



Comparison of analgesic effect of intrathecal morphine alone or in combination with bupivacaine and fentanyl in patients undergoing total gastrectomy: A prospective randomized, double blind clinical trial

Poređenje analgetskog efekta intratekalno primenjenog morfina samog ili u kombinaciji sa bupivakainom i fentanilom kod bolesnika podvrgnutih totalnoj gastrektomiji – prospektivna, randomizovana, dvostruko slepa klinička studija

Zoran Slavković^{*†}, Dušica M. Stamenković^{*}, Veselin Gerić[‡],
Milić Veljović^{*†}, Nebojša Ivanović[§], Aleksandar Tomić^{||}, Tomislav
Randjelović[§], Jelena Rašković[¶], Menelaos Karanikolas^{**}

^{*}Clinic of Anesthesiology and Intensive Care, ^{||}Clinic for Vascular Surgery, Military Medical Academy, Belgrade, Serbia; [†]Faculty of Medicine of the Military Medical Academy, University of Defence, Belgrade, Serbia; [‡]Department of Anaesthesia, [§]Department of Surgery, University Medical Center “Bežanijska Kosa”, Belgrade, Serbia; [¶]Department of Statistics, School of Economics, University of Belgrade, Belgrade, Serbia, ^{**}Department of Anesthesiology, Washington University School of Medicine, Saint Louis, Missouri, USA

Abstract

Background/Aim. Combined spinal-epidural-general anesthesia has several advantages over general anesthesia alone. This study was designed to compare the efficacy of intrathecal (IT) morphine alone, or in combination with bupivacaine and fentanyl, as part of a combined spinal-epidural (CSE) analgesia, in patients undergoing elective total gastrectomy.

Methods. This prospective, randomized double-blind study included 60 patients undergoing total gastrectomy under general anesthesia and CSE. We compared the analgesic effect of lumbar IT morphine 300 µg (the group M, n = 20) vs morphine 300 µg + bupivacaine 2 mg (the group MB, n = 20) vs morphine 300 µg + bupivacaine 2 mg + fentanyl 25 µg (the group MBF, n = 20) given after thoracic epidural catheter placement (T6-7) but before general anesthesia induction. Pain visual analogue scale (VAS) at rest (R), with movement (M) and with cough (C), and the number of analgesia requests were assessed for 72 h and after epidural catheter removal.

Results. Compared to other groups, the MBF group required significantly fewer additional intra-operative epidural bupivacaine doses ($p < 0.001$), whereas the M group required sig-

nificantly more supplemental intraoperative intravenous fentanyl, compared with the MBF ($p = 0.022$) and MB groups ($p = 0.005$). Postoperative pain relief was satisfactory in all the groups at all the time. VAS-R and VAS-M did not differ significantly among the groups. Compared to the M group, VAS-C scores 30 min postoperatively were significantly lower in the MBF ($p = 0.029$) and MB groups ($p = 0.002$). Duration of analgesia was longer in the MBF and MB groups, but the difference reached no significance. The number of supplemental analgesia requests was similar in all the groups in the first 12 h and during 72 h. Additional analgesia requests after epidural catheter removal were similar in all the groups, and side effects were infrequent. **Conclusion.** Compared to IT morphine alone, triple IT combination administered as part of CSE provided better intraoperative analgesia, but conferred no benefit with regards to postoperative analgesia.

Key words: anesthesia, epidural; anesthesia, spinal; methods; fentanyl; bupivacaine; morphine; analgesia; gastrectomy.

