TRANSCERVICAL INTRAPERITONEAL ANALGESIA AFTER OPERATIVE GYNECOLOGICAL LAPAROSCOPY: IS IT AN EFFECTIVE?

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ABSTRACT

The study investigates the effect of transcervical intraperitoneal analgesia with meperidine versus bupivacaine, or combination of both after gynecological laparoscopic ovarian cystectomy.

Sixty patients were enrolled in a randomized double blind study. All patients underwent laparoscopic ovarian cystectomy. Patients were classified into four equal groups, group Meperidine: received intraperitoneal (IP) meperidine 100 mg and IM saline, group Bupivacaine: received IP local anesthetic bupivacaine (10ml saline + 10ml bupivacaine 0.5%) and IM saline, group Bupivacaine+: received IP combination of meperidine 100 mg and bupivacaine (0.25% after dilution in the 20ml syringe) and IM saline, and Control Group: received IP saline and IM meperidine 100 mg. Postoperative pain was assessed both at rest and on movement at arousal, 2, 4, 6, 12, and 24 hours postoperatively. The patients were asked to rate the severity of pain via a visual analog scale (VAS). If the VAS was greater than 3, 2mg morphine was administered IV and could be repeated on demand and the total dose of postoperative morphine were recorded for 24 h.

Throughout the postoperative observational period, the pain scores were significantly less in group bupivacaine+ ($P < 0.01$) than in other goups. The greatest difference was seen at 2, 4 hr ($P < 0.001$) in the pain scores measured at rest and on movement, and the least differences between the four groups was observed at arousal (20-30 min) and at 24 h both at rest and on movement ($P < 0.05$). The total dose of IV morphine used over 24 hr was lower in group bupivacaine+ 4mg used by 2 patients and the highest dose used in group control (22mg). Most of opioid used between 2, and 4 hrs postoperative period. The percentage of patients satisfactions was higher in group bupivacaine+ and lowest in control group during 24 hr observation in the PACU.

IP administration of meperidine combined with bupivacaine provides better postoperative analgesia. Moreover this combination lowers opioid consumption, without side effects, and better patient satisfaction than each one alone after gynecological laparoscopic ovarian syctectomy.

Keywords: Laparoscopy; Local anesthetic; Meperidine; Intraperitoneal.

Accepted for publication: July 22, 2009

INTRODUCTION

Laparoscopic surgery is associated significantly less pain, earlier discharge from hospital, and more rapid convalescence than equivalent procedures performed by minilaparotomy [1,2]. However patients undergoing laparoscopic procedures do experience postoperative pain, especially in the upper and lower abdomen, back, and shoulder regions [3,4]. There are four

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components of pain after laparoscopic gynecologic surgery. Scapular pain secondary to peritoneal insufflations occurred, especially when shoulder holder and exaggerated trendelenberg position are used. This pain tends to increase after the eighth postoperative hour, appears during the night after surgery, and may even hinders sleep. Infiltration of local anesthetics has been reported to decrease scapular pain [5,6]. Visceral pain has its maximal intensity during the first hours and is exacerbated by coughing, respiratory movements, and mobilization. It requires morphine administration when patients awaken from anesthesia. Morphine however, is only partially effective and cannot completely eliminate pain caused by pelvic inflammation and traction on the uterine tubes. The fact that the pain comprises several components accounts for the necessity of multimodal analgesic techniques to provide effective postoperative analgesia.[7] Local anesthetic infiltration attenuates postoperative pain after laparoscopic cholecystectomy [8-11], however only a few reports are available on the efficacy of intraperitoneal (IP) local anesthetic administration for analgesia after laparoscopic gynecologic surgery [12-14]. Some investigators have confirmed that the IP delivery of drugs is a simple and effective method of reducing the intensity of post-laparoscopic pain [13]. However, other investigators have not been able to confirm the analgesic efficacy of IP local anesthetics [9,15]. The administration of IP opioids for the relief of postoperative pain has received little attention. Some reported that IP administration of morphine failed to provide analgesia after laparoscopy [16]. Unlike morphine, meperidine is a synthetic opioid of the phenylpiperidine series, which has local anesthetic effects both in vitro and in vivo [17,18]. Armstrong et al. showed that addition of meperidine to local anesthetic for IV regional anesthesia increased the speed of onset and slowed the recovery of the blockade. IP meperidine may have the potential to provide additional analgesic benefits because of this combined opioid agonistic and local anesthetic properties [18].

