the two groups receiving magnesium and fentanyl as adjuvants in comparison to the group receiving just levobupivacaine.

Besides, the onset of both sensory and motor blocks was significantly faster in the group receiving magnesium and levobupivacaine in comparison to the other two groups.

Postoperative pain control was better achieved in the 2 groups receiving magnesium and fentanyl, as evidenced by a significantly lower VAS as well as a significantly lower number of patients requiring either a first or a second rescue analgesic. Those findings were well noticed throughout the fifth and sixth postoperative hours.

Several studies have evaluated the efficacy of epidural magnesium sulphate as adjuvant to local anesthetics with positive outcomes. To our knowledge, this is the first study designed to assess its efficacy exclusively in elderly and only few studies evaluated its efficacy when added to levobupivacaine.

In the course of comparing epidural to IV analgesia in elderly, Mann C et al. conducted a randomized comparative study on seventy patients aged >70 years undergoing major abdominal Surgery, one group received combined general and epidural anesthesia followed by PCEA in the form of a mixture of bupivacaine and sufentanil, the other group received general anesthesia followed by PCA in the form of intravenous morphine. They found that Pain control was superior in the PCEA group. Regarding the incidence of delirium, it was comparable in both groups, but it improved starting on the fourth postoperative day in the PCEA group. They concluded that epidural route provides superior pain relief and improves mental status in comparison to the intravenous route. The results match the idea of the current study that epidural analgesia is effective and at the same time safe in elderly population [13].

Elderly patients were included in a study done by Bilir et al. in patients subjected to total hip replacement under regional anesthesia, the study showed that postoperative epidural magnesium sulphate given as 50 mg bolus followed by 100 mg/day infusion for 24 h in comparison to epidural saline resulted in significantly lower VAS in the first hour of postoperative period, as well as

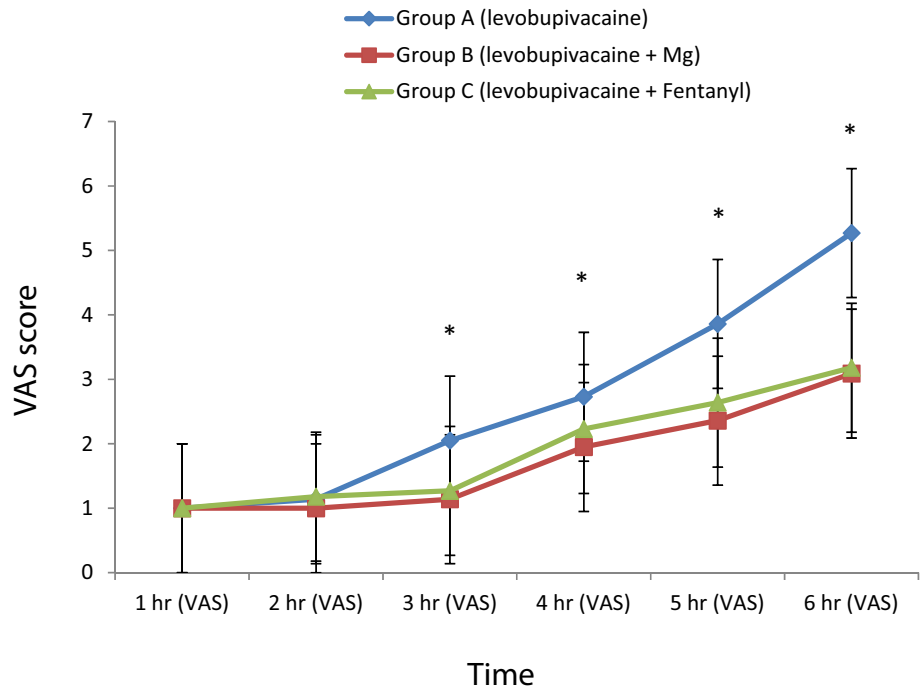

Fig. 3. Comparison between the three groups as regards post operative pain using visual analogue scale (VAS). * denotes statistically significant difference between the 3 groups (p-value < 0.05).