Apstrakt

Uvod/Cilj. Kombinovana spinalno-epiduralno-opšta anestezija ima nekoliko prednosti nad primenom samo opšte anestezije. Cilj ove studije bio je da uporedi efekat intratekalnog (IT) dodavanja fentanila i bupivakaina morfinu, kao

dodatka torakalnoj epiduralnoj analgeziji [kombinovana spinalnoepiduralna analgezija (KSE)], kod bolesnika planiranih za totalnu gastrektomiju. **Metode.** U randomiziranoj dvostruko slepoj studiji poređen je analgetski efekat lumbalno IT primenjenog 300 µg morfina (grupa M, n = 20), 300 µg morfina i 2 mg bupivakaina (grupa MB, n = 20) i trostruke

kombinacije sa 25 µg dodatog fentanila (MBF, $n = 20$), primenjenih nakon postavljanja epiduralnog katetera u torakalni segment (T6-7), ali pre uvida u opštu anesteziju za izvođenje totalne gastrektomije. Za procenu kvaliteta postoperativne analgezije korišćeni su vizuelna analogna skala bola (VAS) u miru (R), pokretu (M) i pri kašlju (C), broj analgetskih zahteva u toku 72 časa i nakon vađenja epiduralnog katetera. **Rezultati.** Intraoperativno, u poređenju sa drugim grupama, u MBF grupi bilo je dodato značajno manje epiduralnog bupivakaina ($p < 0,001$), dok je dodatna količina intravenskog (IV) fentanila bila značajno viša u grupi M u poređenju sa grupom MBF ($p = 0,022$) i MB grupom ($p = 0,005$). Postoperativna analgezija je bila zadovoljavajuća u svim grupama u toku 72 časa. Nije uočena statistički značajna intergrupna razlika za VAS-R i VAS-M ($p > 0,05$). U 30.

minutu postoperativno VAS-C bili su značajno niži u grupi MBF ($p = 0,029$) i MB ($p = 0,002$) u poređenju sa M grupom. Trajanje efektivne analgezije bilo je duže u grupama MBF i MB, ali razlika nije bila statistički značajna ($p > 0,05$). Broj zahteva za dodatnom analgezijom bio je sličan u svim grupama u prvih 12 časova i u toku 72 časa, kao i nakon vađenja epiduralnog katetera. **Zaključak.** Trostruka IT kombinacija kao deo KSE obezbeđuje bolju intraoperativnu analgeziju. Ova studija nije dokazala prednosti ove kombinacije za postoperativnu analgeziju u poređenju sa IT morfinom.

Ključne reči:

anestezija, epiduralna; anestezija, spinalna; metode; fentanil; bupivakain; morfin; analgezija; gastrektomija.

Introduction

Total gastrectomy for gastric cancer is a major surgical procedure with significant morbidity and mortality, depending on several perioperative and postoperative variables¹. Use of intrathecal opioids and local anesthetics in combination with epidural anesthesia/analgesia proved to provide reliable intraoperative and postoperative analgesia in major abdominal surgery, especially colorectal surgery²⁻⁴. This method is suggested in institutions where pumps designed for continuous epidural local anesthetic infusion are not available³.

Combined spinal-epidural-general anesthesia (CSE-GA) offers several advantages over general anesthesia alone⁵. Spinal anesthesia provides rapid onset of muscle relaxation and analgesia, the epidural catheter prolongs anesthesia and improves postoperative analgesia, while general anesthesia provides unconsciousness and controlled ventilation, thus providing excellent operating conditions for the surgeon⁵.

Subarachnoid lipid-soluble fentanyl, which can provide rapid onset of analgesia, combined with preservative-free water-soluble morphine, which provides analgesia with slower onset but longer duration, combined with a small dose of intrathecal bupivacaine has been shown to synergistically produce rapid and sustained analgesia⁶.

Our study was designed to evaluate the potential benefits of intrathecal morphine alone, or in combination with bupivacaine and fentanyl, as part of a combined spinal-epidural analgesia (CSE) regimen, for elective total gastrectomy. Our hypothesis was that the combination of intrathecal bupivacaine, fentanyl and morphine, in addition to thoracic epidural analgesia will improve analgesia in the immediate postoperative period. Postoperative pain at rest, with movement, and with cough was the primary clinical outcome. The need for supplemental intraoperative intravenous (IV) fentanyl and epidural bupivacaine, time to first postoperative analgesia request and postoperative analgesic drug use were designated as secondary outcomes.