This study investigates the effect of transcevical intraperitoneal analgesia with meperidine versus bupivacaine, or combination of both after gynecological laparoscopic ovarian cystectomy.

PATIENTS AND METHODS

This is a randomized double-blinded study. It was conducted at Sohag University Hospitals (SUH) during the period from March 2008 to June 2009. Sixty patients scheduled for laparoscopic ovarian cystectomy and aged 20 years or older were included. The study was approved by the faculty ethical committee. A written informed consent was obtained from those who were welling to participate in this study. All patients were ASA I physical status. Patients with hepatic, vascular, metabolic, or cardiac disease were excluded. Any patient with contraindication to meperidine or local anesthetics was also excluded. Also, patients were withdrawn from the study if the surgical plan was changed, consequently their randomization number were reallocated.

All laparoscopies were conducted under general anesthesia without premedication. Intraoperative monitoring consisted of electrocardiogram, oxygen saturation, $ETCo_2$, and noninvasive blood pressure. Anesthesia was induced with propofol (2.5-3 mg/kg) and fentanyl 2mg/kg IV. Tracheal intubation was facilitated by vecuronium 0.1 mg/kg, and the lungs were ventilated with intermittent positive pressure adjusted to keep $ETCo_2$ between 30-40 mmHg. Anesthesia was maintained with isoflurane 1.5 %. All patients received

ondansetron 8 mg IV after induction of general anesthesia. Surgery was conducted in the lithotomy and trendelenberg position.
At the end of the operation and before abdominal deflation, a 12 F Foley's catheter was introduced through the cervix to the uterine cavity and the balloon inflated with 2-3 ml saline and then syringe 20 ml containing the study drugs according to group allocation injected through the catheter after clamping the distal end. The injected solution must visualized coming through the tube to peritoneal cavity by the laparoscopy.
Patients were assigned to 1 of 4 groups, 15 patients each. Meperidine group: received IP meperidine 100 mg (50 mg/ml) in 18 ml saline and IM 2 ml saline, Bupivacaine group: received IP local anesthetic (LA) bupivacaine (10ml saline + 10ml bupivacaine 0.5%) and IM 2 ml saline, Bupivacaine+ group: recived IP combination of meperidine 100 mg (50 mg/ml) + 10 ml bupivacaine 0.5% + 8 ml saline and IM 2 ml saline and Control group: received IP 20 ml saline and 100 mg meperidine (50 mg/ml) IM. Postoperative observation and follow-up were done by doctors and nurses unaware of study group allocation.
Postoperative pain was assessed both at rest and on movement (patients was asked to move from supine to the sitting position) at arousal (20-30 min), 2, 4, 6, 12, and 24 hours postoperatively. The patients were asked to rate the severity of pain via a visual analog scale (VAS) ranging from no pain (0 cm) to worst possible pain (10 cm). The use of these measures was explained to all patients before surgery. An independent investigator blinded to the treatment group obtained the scores. If the VAS was greater than 3, 2mg morphine was administered IV and could repeated on demand and total doses of postoperative morphine were recorded until 24 hour. In the PACU and at 2 hours, patients were questioned directly about symptoms potentially suggested of local anesthetic toxicity (e.g., tinnitus, circum-oral numbness, twitching). At 2, 4, 6, 12, and 24 hours, post-operative nausea and vomiting (PONV) was rated on four point scale (0 = no PONV, 1 = only nausea, 2 = mild vomiting successfully treated by ondansetron 4mg, 3 = heavy vomiting requiring repeated dose of ondansteron 4mg and additional of other treatments). At 24 hour, patients were asked about the intermittent cramping pain, indicative of visceral pain; shoulder tip pain, indicative of sub diaphragmatic peritoneal pain; and satisfaction with pain relief according to Kubler-Ross scores (denial=1, anger=2, depression=3, bargaining=4, acceptance=5) and we considered that score 4 and 5 was satisfaction.

