Intraperitoneal ropivacaine or ropivacaine plus meperidine for laparoscopic gynecological procedures

Jinekolojik laparoskopik cerrahide intraperitoneal ropivakain ve ropivakain ile meperidin kombinasyonu

Semra KARAMAN,[1] Seden KOCABAŞ,[1] Sedat ERGUN,[1] Vicdan FIRAT,[1] Meltem UYAR,[2] Fatih ŞENDAĞ[3]

Summary

Objectives: Postoperative pain after laparoscopic surgery is less intense than after laparotomy and patients may benefit from an intraperitoneal injection of local anesthetic and opioids. We aimed to compare intraperitoneal 0.75% ropivacaine with 0.75% ropivacaine plus meperidine for postoperative analgesia in patients undergoing gynecologic laparoscopy.

Methods: At the end of gynecologic laparoscopy, in a double-blind, randomized manner, one of the following injections was given intraperitoneally. Patients were allocated into three groups: Patients in R Group (n=18) were given 0.75% ropivacaine 3 mg/kg in 200 mL saline; patients in RM Group (n=17) were given meperidine 50 mg plus 0.75% ropivacaine 3 mg/kg in 200 mL saline; patients in C Group (n=18) were given 200 mL saline through the trocars. All patients were given diclofenac sodium when they had pain (VAS 3) and 1 mg/kg meperidine i.v. was also given when pain persisted.

Results: The pain scores and analgesic requirements during the first postoperative hour were significantly lower in the RM Group than those in the R and C Groups. Beyond that time, the pain scores were similar in all groups and there were no differences in total analgesic requirement in 24 h between groups. The three groups were comparable for shoulder pain and side effects.

Conclusion: The intraperitoneal infiltration of 0.75% ropivacaine plus meperidine reduced pain scores and analgesic requirement during the first one hour after gynecologic laparoscopy compared with the intraperitoneal infiltration of ropivacaine or saline.

Key Words: Intraperitoneal analgesia; laparoscopy; meperidine; ropivacaine.

Özet

Amaç: *Laparoskopik cerrahi sonrası postoperatif ağrı laparatomiye göre daha hafiftir ve hastalar intraperitoneal lokal anestezik ve opioid uygulamalarından fayda görebilir. Çalışmamızda jinekolojik laparoskopik cerrahi uygulanacak hastalarda intraperitoneal uygulanan %0.75'lik ropivakain ve meperidinle kombinasyonun postoperatif analjezi üzerine etkilerini karşılaştırmayı amaçladık.*

Gereç ve Yöntem: *Jinekolojik laparoskopi sonunda, randomize çift-kör çalışma protokolüne göre intraperitoneal enjeksiyon uygulandı. Hastalar üç gruba ayrıldı: R Grubuna (n=18) %0.75'lik ropivakain 3 mg/kg 200 ml salin içinde; RM Grubuna (n=17) %0.75'lik ropivakain 3 mg/kg ve meperidin 50 mg 200 ml salin içinde; K Grubuna (n=18) 200 ml salin trokarla uygulandı. Hastalara ağrısı olduğunda (VAS 3) diklofenak sodyum ve eğer ağrısı geçmezse 1 mg/kg meperidin i.v. uygulandı.*

Bulgular: *Ağrı skorları ve analjezik gereksinimi postoperatif ilk bir saat için RM grubunda daha düşük bulundu. Daha sonraki dönemde ağrı skorları tüm gruplar için benzerdi ve 24 saatlik total analjezik tüketimi açısından fark saptanmadı. Her üç grup arasında omuz ağrısı ve yan etkiler yönünden fark saptanmadı.*

Sonuç: *Jinekolojik laparoskopik cerrahi sonrası intraperitoneal %0.75'lik ropivakain ile meperidin kombinasyonu ropivakain ya da saline göre postoperatif ilk bir saatte daha düşük ağrı skorları ve analjezik tüketimi sağlamaktadır.*