Methods

This prospective, randomized, double blind clinical trial was approved by the University Expert Council for Medical Science, and written informed consent was obtained from all

patients before they entered the study. In total, 60 American Society of Anesthesiologists (ASA) physical status 1–3 adult patients requiring total gastrectomy for malignancy were recruited. Exclusion criteria were: patient's disapproval, significant comorbidity, preoperative opioid or nonsteroidal anti-inflammatory drugs (NSAID) consumption, drug addiction, psychiatric disorders, spinal problems, local infection, coagulation abnormality, neurological problems, allergy to medications used in the study, and any contraindications to neuraxial anesthesia. Preoperative preparation included patient education in order to explain the goals of the study, and familiarize patients with the visual analogue scale (VAS) scale, which was used to quantify pain in the postoperative period. A computer-generated randomization schedule was provided by an independent investigator who prepared and dispensed drugs for the trial. The patients and medical personnel were blinded to group assignment. All surgical procedures were performed by the same surgeon, who specializes in esophagogastric surgery and all anastomoses were hand sewn.

All the patients received midazolam 2.5 mg IV for premedication. Hartman's solution 1 L was given as fluid preload, and antibiotic prophylaxis consisted of ceftriaxone 2 g and metronidazole 500 mg in all cases. All neuraxial blocks were performed in the operating room, with the patients being awake and lying in the right lateral decubitus position. CSE was conducted using the double-space technique: an epidural catheter was inserted at the T6-7 interspace (paramedian approach) (Perifix, Tuohy needle 18 G, catheter 3 lateral eyes), followed by an intrathecal injection at the L2-3 interspace using a 25 G Pencan spinal needle. A test dose of lidocaine 2% and epinephrine 1 : 200 000, total volume 3 mL, was given via the epidural catheter to confirm appropriate catheter placement.

The patients were randomized to receive one of three intrathecal solutions (total volume was 1.2 mL in all the groups): morphine 300 µg, fentanyl 25 µg and bupivacaine (0.25%) 2 mg (MBF group), vs morphine 300 µg, bupivacaine (0.25%) 2 mg and normal saline 0.5 mL (MB group) vs morphine 300 µg and normal saline 0.9 mL (group M). In addition, all the patients received 10 mL of bupivacaine 0.25% through the epidural catheter before anesthesia induction.

General anesthesia was induced with midazolam 2 mg, fentanyl 100 µg and propofol 2 mg kg⁻¹. Suxamethonium 1 mg kg⁻¹ was given IV to facilitate tracheal intubation, followed by IV pancuronium 4 mg. Anesthesia was maintained with sevoflurane (1 MAC end-tidal) in O₂/air, supplemented by intermittent epidural bupivacaine boluses and IV fentanyl boluses as needed. Muscle relaxation was maintained using IV pancuronium 1 mg, when requested by the surgeon. A second bolus of epidural bupivacaine 0.25% 5 mL was administered before incision, and was followed by epidural bupivacaine 0.25% 5 mL boluses every hour for the remainder of the case. Intraoperative signs of insufficient analgesia (hypertension, tachycardia, lacrimation, flushing, sweating, swallowing or movement) were treated with additional 3 mL of epidural bupivacaine 0.25%. If signs of insufficient analgesia persisted, IV fentanyl 50 µg was also given.

Crystalloid and colloid solutions were infused as needed to meet fluid maintenance requirements and compensate for blood loss, respectively. Ephedrine 5 mg IV was administered when mean arterial pressure (MAP) fell below 60 mmHg despite adequate fluid infusion. At the end of surgery, residual neuromuscular blockade was reversed with neostigmine 2.5 mg and atropine 0.8 mg, and the patient was extubated. Extubation criteria were recovery from anesthesia, spontaneous breathing, hemodynamic stability and normothermia, but the decision for extubation was at the discretion of the anesthesia and surgery providers. Postoperatively, patients were transported either to the Intensive Care Unit (ICU) (if left on mechanical ventilation) or to a high dependency unit.