Statistical analysis

Statistical analyses were performed using SPSS version 13 for windows (SPSS Inc., Chicago, IL, USA). Most of data were presented as mean±SD, other data were presented as number and percentage. Comparison among groups was done using kruskal-Wallis test and for comparison between two groups Mann-Whitney test was used for non parametric data. ANOVA test was used for comparison among groups and t-test was used for comparison between two groups for parametric data. Percentages were compared using Chi-squared analysis test. P values < 0.05 were considered statistically significant.

RESULTS

Ten patients ask for discharge from the hospital after 12 hour, 4 of them were from Bupivacaine+ group, 3 from Meperidine group, 2 from Bupivacaine group, and 1 from Control group. The ages, heights and weights of the patients were comparable in the four groups (Table I).

Table I. Patients characteristics

	Meperidine n = 15	Bupivacaine n = 15	Bupivacaine+ n = 15	Control n = 15
Age in years	34.7±4.2	32.5±6.5	37.5±4.6	38.2±5.7
Weight in kg	80.3±2.7	77.3±3.8	75.5±7.5	78.4±5.3
Height in Cm	165.6±6.8	170.4±5.7	173.8±4.7	168.8±5.9

Data are expressed as mean±SD

There was no significant difference between the 4 groups regarding cyst diameter, operative time and Co_2 consumptions (Table II).

Table II. The operative data in each group

	Meperidine n = 15	Bupivacaine n = 15	Bupivacaine+ n = 15	Control n = 15
Cyst diameter(Cm)	8.7±1.2	7.2±0.8	9.1±0.6	8.6±0.9
Operative time (min)	67.3±19.3	72.5±21.1	69.6±15.2	6 3.4±18.3
Co2 consumptions(liter)	48.2±15.6	53.5±10.3	47.6±14.3	44.1±14.8

Data are expressed as mean±SD

Throughout the postoperative observational period, the pain scores were significantly less in Bupivacaine+ group ($P < 0.01$) than in other goups. The greatest difference was seen at 2, 4 hours ($P < 0.001$) in the pain scores measured at rest and on movement, and the least differences between the four groups was observed at arousal and at 24 h both at rest and on movement ($P < 0.05$) (Table III and IV).

Table III. Pain scores (VAS) at rest in each group

	Meperidine n = 15	Bupivacaine n = 15	Bupivacaine+ n = 15	Control n = 15
After arousal	2.3±0.9	2.9±0.9	2.1±0.9	3.5±1.8
2 hour	2.1±0.8	2.9±0.8	0.9±0.5	2.9±1.8
4 hour	1.9±0.6	1.5±0.8	0.7±0.4	2.2±1.5
6 hour	1.6±0.6	1.4±0.7	0.7±0.2	2.1±0.8
12 hour	0.9±0.5	1.4±0.6	0.4±0.6	2.2±0.8
24 hour	0.7±0.4	1.2±0.5	0.3±0.1	2.2±0.4

Data are expressed as mean±SD

Table IV. Pain scores (VAS) on movement in each group

	Meperidine n = 15	Bupivacaine n = 15	Bupivacaine+ n = 15	Control n = 15
After arousal	2.5±0.8	3.2±0.2	2.8±0.9	3.5±1.9
2 hour	2.3±0.8	2.9±0.8	1.2±0.5	2.9±1.9
4 hour	1.9±0.6	1.8±0.8	0.9±0.4	2.1±1.5
6 hour	1.9±0.3	1.4±0.7	0.7±0.3	2.9±0.6
12 hour	0.9±0.7	1.4±0.6	0.4±0.8	2.8±0.7
24 hour	0.7±0.6	1.2±0.5	0.3±0.2	2.2±0.5

Data are expressed as mean±SD

The total dose of IV morphine used over 24 hour was lowest in Bupivacaine+ group and the highest dose used in Control group ($P < 0.05$). The percentage of patients satisfied was highest in Bupivacaine+ group and lowest in Control group ($P<0.05$) (Table V).