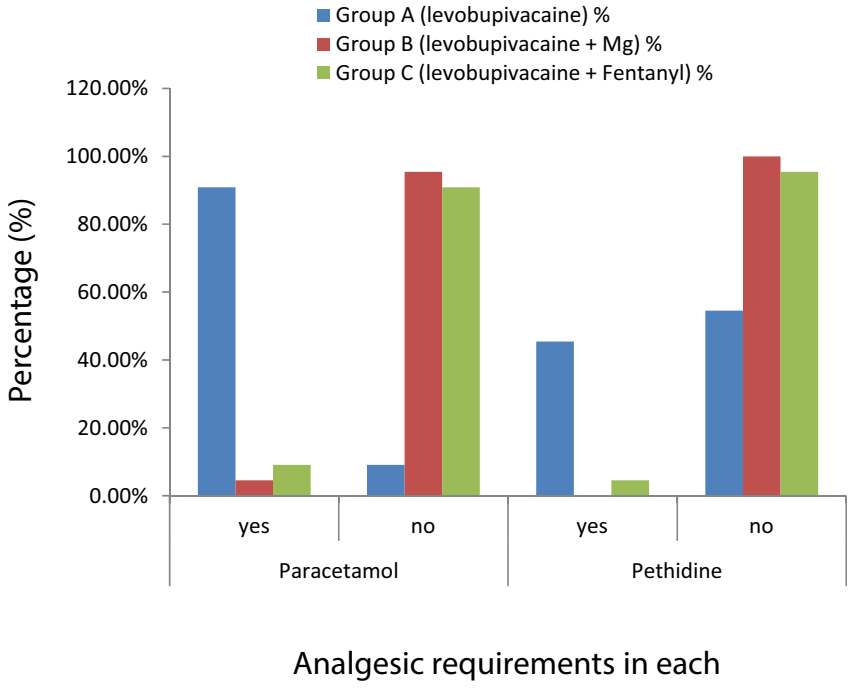

Fig. 4. Comparison between the three groups as regards paracetamol and pethidine requirements in the six hours following recovery.

reduced epidural fentanyl consumption in 24 h postoperatively. The results goes with the current study in that co administration of magnesium to epidural infusion improves postoperative analgesia and decrease analgesic requirements without side effects, though it differs in the time of administration and the co administered drugs [14].

The onset of sensory and motor blocks after adding magnesium sulphate to epidural anesthesia was studied by Ghatak et al. on 90 patients aged 18–60 years undergoing lower abdominal and lower limb surgeries. Patients received epidural bupivacaine with either 50 mg magnesium or 150 μg clonidine, whereas in control group patients received epidural bupivacaine with saline. The onset of