Anahtar sözcükler: *İntraperitoneal analjezi; laparoskopi; meperidin; ropivakain.*

Departments of [1]Anesthesiology and Reanimation, [2]Algology, [3]Obstetrics and Gynecology, Ege University Faculty of Medicine, İzmir, Turkey

Ege Üniversitesi Tıp Fakültesi, [1]Anesteziyoloji ve Reanimasyon Anabilim Dalı, [2]Algoloji Bilim Dalı, [3]Kadın Hastalıkları ve Doğum Anabilim Dalı, İzmir

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Correspondence (*İletişim*): Semra Karaman M.D. Ege Üniversitesi Tıp Fakültesi, Anesteziyoloji ve Reanimasyon Anabilim Dalı, İzmir, Turkey
Tel: +90 - 232 - 390 21 42 **e-mail (*e-posta*):** semra.karaman@ege.edu.tr

Introduction

Laparoscopic surgery is associated with significantly less pain, earlier discharge from the hospital, and more rapid convalescence than equivalent procedures performed by mini-laparotomy.[1,2] However, patients undergoing laparoscopic procedures do experience postoperative pain, especially in the upper and lower abdomen, back, and shoulder regions.[3, 4] Collins et al.,[5] reported the incidence of postoperative abdominal pain after outpatient gynecologic diagnostic laparoscopy to be 61.8%, 71.4%, and 55.1% immediately after surgery, at postoperative 24 h and 48 h, respectively. The pain experienced by patients undergoing laparoscopic surgery has a visceral component, as a result of surgical handling and diafragmatic irritation by dissolved carbon dioxide and a somatic component due to the holes made in the abdominal wall for the trocars.[6] Shoulder pain, which is associated with peritoneal insufflation, especially when shoulder houlders and an exaggerated Trendelenburg position have been used frequently complicates the postoperative period after laparoscopic surgery.[7]

The intraperitoneal (IP) administration of local anaesthetics (LA) in reducing the intensity of postlaparoscopic pain is a conflicting subject. Although some investigators have reported that the IP delivery of LA is an effective method of providing analgesia after laparoscopic surgery,[8,9] other investigators have not been able to confirm the analgesic efficacy of IP LA.[10,11] There are many studies on the use of IP bupivacaine and lidocaine for postoperative analgesia. Ropivacaine, an amide local anaesthetic that has similar efficacy to bupivacaine at a large dose, also leads to reduced systemic and cardiac toxicity.[12,13]

The peripheral analgesic effects of opioids have been investigated in a number of studies.[14-16] Some investigators reported that the IP administration of morphine failed to provide analgesia after laparoscopy.[14] Peach et al.[17] reported no benefit from the IP instillation of ropivacaine plus meperidine. However, Colbert et al.,[9] reported that the combination of IP bupivacaine plus IP meperidine provides satisfactory pain relief after laparoscopic tubal ligation. These findings have not been confirmed in a larger clinical trial. The aim of this study was to investigate whether IP ropivacaine or a combination of IP ropivacaine and meperidine provide effective pain relief after gynecologic laparoscopy and to record the analgesic profiles.

Material and Methods

The study was approved by our ethics committee, and all patients gave their written, informed consent. Fifty-three patients with ASA physical status I-II (aged 18-50 years) scheduled to undergo laparoscopic gynecology were included in this prospective, randomized, placebo-controlled, and double-blinded study. Criteria for exclusion were: psychiatric disease, allergic reactions to opioids or local anesthetics, previous history of opioid intake, morbid obesity and severe chronic disease. Patients were randomized according to a table of random numbers.