Postoperative epidural analgesia started 12 hours after surgery and consisted of intermittent bolus of morphine 2 mg with 0.125% bupivacaine 8 mL every 8 hours. Pain was assessed using the VAS scale (0 = no pain, 100 mm = the worst pain imaginable) at rest (VAS-R), on movement from the supine to the sitting position (VAS-M) and with cough (VAS-C). Tramadol 100 mg was added as slow IV infusion to supplement analgesia if VAS-R score was > 30 mm or VAS-M was > 40 mm. The patients were assessed for technical causes of epidural failure (catheter dislodgment or migration) after each analgesia request. Time to first analgesia request was defined as the time between the application of the surgical dressing (end of surgery) and the first analgesia request. The number of additional analgesics given while epidural analgesia was in use, and after epidural catheter was removed, were recorded. If a patient was asleep, VAS score was recorded as 0. Epidural analgesia was used for 72 hours postoperatively, and then the catheter was removed. In cases where the epidural catheter was dislodged earlier, analgesia was provided with IV tramadol (100 mg) every 6 hours. As we performed statistical analysis based on "Intention to treat", patients with dislodged catheter had data recorded until the time the epidural catheter fell off, and were included in the statistical analysis, in the groups in which they were randomized.

VAS and hemodynamic data were collected, starting at the time of surgery, and continuing for 72 hours postoperatively, at predefined intervals (0 min, 30 min, 1st, 2nd, 3rd,

4th, 6th, 12th, 18th, 24th, 48th and 72nd hour). Postoperative fluids were administered in accordance with hospital protocol. The Bromage scale was used for motor block assessment and the Ramsey scale was used for sedation assessment. Side effects, including nausea, vomiting, pruritus (none, mild, moderate, severe), respiratory depression (defined as respiratory rate < 8 breaths per min), hypotension (MAP < 60 mmHg), VAS mood (0 = the worst mood, 100 mm = the best mood), postoperative complications and complications related to neuraxial anesthesia were recorded. Since all the patients had urinary catheter, urinary retention was not a problem in any patient.

Power analysis was conducted using Graph Pad Stat-Mate 2.00 (GraphPad Software, Inc., La Jolla, California, USA), based on the following assumptions: difference of mean VAS-R between-groups 20 mm, standard deviation 17 mm, power 70%, and significance level (alpha) 0.05 (two-tailed). These assumptions were based on data from previous similar studies^{7,8}. Power analysis estimated that this study would need 18 cases per group. Therefore, we decided to include 20 patients per group, in order to allow for possible patient attrition or missing data. Normality of data distribution was evaluated with the Kolmogorov Smirnov test. Depending on data distribution, data are presented as mean (standard deviation) or median (range). Parametric and non-parametric statistical tests were applied as appropriate. Demographic data were analyzed using analysis of variance or chi-square test as appropriate. Because of their distribution, VAS data were treated as ordinal, and comparisons between the groups were conducted using the Kruskal-Wallis test, whereas the Mann-Whitney test was used for post-hoc comparisons. Nominal data were analyzed using Chi-square. *p* – values < 0.05 were considered significant for all the tests. All analyses were performed using SPSS 12.0 (SPSS Inc., Chicago, Illinois, USA).

Results

A total of 60 patients were enrolled in the study. Demographic characteristics did not differ significantly among all the groups (Table 1).

The thoracic epidural and lumbar intrathecal spaces were successfully identified in all the patients. There were no differences among the groups with regards to the duration of anesthesia and surgery (Table 2). Compared to all other groups, the MBF group required significantly fewer additional epidural bupivacaine doses (*p* < 0.001). Supplemental IV fentanyl requirements were significantly higher in the group M compared to the groups MBF (*p* = 0.022) and MB (*p* = 0.005) (Table 2). Intraoperative pancuronium use did not differ among the groups (*p* = 0.093; Table 2). Compared to the groups MBF and MB, more patients in the group M were extubated immediately after the surgery, but this difference was not statistically significant (Table 2).