Table V. Total dose of morphine used and patients satisfaction in each group

	Meperidine n = 15	Bupivacaine n = 15	Bupivacaine+ n = 15	Control n = 15
Total dose in mg in 24 hour	10±3.5	20±2.8	4±2.6	22±4.9
No. of pt. satisfied Percentage	12 (80%)	6 (40%)	14 (93.3%)	3 (20%)

Data are expressed as mean±SD, number and percentage

There was no significant difference between the four groups as regard PONV. No patient reported symptoms of either local anesthetic or meperidine toxicity during 24 hour observation in the PACU.

DISCUSSION

Our trial to inject the analgesics through Foley's catheter, as the analgesics passed from the uterus to the peritoneum through the fallopian tube came in contact with the operative sites with better spread into the peritoneum and solutions injected would not washed out. Also, of great concern, passing of injected fluids through the tube eliminate an important component of pain due to traction on the follapian tubes and this is in agreement to Andrei Goldstein et al 2000, who stated that tubal traction is one of important cause of pain after laparoscopy[7]. In the present study, after gynecological laparoscopic ovarian cystectomy, the administration of IP meperidine and bupivacaine through Foley's catheter passing the cevix resulted in lowest pain scores (both at rest and on movement) and reduction of postoperative opioid administration. Also satisfactory postoperative analgesia was significant after IP meperidine than that of IP bupivacaine and IM meperidine. Schulte-steinberg et al.[16] examined pain after laparoscopic cholecystectomy in patients receiving IP morphine and

found no analgesic effects. 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 local anesthetic properties of meperidine appear to be superior to the other opioids. The effects of meperidine appear to be produced by its actions on two independent pathways: the opioids receptor pathways, which sub serve local anesthetic action[17].these local anesthetic actions appear to be independent of its opioid analgesic activity when administered topically in the subarachnoid space, epidural, or on exposed nerve in experimental studies. Meperidine, a side from producing a local anesthetic effect when used alone, has also been shown to potentiate the degree of block produced by other established local anesthetics[18]and this explained superior analgesia in group of combined IP meperidine and bupivacaine than each one alone. The effects of meperidine in our study may result from systemic activity. It 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. Although the same dose of meperidine was administered IM in the control group, it is difficult to separate the local and systemic effects of meperidine in this study. Our results which essentially compared the analgesic effects produced by equivalent doses of meperidine administered IM or IP with or without local anesthetic, suggest that the observed differences may be produced by the local effects of meperidine, specifically its known local analgesic properties acting on visceral peritoneum. Shaw et al.[19] reported no benefit from the IP instillation of very dilute LA at gynecological laparoscopic surgery. The influence of volume on efficacy or absorption from the peritoneal cavity is unknown, but our use of a high concentration should have maximized the chance of detecting an improvement on pain relief.[20] Studies comparing pre-surgical and post-surgical instillation of IP LA have produced conflicting results,[21]but recent meta-analysis indicates a larger reduction in pain when administered before surgical dissection,[6-11]however Goldstein et al.[22]reported opioid dose-sparing after gynecologic laparoscopy when bupivacaine was instilled, both at the surgical site and bilaterally under the diaphragm and this was consistent with our findings. Also a subsequent study revealed that plasma concentrations of lidocaine and bupivacaine after IP instillation of quite large doses of local anesthetic did not approach toxic plasma concentrations.[23]Subsequently, it was shown that after laparoscopic cholecystectomy, pain was reduced after administration of 20 ml of 0.25% bupivacaine into the region of the gall bladder during surgery; although plasma concentrations of local anesthetic were not measured, no patient exhibited clinical signs of toxicity.[24]Our findings were also consistent with these studies.

In conclusion, an analgesic regimen involving the IP administration of meperidine (100mg) combined with bupivacaine (20 ml 0.25%) provide better postoperative analgesia after gynecological laparoscopic ovarian cystectomy. Moreover this combination lowers opioid consumption, without side effects and better patient satisfaction than each drug alone and this IP instillation can be successively administered through Foley's catheter passing through the cervix.

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