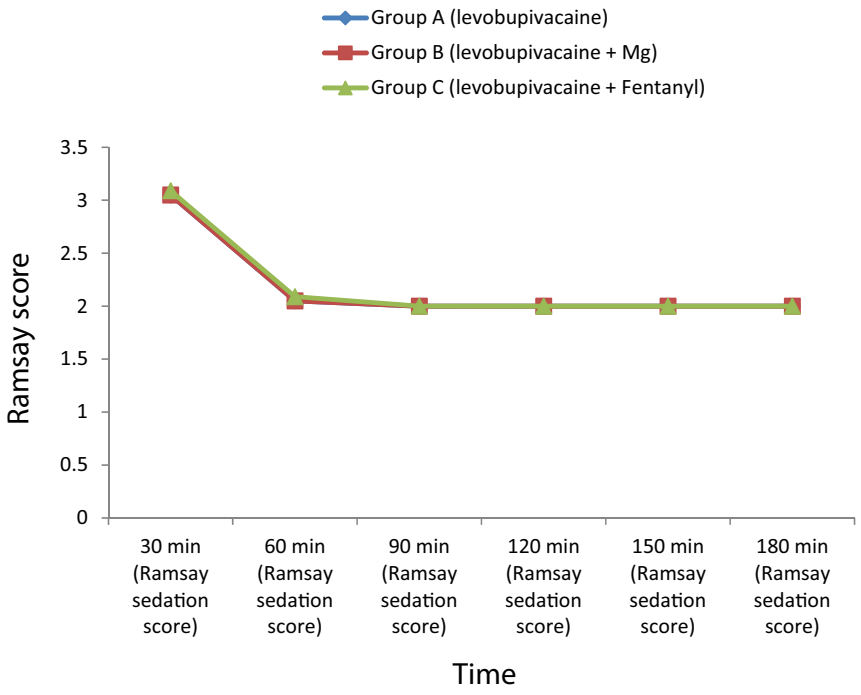

Fig. 5. Comparison between the three groups as regards post operative sedation using (Ramsay sedation score).

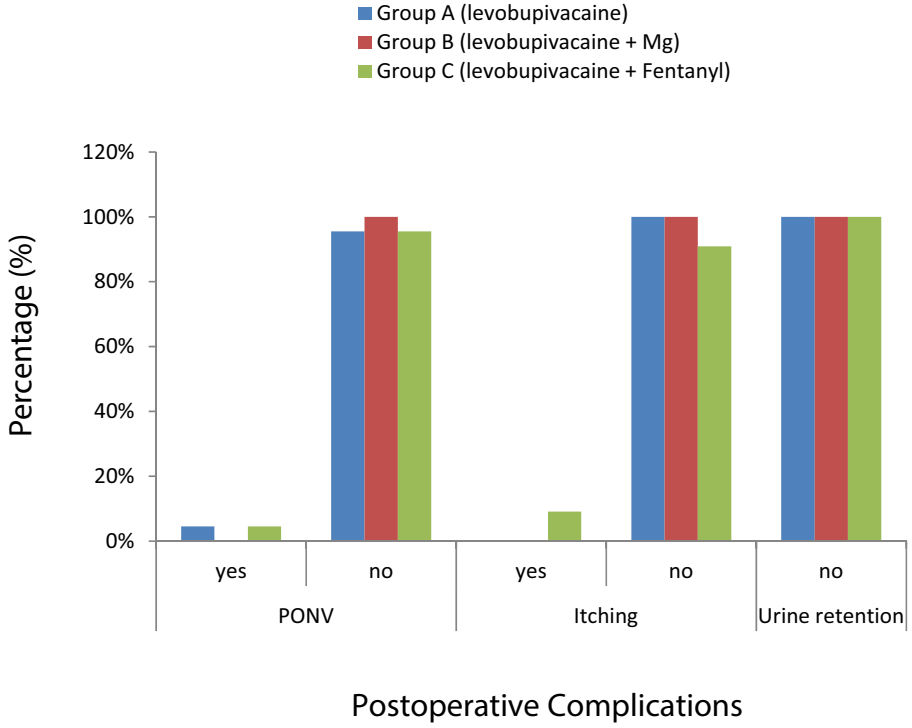

Fig. 6. Comparison between the three groups as regards post operative nausea, vomiting, itching and urine retention.

sensory and motor blocks was faster in the magnesium group, while the duration of anesthesia was longer in the clonidine group followed by the magnesium group and then the control group. Sedation was higher in the clonidine group and VAS was lower than in other groups but there was increased incidence of shivering. The groups were similar in respect to hemodynamic variables, nausea and vomiting. Although the difference in co administered drugs the results match those of the current study in that magnesium showed rapid onset of motor and sensory blocks in comparison to fentanyl and levobupivacaine [2].

