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Research Article

Vaginal Cuff Infiltration with a Local Anesthetic for Postoperative Pain after Laparoscopic Hysterectomy: A Randomized Control Trial

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2. Key words

Laparoscopy; Hysterectomy; Local analgesia;Vaginal wound; Postoperative pain

1. Abstract

1.1. Objective: To assess the effect of local infiltration of anesthetic to the vaginal cuff on postoperative pain after laparoscopic hysterectomy.

1.2. Methods:A single-center, randomized trial. Women assigned to laparoscopic hysterectomy were randomly divided into two groups. In the intervention group (n=41) the vaginal cuff was infiltrated with 10 ml of ropivacaine (7.5 mg/ml) at four points, in addition to trocar-site anesthesia. In the control group (n=40) only trocar incisions were infiltrated with local anesthetic.The primary outcomes were postoperative opioid (oxycodone) use, and postoperative pain in visual analog scale (VAS). Secondary outcomes were emesis, bleeding, operative time, time to discharge and complications.

1.3. Results: The number of patients with minimal pain i.e. VAS scores for pain below 3 was significantly higher in the intervention group than in the control group (17 vs. 8, p=0.04). Otherwise, there were no significant differences between the groups in VAS scores for pain, the use of opioids or in any other variables.

1.4. Conclusion: Injection of local anesthetic into the vaginal cuff along with trocar sites analgesia did not affect the use of oxycodone, but increased the number of women experiencing only minor pain after laparoscopic hysterectomy. Local anesthesia of the vaginal cuff was feasible and safe.

3. Introduction

Laparoscopy is the preferred surgical approach in gynecologic surgery because it diminishes pain and enhances recovery. Laparoscopic hysterectomy is one of the most common gynecological procedures in Finland: Forty-four % of the 5279 hysterectomies performed in 2006 were vaginal, 32% laparoscopic and 24% abdominal [1, 2]. Patients undergoing the laparoscopic approach still require opioid analgesics in the early postoperative period, which increases the risk of opioid-related side effects, such as vomiting, nausea, obstipation and sedation. These symptoms may delay mobilization, home discharge and recovery. Opioid-free or opioid-reduced analgesia are used to reduce postoperative pain and opioid-related side effects in multimodal regimens [3-6]. The one of basic principles of ERAS (Enhanced Recovery after Surgery) is a focus on regional anesthetic and no opioid analgesic approaches [7]. Local analgesia/anesthetic infiltration is effective for the early treatment of postoperative pain in various surgical procedures [8-12]. Infiltration relieves postoperative pain and reduces opioid use after abdominal/and vaginal hysterectomy [8, 9], genital prolapse surgery [10, 11] and gynecologic

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laparoscopic surgery [13]. However, vaginal cuff infiltration with a local anesthetic for pain relief after laparoscopic hysterectomy has not been described or assessed. The present randomized controlled study tested the hypothesis that local infiltration of the vaginal cuff at the end of laparoscopic hysterectomy could decrease postoperative pain and opioid use.

4. Materials and Methods

This randomized controlled, open-label trial was performed at department of Obstetrics and Gynaecology, Helsinki University Hospital between November 2014 and May 2015. All gynaecologic surgery in the Helsinki metropolitan region is centralised in this tertiary referral hospital. Women scheduled for laparoscopic hysterectomy with salpingectomy or salpingo-oophorectomy for benign conditions or a malignant condition that only required simple hysterectomy (e.g., cervical in situ carcinoma, low-risk endometrial cancer or prophylactic hysterectomy with an inherited risk of genital cancer) were assessed for eligibility. All candidates were interviewed at the preoperative visit to obtain a detailed general, gynaecologic and operative history. A complete physical and gynaecological examination, including body mass index (BMI) measurement and transvaginal ultrasonography, were performed. The exclusion criteria were endometriosis, contraindications to any of medications used in the study (oxycodone, ketoprofen, or paracetamol), language difficulties (inability to understand and speak Finnish or Swedish). The criterion for inclusion was a uterine size less than uterine size at 14 weeks of pregnancy. Participants were given information orally and in writing, and a signed consent form was obtained from all women. Participants were randomly allocated into two groups: an intervention group (IG; n=41) that received local anaesthetic infiltration to the vaginal cuff, and a control group (CG; n=40) that did not receive vaginal cuff infiltration.

Therandomizationofparticipantsintotheirrespectivegroupswas performed using a computer-generated randomization program. The personnel responsible for generating the randomization list and sealing the envelopes did not participate in the allocation. The allocation cards were sealed in opaque, sequentially numbered envelopes. A surgeon opened the envelopes in the operating room prior to surgery.