Patients were not premedicated. Anesthetic management was standardized. After insertion of an intravenous cannula and placement of routine intraoperative monitoring devices such as an electrocardiograph, pulse oximetry, capnograph and noninvasive blood pressure monitor, all patients breathed 100% oxygen before induction of anesthesia. Anesthesia was induced with 10 µg/kg atropin, 1 µg/kg remifentanil, 2 mg/kg propofol and 0.1 mg/kg vecuronium was given to facilitate endotrachael intubation. Anesthesia was maintained with 1–2% end-tidal sevoflurane in 50% O_2-N_2O and remifentanil infusion. Remifentanil infusion rate of 0.5 µg/kg/min was maintained for 5 minutes after induction, followed by 0.25 µg kg/min until the last surgical suture. Vecuronium 0.02 µg/kg was used as necessary. Ventilation was adjusted to maintain end-tidal carbondioxide between 34 and 40 mmHg. Surgery was conducted in the lithotomy and Trendelenburg position. During laparoscopy, intraabdominal pressure was limited to 14 mmHg. All patients received metoclopramide 10 mg i.v. during operation.

At the end of successful gynecologic laparoscopy, patients were allocated randomly to one of three groups: patients in R Group (n=18) were given 0.75% ropivacaine 3 mg/kg in 200 mL saline; patients in RM Group (n=17) were given meperidine

50 mg plus 0.75% ropivacaine 3 mg/kg in 200 mL saline, and patients in C Group (n=18) were given 200 mL saline intraperitoneally through the trocars. The anesthesiologist and the surgeon administering the solutions intraperitoneally through the trocars were not informed about the contents of the solution. Carbondioxide was then evacuated from the peritoneal cavity. Surgical wounds were not infiltrated with local anesthetic solution. Anesthesia was discontinued, and neuromuscular blockade was reversed with 0.05 mg/kg neostigmine and 0.01 mg/kg atropine at the end of surgery.

All patients were informed about the visual analog scale (VAS) on the day before operation. Postoperative intra-abdominal pain was assessed both at rest and on coughing at 30 min, 1 h, 2 h, 6 h, 12 h, and 24 h. The patients were asked to rate the severity of pain via VAS ranging from no pain (0 cm) to the worst possible pain (10 cm). A standard postoperative analgesic regimen was used in all patients, with non-steroidal anti-inflammatory drugs and meperidine. During the first 24 h postoperatively, all patients were given (up to every 8 h) diclofenac sodium (Voltaren®, Novartis, Swiss) 75 mg im as necessary (VAS ≥3). Meperidine (Aldolan®, Gerot Pharmazeutika GmbH, Austria) 1 mg/kg i.v. was also given when pain persisted. In the postoperative period, the time to first analgesic administration and total diclofenac sodium and meperidine requirements were recorded. The presence of postoperative shoulder pain and side effects such as nausea, vomiting, headache, pruritus, urinary retention or shivering were recorded by an independent investigator blinded to the treatment groups.

Statistical analyses were performed using SPSS (SPSS for Windows Release 10.0) statistical package. The results are presented as mean ± standard deviation, median (range), or frequencies as appropriate. Statistical analysis was performed with ANOVA and $p<0.05$ was considered statistically significant. The VAS values were compared between groups by using the Kruskal-Wallis test followed by the Wilcoxon Matched Pairs Rank test. The occurrence of postoperative side effects was compared between groups by using a χ^2 test.

Results

In the RM Group, one patient who had conversion to open surgery did not complete the study and was excluded. The groups were similar with regard to age, height, weight, ASA classification, and duration of surgery (Table 1). There were no statistically significant differences among the groups regarding

Table 1. Patient characteristics and surgical data

	Group R (n= 18)	Group RM (n= 17)	Group C (n= 18)
Age (year)	33.1±7.4	33.8±6.7	32.4±4.5
Weight (kg)	66.5±10.4	64.1±11.4	63.2±7.2
Height (cm)	161.6±5.2	163.7±5.4	162.3±4.8
ASA (I/II)	11/7	12/5	12/6
Duration of surgery (min)	92.5±41.1	98.2±36.5	100.3±24.5

Values are mean ± SD. There were no significant differences among groups.