Pain relief was satisfactory in all the groups throughout the entire 72 h postoperative period. Compared to the group M, VAS-C scores were significantly lower in the group MBF (*p* = 0.029; Figure 1) and MB (*p* = 0.002; Figure 1) in the

Table 1

Demographic characteristics of the patients

Preoperative characteristics	Groups of patients			p
	MBF (n = 20)	MB (n = 20)	M (n = 20)	
Age (years)	59.8 ± 8.1	58.3 ± 9.9	56.7 ± 10.8	0.602
Weight (kg)	72.1 ± 14.0	66.1 ± 14.1	69.8 ± 14.4	0.419
Height (cm)	172.3 ± 8.9	169.6 ± 10.3	169.8 ± 7.9	0.587
Sex M/F (n)	15/5	13/7	16/4	0.495
ASA 1/2/3 (n)	5/14/1	2/14/3	5/13/2	0.600

Data are presented as mean ± SD or number (n); M – male; F – female;
 ASA – American Society of Anesthesiologists Physical Status Classification
 (1 – normal healthy patient; 2 – patient with mild systemic disease; 3 – patient with severe systemic disease); M – the group that received morphine; MB – the group that received morphine and bupivacaine; MBF – the group that received morphine, bupivacaine and fentanyl.

Table 2

Intraoperative data

Variables	Groups of patients			p
	MBF (n = 20)	MB (n = 20)	M (n = 20)	
GA duration (min)	306.2 ± 99.5	242.53 ± 71.1	265.0 ± 77.4	0.06
Additional epidural bupivacaine (mg)	20.1 ± 4.4 ^{††}	27.9 ± 6.8	30.6 ± 6.5	0.001
Fentanyl (µg)	247.5 ± 237.0 [†]	278.9 ± 161.0 [‡]	475.0 ± 247.9	0.003
Pancuronium (mg)	15.4 ± 4.8	12.6 ± 4.7	12.9 ± 3.5	0.093
Colloids (mL)	955.0 ± 671.6	1052.63 ± 621.3	1337.5 ± 844.0	0.228
Blood (mL)	839.5 ± 451.0	692.6 ± 866.8	1006.5 ± 821.7	0.416
Extubation in OR [n (%)]	8 (40%)	11 (57.9%)	13 (65%)	0.263

Values are presented as mean ± SD, patient number (n), or percentage (%); GA – general anaesthesia; M – the morphine group; MB – the morphine + bupivacaine group; MBF – the morphine + bupivacaine + fentanyl group; OR – operating room;
[†]p < 0.05 comparing the group MBF vs MB; ^{††}p < 0.05 comparing the group MBF vs M; [‡]p < 0.05 comparing the group MB vs M

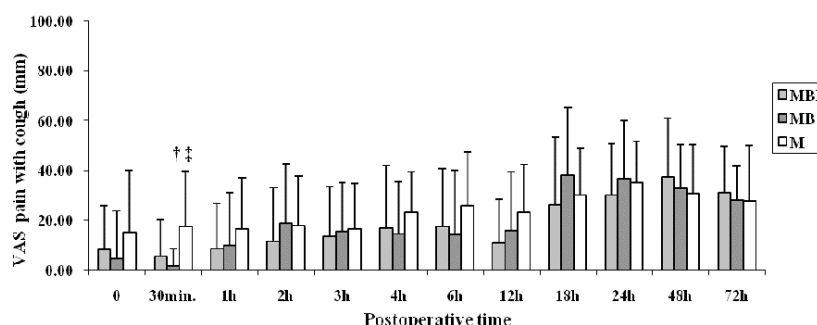


Fig. 1 – Visual analogue scale (VAS) pain scores with cough recorded during the first 72 h.