The effect of adding a single dose of epidural magnesium sulphate on the duration of either intraoperative or postoperative

analgesia was tested in several studies. One of the studies was conducted by Banwait et al. in sixty patients aged between 18 and 65 years undergoing hip replacement surgeries by means of combined spinal–epidural anesthesia. At the end of the surgery, patients were randomized into two groups, either receiving epidural fentanyl 1 μg/kg or epidural magnesium 75 mg with fentanyl 1 μg/kg, if Verbal Rating Score (VRS) > 4 supplementary 50 mg intravenous tramadol were given. The duration of analgesia was superior (P 0.001) and the rescue analgesic requirements were significantly less (P 0.001) in the group receiving epidural magnesium [7]. Besides, in another study done by Hasanein et al. found that a single dose of magnesium sulphate 50 mg added to epidural bupivacaine 0.125% and fentanyl 50 μg in labor significantly fastened the onset and prolonged the duration of epidural analgesia, moreover there was a significant decrease in the number of women requiring additional boluses of bupivacaine (P 0.016) [15]. Moreover, the results of a study done by Gupta et al. in patients undergoing lower abdominal surgeries by means of epidural anesthesia showed that there was significant difference between groups favoring the group receiving magnesium sulphate 50 mg, in the time to first analgesic requirement, the number of doses of epidural fentanyl given as rescue analgesics as well as the cumulative fentanyl consumption in 24 h. The results of the three studies are congruent with those of the current study in that adding magnesium sulphate to epidural local anesthetic prolongs post operative analgesia without side effects, but they are in variance as regards the study group, the dose, the way of drug administration and the mode of anesthesia [16].

Comparable to our study Farouk S. evaluated the effect of epidural magnesium 50 mg given before induction of anesthesia (pre-magnesium group) and followed by infusion of 10 mg/h against epidural magnesium 50 mg given at the end of surgery (post-magnesium group) and epidural saline within the same times (control group). After the end of the operation, patients in both magnesium groups received patient controlled epidural analgesia (PCEA) in the form of fentanyl 1 μg/ml, bupivacaine 0.08% (0.8 mg/ml) and magnesium 1 mg/ml running at an initial rate of 2.5 ml/h, while, patients in the control group received PCEA in the form of fentanyl 1 μg/ml and bupivacaine 0.08% (0.8 mg/ml) running at an initial rate of 2.5 ml/h. The results showed that there were significantly lower pain scores and lower analgesic consumption in the pre-magnesium group compared with the post-magnesium and control groups ($P < 0.05$), moreover, the dose consumed in the post-magnesium group was significantly smaller than the control group ($P < 0.05$) [17]. Furthermore, a recent study was conducted by Kogler et al. on seventy patients including elderly undergoing thoracic surgery, patients were allocated either to receive sufentanil 0.2 μg/kg in combination with levobupivacaine 10 mg 0.5% and magnesium sulphate 50 mg or sufentanil 0.2 μg/kg in combination with levobupivacaine 10 mg 0.5% 15 min before induction of general anesthesia, followed by epidural infusion of magnesium sulphate 10 mg/h in the first group, whereas the second group received the same volume of saline. After the end of the surgery and for 48 h postoperatively, the first group received epidural infusion of sufentanil 1 μg/mL along with levobupivacaine 1 mg/ml and magnesium sulphate 1 mg/ml, while the second group received an epidural infusion of sufentanil 1 μg/mL and levobupivacaine 1 mg/ml [18]. The results are in favor with that of the present study as they showed that the preoperative use of epidural magnesium followed by infusion resulted in better postoperative analgesia as well as less analgesic consumption, but they differ in the study population though the study by Kogler et al. included elderly, the co-administered drugs and the continued use of epidural analgesia postoperatively.

5. Conclusion and limitations

From the current study we can conclude that using magnesium sulphate as an additive to epidural levobupivacaine infusion that started before the operation and continued till the end of the surgery provides good analgesia without side effects, it proved to fasten the epidural block in comparison to both the levobupivacaine and the levobupivacaine fentanyl groups, besides it increased the duration of post operative analgesia and decreased the total analgesic consumption in the first six postoperative hours in comparison to levobupivacaine group.