Table 2. Surgical procedures

	Group R (n= 18)	Group RM (n= 17)	Group C (n= 18)
Salpingectomy (n/%)	2 / 11.1	3 / 16.6	2 / 11.1
Ovarian cystectomy (n/%)	8 / 44.4	6 / 33.3	8 / 44.4
Myomectomy (n/%)	4 / 22.2	3 / 16.6	3 / 16.6
LAVH (n/%)	4 / 22.2	5 / 27.7	5 / 27.7

LAVH: Laparoscopic-assisted vaginal hysterectomy. There were no significant differences among groups.

Table 3. Analgesic requirements

	Group R (n= 18)	Group RM (n= 17)	Group C (n= 18)
Diclofenac sodium in 1h (mg)	62.5±28.7	35.2±31.5*	70.8±17.6
Diclofenac sodium in 24h (mg)	108.3±46.1	88.2±29.4	125±62.9
Meperidine in 24h (n)	4 (22.2%)	3 (17.6%)	8 (44.4%)

Values are mean ±SD or number of patients n (%). * p<0.05, Group RM versus Group R and Group C.

Table 4. Postoperative characteristics and side effects.

	Group R (n= 18)	Group RM (n= 17)	Group C (n= 18)
Nausea	6 (33.3%)	7 (38.8%)	9 (50.%)
Vomiting	2 (11.1%)	2 (11.1%)	3 (16.6%)
Shoulder pain	9 (50%)	10 (59%)	11 (61%)

Values are number of patients n (%) or mean ±SD. There were no significant differences among groups in the overall incidence of side effects.

the different types of surgical procedures (Table 2).

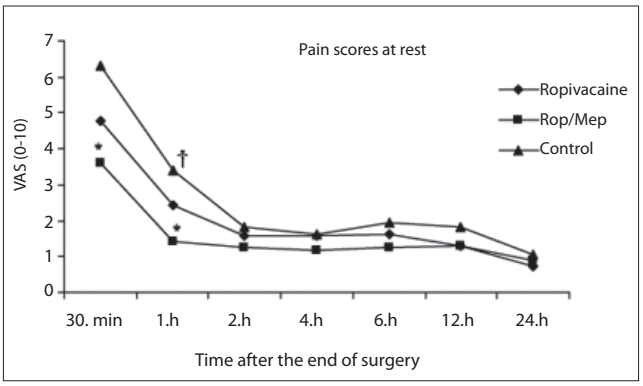
Pain scores were highest at 30 min after the laparoscopic procedure in all groups. There were no significant differences between the three groups with regard to pain scores (at rest or on coughing) throughout the study period except in the first postoperative hour. In the RM Group, pain scores at rest and on coughing were lower than those in the R and C Groups at postoperative 30 min and 1 h (Figure 1, 2).

At the end of the first postoperative hour, the amount of diclofenac sodium required was significantly lower in RM Group than in R and C groups (Table 3) (p <0.05). The total amount of diclofenac sodium consumption in 24 h were similar in all groups (Table 3). The number of patients receiving meperidine treatment in the postoperative period were similar between groups (Table 3) (p>0.05).

No differences in the incidence of nausea, vomiting and shoulder pain were observed between R Group, RM Group and C Group (p>0.05) (Table 4). There were no cases of shivering, headache, pruritus or urinary retention reported in any of the groups.

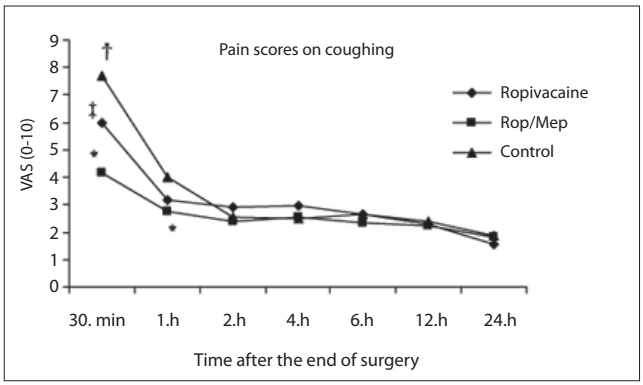
Discussion

The results of the present study suggest that the IP infiltration of ropivacaine/meperidine was more effective in reducing pain immediately after operative laparoscopy when compared with IP ropivacai-



* p<0.05, Group RM versus Group C. † p<0.05, Group C versus Group RM and Group R.