The values are reported as mean ± SD; ^{*}p < 0.05 comparing MBF vs MB group; [‡]p < 0.05 comparing MB vs M group; M – the morphine group; MB – the morphine + bupivacaine group; MBF – the morphine + bupivacaine + fentanyl group.

first 30 minutes after the surgery, but VAS-R and VAS-M pain scores did not differ significantly between the groups at any time ($p > 0.05$; Figure 2 and Figure 3).

Time to first analgesia request was longer in the groups MBF and MB, but the difference did not reach statistical significance (Table 3). The number of supplemental analgesia requests was similar in all the CSE groups in both the first 12 hours and the first 72 hours (Table 3). Similarly, the number of supplemental analgesia requests after epidural catheter removal were similar in all the groups (Table 3).

Intraoperatively, mean pressure was higher in the MBF compared to the MB group at only 90 minute measuring point

(Figure 4). Postoperatively, the group MBF had higher mean pressure compared to the group M 30 minutes after the surgery. The group MB had higher mean pressure compared to the group M at 3 hours and 72 hours after the surgery (Figure 5).

The frequency of vomiting, hypotension and sedation was similar in all the groups. VAS mood was significantly higher in the group M compared to the group MB after 18 hours ($p = 0.034$) and 24 hours ($p = 0.002$), and compared to the MBF group after 24 hours ($p = 0.029$) (Figure 6). All the patients were able to walk the morning after surgery. There were no deaths, and there was no nerve injury or central nervous system complication related to neuraxial blockade.

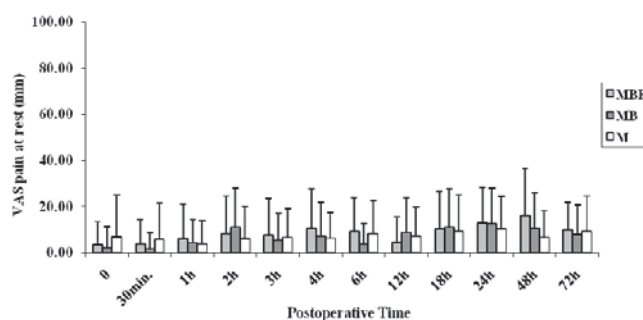


Fig. 2 – Visual analogue scale (VAS) pain scores at rest recorded during the first 72 h
The values are reported as mean $\pm$ SD; M – the morphine group; MB – the morphine + bupivacaine group;
MBF – the morphine + bupivacaine + fentanyl group.

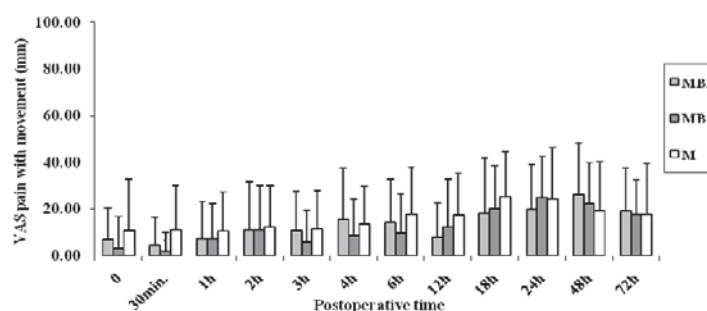


Fig. 3 – Visual analogue scale (VAS) pain scores with movement recorded during the first 72 h
The values are reported as mean $\pm$ SD; M – the morphine group; MB – the morphine + bupivacaine group;
MBF – the morphine + bupivacaine + fentanyl group.