All surgeries were performed under general anesthesia. The anesthesiology protocol and use of local anesthetics were standardized. Each patient received 1 g paracetamol as premedication and antibiotic prophylaxis at induction (cefuroxime, 1.5 g or clindamycin, 600 mg in cases of allergy). Standard monitoring was used in the operating theatre. Anesthesia was induced and maintained with a controlled infusion of propofol and remifentanil. Tracheal intubation was facilitated with rocuronium. Patients were ventilated with a mixture of oxygen and air. The stomach was always aspirated. All patients received dexamethasone (5 mg) at the start of anaesthesia and ondansetron (4 mg) with droperidol (0.1 mg/10 kg) at the end of surgery to prevent postoperative emesis. Each patient also received fentanyl (1 mg/kg) and ketoprofen (100 mg) at the end of the procedure for pain control.

Patients were placed in the lithotomy position for the standardized laparoscopic procedure. A uterine manipulator (Valtchev Uterine Mobilizer, Conkin surgical instruments, Vancouver, Canada) was used to expose the uterus and pelvic structures. Pneumoperitoneum was created using a Veress needle (Mock Medical, Milford, USA) through the umbilicus, and a 10-mm umbilical trocar was inserted for optics. Three 5-mm trocars were inserted in the left and right paramedian regions and the suprapubic region under direct visualization. Bipolar cautery was performed to coagulate vessels, and scissors were used to dissect tissue. The uterus and fallopian tubes, with or without ovaries, were detached, circular colpotomy was performed, and the uterus was removed through the vagina. The vaginal cuff was closed using a continuous vertical Biosyn 2-0 (Covidien, Dublin, Ireland) suture vaginally. In the intervention group the vaginal cuff was infiltrated with 10 ml of ropivacaine (7.5 mg/ml) at four points around the wound in equal 2.5 ml volumes, 4–5 mm deep. In both groups the fascia of the 10-mm port and all skin incisions were closed using absorbable sutures. Five milliliters of ropivacaine (20 ml in total, 7.5 mg/ml) was infiltrated into each trocar incision between the skin and fascia in both groups. A Foley catheter was left in place until the next morning, but no abdominal drains were used. Postoperative pain was treated using intravenous or intramuscular oxycodone, and the amount of medication was recorded. Patients also received ibuprofen (600 mg) and paracetamol (1 g) three times daily, which they continued at home. The use of oxycodone was liberal. The women were asked to scale their pain, and they received oxycodone (3 mg) if they reported a VAS score >5 in the post-anesthesia care unit and surgical ward. Patients recorded the severity of incisional pain using VAS score (0 indicated no pain, and 10 indicated unbearable pain) at 1, 3, 6, 12 and 24 hours after surgery. VAS-rating of <4 correspond to mild pain, 4-6 to moderate pain, and 7-10 to severe pain [14]. The operative time, emesis, amount of operative bleeding, uterus weight and complications were retrieved from patient files. The length of hospital stay was counted from the end of surgery until discharge.

The local Ethics Committee of Helsinki and Uusimaa district approved the study design (98/13/03/03/2014/2). This study was

also registered at clinicaltrials.gov as NCT02767544 retrospectively.

4.1. Power calculation

The size of the sample was estimated from previous publications. Based on earlier data from our clinic we assumed that the need for oxycodone would be 30 mg within 24 hours after laparoscopic hysterectomy [15-17]. Vaginal wound infiltration with local anesthetic was estimated to reduce the need of oxycodone to 10 mg (SD 15). The study would require 37 patients per group with 80% power (a=0.05) using a two-sample t-test. A 10% drop-out rate was assumed, and 40 patients were needed in each group.

4.2. Statistical analysis

All analyses were performed using SPSS software, version 20 (IBM SPSS Inc., IL, USA). Data are presented as medians and interquartile ranges (IQRs) or n (%). Differences in continuous variables were analysed using the Mann–Whitney U-test for skewed data. Chi-square or Fisher's exact tests were used for independent nominal data where appropriate. Statistical significance was defined as $p<0.05$. The 95% Confidence Interval (CI) for differences of proportions were calculated using Newcombe's method.

5. Results

The eligibility of 105 women was assessed for this trial. Nineteen women were excluded because they did not fulfil the inclusion criteria (four did not speak Finnish or Swedish, six had medical contraindications and nine declined the invitation to participate). Eighty-six women were randomised (n=43 per group). There were two drop-outs in the intervention group (protocol violation) and three drop-outs in the control group (two laparoscopy converted to laparotomy and one protocol violation). Therefore, 81 cases were analysed (**Figure1**). **Table 1** describes the basic demographic characteristics of these women, and **Table 2** presents the indications for hysterectomy. There were no significant demographic differences between groups in the age, BMI, painkiller chronic use, previous abdominal surgery, ASA physical status and parity.