Fig. 1. Pain scores at rest in each group at each of the time periods examined. Values are median.



* p<0.05, Group RM versus Group C. † p<0.05, Group C versus Group RM and Group R, ‡ p<0.05, Group R versus Group RM.

Fig. 2. Pain scores on coughing in each group at each of the time periods examined. Values are median.

ne alone or IP saline, but the effect was not seen beyond one hour. The pain scores and analgesic requirement in the RM Group were lower than those in the R and C groups during the first hour after surgery, but cumulative analgesic consumption in 24 h was similar in all groups. This suggests that, although IP injection of ropivacaine/meperidine has some effect on postoperative pain, it remains a weak analgesic technique.

Bisgaard et al.,[18] suggested that pain after laparoscopic cholecystectomy was divided into three components: incisional pain, which dominated over visceral pain, which in turn dominated over shoulder pain. Several investigators have reported that the visceral pain experienced after laparoscopic cholecystectomy can be theoretically blocked by IP infiltration.[19] In the present study, IP infiltration with ropivacaine or ropivacaine plus meperidine was found to ineffective in preventing visceral pain after gynecologic laparoscopy beyond one hour. The results of the present study seem to be in accordance with the findings of Bisgaard et al.,[18] who reported that IP infiltration of local anaesthetics or opioids is ineffective in blocking incisional pain.

The efficacy of IP local anaesthetic infiltration has been demonstrated in numerous studies on laparoscopic cholecystectomy, but there is no consensus regarding the dose, concentration, site and manner of administration.[9,10,13,16] Although the IP administration of bupivacaine 50-150 mg was found to be effective in preventing postoperative pain after laparoscopic cholecystectomy in some studies,[6,20] there are others who reported IP bupivacaine to be inefficient for analgesia after laparoscopic cholecystectomy.[10,21] Scheinin et al.,[21] reported that IP instillation of 0.15% bupivacaine 150 mg at the end of surgery had no effect on pain after laparoscopic cholecystectomy. Joris et al.,[10] investigated the effects of administering 0.125% bupivacaine (80 mL) or saline (80 mL) intraperitoneally at the end of laparoscopic cholecystectomy. The investigators reported IP bupivacaine to be ineffective for treating pain after laparoscopic cholecystectomy.

In gynecologic laparoscopy, decreased postoperative pain scores after IP local anesthetic administration have been reported.[8,22,23] Here as well, however, the mode of administration lacks standardization, e.g., infiltration on the trajectory of the trocars, infiltration of the uterine tubes, and peritoneal instillation before and after insufflation. Goldstein et al.,[7] reported that the IP instillation of 20 mL of either 0.5% bupivacaine or 0.75% ropivacaine prevented postoperative pain and decreased the need for postoperative analgesia, when compared with placebo in patients undergoing laparoscopic gynecologic surgery. Callesen et al.,[23] combined port site and mesosalpinx infiltration and peritoneal instillation by using 285 mg of ropivacaine (50 mL) in a double-blinded, randomized, placebo-controlled study on 80 patients undergoing laparoscopic tubal sterilization. The investigators demonstrated significant improvement of pain scores over the first 8 h on coughing and during mobilization in the ropivacaine group when compared with the placebo group. In contrast with the studies mentioned above, we used relatively higher volumes of IP infiltration (3 mg/kg ropivacaine in 200 mL saline). Since there is a close relationship between the concentration of a local anaesthetic acting on a nerve and the degree of conduction blockade that occurs, failure of the technique in the present study could be due to the low concentration of ropivacaine. Higher volumes of IP local anaesthetic infiltration have also been used in some studies, such as the study by Maestroni et al.,[24] in which 5 mg/kg ropivacaine in 200 mL saline or placebo was administered intraperitoneally before creation of the pneumoperitoneum for laparoscopic cholecystectomy. The investigators found decreased postoperative pain scores with the preemptive administration of IP ropivacaine when compared with IP saline. In this study, unlike the study by Maestroni et al.,[24] where IP local anesthetic was given preemptively, 3 mg/kg ropivacaine was administered through the trocars into the peritoneal cavity at the end of surgery.