Data on postoperative analgesia and hospital stay of patients

Table 3

Variables	Groups of patients			p
	MBF (n = 20)	MB (n = 20)	M (n = 20)	
Time to first analgesia request (min), mean $\pm$ SD (min-max)	220.6 $\pm$ 206.7 (1–585)	312.3 $\pm$ 317.3 (0–1065)	155.2 $\pm$ 170.2 (0–570)	0.310
Analgesia requests during 12 hours, n	0–1	0–2	0–2	0.392
Analgesia requests during 72 hours, n	0–4	0–5	0–8	0.707
Analgesia requests after EC removal, n	0–32	0–22	0–30	0.673
Hospital stay (days)	5–30	8–32	9–23	0.321

EC – epidural catheter;

M – the group that received morphine; MB – the group that received morphine and bupivacaine;

MBF – the group that received morphine, bupivacaine and fentanyl.

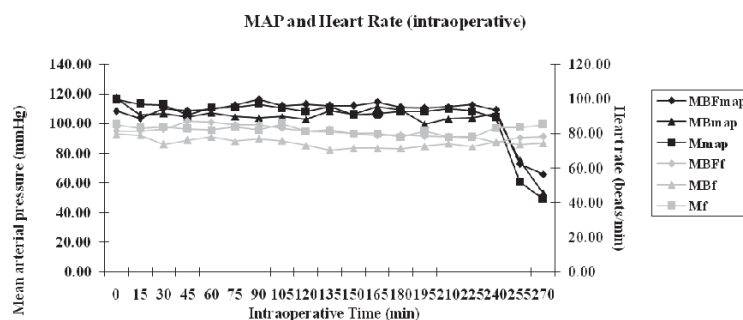


Fig. 4 – Intraoperative heart rate and mean arterial pressure (MAP)

The values are reported as mean $\pm$ SD; * $p < 0.05$ comparing the MBF group with the MB group; f – frequency of heart rate; M – the morphine group; MB – the morphine + bupivacaine group; MBF – the morphine + bupivacaine + fentanyl group.

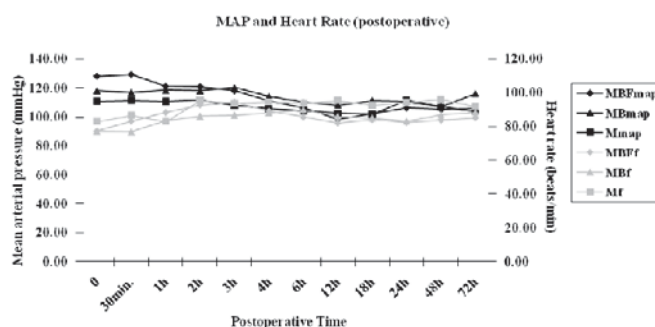


Fig. 5 – Postoperative heart rate and mean arterial pressure (MAP) recorded during the first 72 h.

The values are reported as Mean $\pm$ SD; $\dagger p < 0.05$ comparing MBF vs. M group; $\ddagger p < 0.05$ comparing MB vs. M group; f – frequency of heart rate; M – the morphine group; MB – the morphine + bupivacaine group; MBF – the morphine + bupivacaine + fentanyl group.

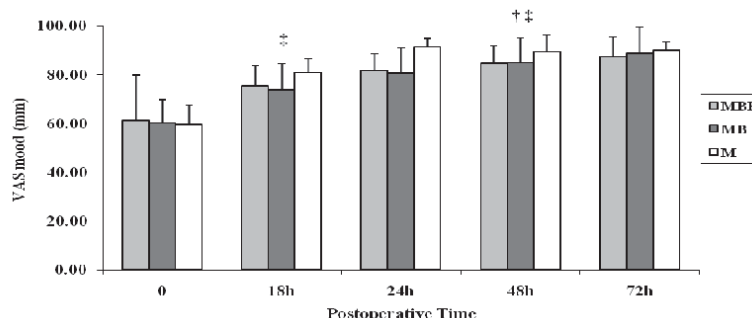


Fig. 6 – Visual analogue scale (VAS) mood scores recorded during the first 72 h

The values are reported as mean $\pm$ SD; $\dagger p < 0.05$ comparing MBF vs. M group; $\ddagger p < 0.05$ comparing MB vs. M group; M – the morphine group; MB – the morphine + bupivacaine group; MBF – the morphine + bupivacaine + fentanyl group.