The current study found no difference in duration of post operative analgesia between both levobupivacaine plus magnesium and levobupivacaine plus fentanyl groups so increasing the sample size and increasing the duration of post operative monitoring of analgesic effect as well as recording of the number of rescue analgesics and the doses required during that time may be of value in further studies.

References

[1] Griffiths R, Beech F, Brown A, Dhesi J, Foo I, Goodall J, et al. Perioperative care of the elderly 2014: Association of anesthetists of Great Britain and Ireland. Anaesthesia 2014;69:81–98.
[2] Ghatak T, Chandra G, Malik A, Bahatia VK. Evaluation of the effect of magnesium sulphate vs. clonidine as adjunct to epidural bupivacaine. Indian J Anaesth 2010;54:308–13.
[3] Dubé Laurent, Granry Jean-Claude. The therapeutic use of magnesium in anesthesiology, intensive care and emergency medicine: a review. CJA 2003;50:732–46.
[4] Buvanendran A, Kroin JS. Useful adjuvants for postoperative pain management. Best Pract Res Clin Anaesthesiol 2007;21:31–49.
[5] Uzuner A, Saracoglu K, Saracoglu A, Erdemli O. The comparative study of epidural levobupivacaine and bupivacaine in major abdominal surgeries. J Res Med Sci 2011;16:1159–67.
[6] Bajwa SJS, Arora V, Kaur J, Singh A, Parmar SS. Dexmedetomidine vs fentanyl in epidural anaesthesia. Saudi J. Anaesthesia 2011;5:365–70.
[7] Banwait S, Sharma S, Pawar M, Garg R, Sood R. Evaluation of single epidural bolus dose of magnesium as an adjuvant to epidural fentanyl for postoperative analgesia: a prospective, randomized, double-blind study. Saudi J Anaesth 2012;6:273–8.
[8] Starr KNP, Bales CW. Excessive body weight in older adults: concerns and recommendations. Clin Geriatr Med 2015;31:311–26.
[9] Bromage PR. A comparison of the hydrochloride and carbon dioxide salts of lidocaine and prilocaine in epidural analgesia. Acta Aneaesthesiol Scand Suppl 1965;75:193–200.
[10] Huskisson EC. Measurement of pain. Lancet 1974;2:1127–31.
[11] Riker RR, Picard JT, Fraser GL. Prospective evaluation of the sedation -agitation scale for adult critically ill patients. Crit. Care Med. 1999;27:1325–9.
[12] McKeown JL. Pain management issues for the geriatric surgical patient. Anesthesiol Clin 2015;33:563–76.
[13] Mann C, Pouzeratte Y, Boccara G, Peccoux C, Vergne C, Brunat G, et al. Comparison of intravenous or epidural patient controlled analgesia in the elderly after major abdominal surgery. Anesthesiology 2000;92:433–41.
[14] Bilir A, Gulec S, Erkan A, Ozcelik A. Epidural magnesium reduces postoperative analgesic requirement. Br J Anaesth 2007;98:519–23.
[15] Hasanein R, El-Sayed W, Khalil M. The value of epidural magnesium sulphate as an adjuvant to bupivacaine and fentanyl for labor analgesia. Egypt J Anaesth 2013;29:219–24.
[16] Gupta A, Goyal VK, Gupta N, Mane R, Patil MNC. A randomized controlled trial to evaluate the effect of addition of epidural magnesium sulphate on the duration of postoperative analgesia in patients undergoing lower abdominal surgeries under epidural anaesthesia. Sri Lankan J Anaesthesiol 2013;21:27–31.
[17] Farouk S. Pre-incisional epidural magnesium provides pre-emptive and preventive analgesia in patients undergoing abdominal hysterectomy. Br J Anaesth 2008;101:694–9.
[18] Kogler J, Peric M, Hrabac P, Bekavacmisak V, Karaman-Ilic M. Effects of epidural magnesium sulphate on intraoperative sufentanil and postoperative analgesic requirements in thoracic surgery patients. Signa Vitae 2016;11:56–73.