The opioid chosen for this study was meperidine, rather than morphine or fentanyl, because of the dual local anesthetic and analgesic properties of meperidine. The effects of meperidine appear to be produced by its actions on two independent pathways: the opioid receptor pathways, which subserve analgesic action, and the sodium channels, which subserve local anesthetic action. These local anesthetic actions appear to be independent of its opio-

id analgesic activity when administered topically in the subarachnoid space, epidurally, or on exposed nerve in experimental studies. After IP administration, meperidine is absorbed from the peritoneal cavity and has a central analgesic action. The speed of absorption and the rapidity of onset of action when administered by this route are uncertain in patients undergoing laparoscopy.[9] Colbert et al.,[9] reported that the combination of IP bupivacaine plus IP meperidine achieved adequate pain relief after laparoscopic tubal ligation. These authors suggested that the observed analgesia was probably produced by the local anesthetic effect of meperidine observed both in vitro and in vivo. In the present study, the lower pain scores and analgesic requirement in the RM Group than those in the R and C Groups during the first hour after surgery suggest that meperidine was effective as an opioid in preventing early postoperative pain.

Shoulder pain may occur in as many as 63% or as few as 35% of patients undergoing laparoscopic surgery.[3] The prolonged presence of shoulder tip pain suggests excitation of the phrenic nerve. This pain is present often after laparoscopy associated with persistent pnemoperitoneum, sometimes for as long as three days. There is a statistically significant correlation between the width of the gas bubble and pain score, and this can be reduced by aspiration of the gas under the diaphragm, the use of a gas drain or application of local anaesthesia under the diaphgram under direct vision, through an irrigation device or through a sub-phrenic catheter.[3] The incidence of shoulder pain was found to be 50-75% in the present study, where the gas under the diaphragm was repeatedly suctioned.

We did not observe any side-effects attributable to the local anesthetic, such as shivering, nausea, dizziness, confusion, seizures or cardiac arryhthmias. The plasma concentrations of local anesthetic were not measured, but the doses of ropivacaine used in our study were lower than those thought to cause systemic toxicity. Some reports have shown the range of mean plasma concentration to be 2.93-3.76 µg/mL after the IP administration of 150-300 mg plain ropivacaine.[19] Maestroni et al.,[24] found the lowest plasma concentration of ropivacaine to be 0.35 µg/mL at 15 min and the highest plasma concentration of ropivacaine to be 2.2 µg/mL at 2 h after administering 5 mg/kg ropivacaine in 200 mL saline through the IP route in patients undergoing laparoscopic cholecystectomy. Labaille et al.,[19] reported no systemic toxicity after the IP administration of 300 mg ropivacaine in patients undergoing laparoscopic cholecystectomy and similar to our study, no plasma concentrations were determined.

In summary, the IP infiltration of 7.5% ropivacaine plus meperidine reduced pain scores and analgesic requirement during the first one hour after gynecologic laparoscopy compared with the IP infiltration of ropivacaine or saline. Although the present study failed to show the efficacy of IP ropivacaine or ropivacaine plus meperidine in preventing postoperative pain beyond one hour, further research is needed to evaluate the timing and the localization of IP analgesia for gynecologic laparoscopy.

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