Discussion

The study was designed to evaluate the potential benefits of intrathecal morphine alone or in combination with bupivacaine and fentanyl as part of CSE in patients undergoing total gastrectomy. The combination of intrathecal morphine, bupivacaine and fentanyl has been shown to provide useful analgesia in gynecology and obstetrics^{9–11}. In this study we investigated whether a similar benefit could be demonstrated for total gastrectomy.

The choice of study medications was based on the concept of anti-nociceptive synergy: intrathecal fentanyl provides rapid (within 5–10 min) analgesia onset, improves surgical blockade quality¹² and enhances the effect of small intrathecal bupivacaine doses¹³, whereas intrathecal morphine provides prolonged analgesia¹⁴. Similarly, intrathecal bupivacaine potentiates epidural bupivacaine¹⁵ and the anti-nociceptive effect of intrathecal morphine¹⁶. Adequate analgesia after total gastrectomy (at rest, with movement and with cough) was the main study endpoint. Reduction of intraoperative analgesia requirements, time to first postoperative analgesia request and postoperative analgesic drug use, were designated as secondary study endpoints.

Our results suggest that the main benefit of adding fentanyl and bupivacaine to intrathecal morphine were reduced intraoperative IV fentanyl and epidural bupivacaine use in the MBF group. Because the same surgeon performed all procedures, observed differences between groups are proba-

bly not related to differences in surgical technique or complications.

Because the visceroperitoneal organs receive multiple innervations by the spinal nerves (T5–T12), the vagus nerve and the phrenic nerve (C3–C5) in the upper abdomen¹⁷, pain perception during gastrectomy is regulated by multiple mechanisms¹⁷. The complex nature of postoperative pain after gastrectomy was the reason we decided to study the role of CSE analgesia in these patients. Postoperative analgesia was satisfactory in all the patients, and VAS pain scores, time to first analgesia request, number of analgesia requests at 12 hours and 72 hours postoperatively, and after epidural catheter removal did not differ significantly among the groups. Since all the patients had access to adequate pain relief, and pain scores did not differ significantly among the groups, postoperative analgesia requirements are a reasonable way to detect differences in the quality of analgesia among the groups. The absence of a difference with regards to postoperative analgesia between the groups could be due to intrathecal morphine effectively suppressing pain in all the patient groups.

The use of epidural morphine and bupivacaine combination for postoperative analgesia was based on the concept of synergistic anti-nociceptive effect from concurrent administration of pain-inhibiting drugs, which allows a dose reduction for each drug¹⁸. Moreover, data show that epidural morphine can provide prolonged analgesia¹⁹ and reduce epidural local anesthetic requirements, thereby minimizing

lower extremity motor blockade and facilitating early ambulation. Indeed, all the patients in our study ambulated the morning after the surgery. The widespread worldwide use of epidural morphine for postoperative analgesia suggests that this technique is safe²⁰. We opted for the same dose of medications for neuraxial blocks in all the patients, because this approach is simple, less time-consuming and less prone to errors during medication preparation. In order to prevent under-treatment of pain, we instructed the patients to request additional analgesia for VAS-R score > 30 mm or VAS-M > 40 mm. We used IV tramadol for breakthrough pain, because in our experience, IV tramadol is better tolerated than morphine (i.e. causes less nausea) in our patient population. Of note, our study did not have adequate power to assess the impact, if any, of CSE on morbidity and mortality.

Conclusion

Our findings suggest that addition of fentanyl and/or bupivacaine to intrathecal morphine reduces the need for additional intraoperative epidural bupivacaine and IV fentanyl, but does not improve postoperative VAS pain scores after gastrectomy. Well designed prospective clinical studies are needed to further evaluate the potential benefit of adding subarachnoid fentanyl and/or bupivacaine to subarachnoid morphine for total gastrectomy.

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