The total dose of oxycodone used was equal (10 mg [6–16 mg] and 10 mg [6–17 mg]; p=0.63) in the intervention and control groups, respectively (**Table 3**). VAS scores for pain at 1, 3, 6, 12 and 24 hours after surgery and median maximal pain did not differ statistically significantly between groups. No differences in the operative bleeding, operative time, time to discharge, postoperative emesis or major complications between the study groups were found. The mean uterine weight was similar in the two groups (81 g vs. 81.5 g; p=0.82). Morcellation was not used for uterine removing. However, all asked VAS scores for pain at 1, 3, 6,12 and 24 hours postoperatively were less than 3 during the entire postoperative study period in 17 patients in the intervention group and eight patients in the control group, which was statistically significant (p=0.04). No complications (allergic reaction, iv injection or the use of the anesthetic itself) were related to the vaginal cuff infiltration with local anesthetic.

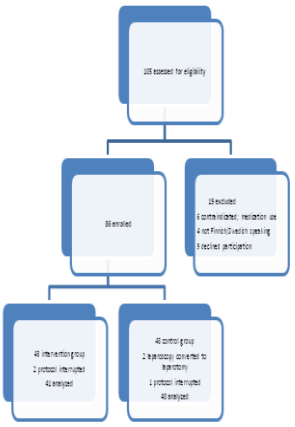

Figure 1: Flow chart of study randomization.

Picture 1. Ropivacaine injection sites around vaginal incision.

Table 1. Demographics of the women undergoing laparoscopic hysterectomy

Variable	Intervention group (n=41)	Control group (n=40)
Age (years)	56 (48–66)	58 (45–69)
BMI (kg/m^2)	27 (22–31)	25 (23–29)
Painkiller chronic use	4 (9%)	1 (2%)
Previous abdominal surgery	27 (66%)	21 (53%)
ASA physical status		
I A normal healthy patient	10 (24%)	17 (43%)
II A patient with mild systemic disease	24 (59%)	17 (43%)
III A patient with severe systemic disease	7 (17%)	6 (14%)
Nulliparous	9 (22%)	8 (20%)
Previous vaginal delivery	32(78%)	32 (80%)

Data are presented as median (IQR) or n (%).
ASA: American Society of Anesthesiologists

Table 2. Indications for laparoscopic hysterectomy.

	Intervention group (n=41)	Control group (n=40)	*p*-value
Atypical adenomatous hyper-plasia	12 (29%)	14 (35%)	0.58
In situ cervical carcinoma	7 (17%)	7 (17%)	0.96
Low-risk endometrial cancer	5 (13%)	5 (13%)	0.97
Menorrhagia	13 (32%)	11 (28%)	0.68
Adenomyosis	1 (2%)	2 (5%)	0.54
Prophylactic hysterectomy (increased inherited risk of genital cancer)	3 (7%)	1 (2%)	0.32

Values are n (%).

Table 3. Use of oxycodone, pain (VAS scores), operative time, bleeding and time to discharge among the women undergoing laparoscopic hysterectomy.

Variable	Intervention group n=41	Control group n=40	*p*
Oxycodone (mg)	10 (6 to 16)	10 (6 to 17)	0.63
VAS 1h	2 (0 to 2)	3 (0 to 4)	0.76
VAS 3h	1 (0 to 2)	0 (0 to 3)	0.68
VAS 6h	0 (0 to 2)	1 (0 to 2)	0.16
VAS 12h	0 (0 to 1)	0 (0 to 1)	0.88
VAS 24h	1 (0 to 3)	1 (0 to 2)	0.96
VAS < 3 continuously for 24h	17 (41.5%)	8 (20.0%)	0.04*
VAS max	3 (2 to 4)	4 (2 to 4)	0.31
Postoperative emesis	5 (12)	5 (13)	0.97
Operative time (min)	100 (70–133)	115 (80–125)	0.41
Bleeding (ml)	50 (0–200)	100 (0–200)	0.793
Major complication	0	0	n. s.
Time to discharge (hours)	22.25 (20.75-24.00)	22.25 (21.00-23.95)	0.97
Uterine weight (g)	81 (60–134)	81.5 (57–146)	0.82

* Difference 21.5, 95% Confidence Interval 1.3 to 39.4)
Data are presented as median (IQR) or n (%)

6. Discussion

To our knowledge, this report is the first study of the effect of vaginal cuff infiltration with local anesthetic in laparoscopic hysterectomy. We performed a randomized study to evaluate the feasibility and safety of local vaginal anaesthesia to relieve postoperative pain. Minimising the use of opioids supports enhanced recovery and discharge and prevents opioid-related side effects. There was no difference in the total use of oxycodone. However, postoperative local infiltration of the vaginal cuff with abdominal trocar incision analgesia increased the number of women who experienced only minor postoperative pain.

No difference in the use of oxycodone was found between the groups, and the quantity of opioids used was equally minimal. A recent observational study [18] investigated the effect of pain medication after laparoscopic hysterectomy, without local anaesthesia, but using a delicate surgical technique. VAS pain scores in their study were low (mean VAS score <4), and the investigators discharged patients five hours after surgery. Paracetamol, naproxen and tramadol were used for pain medication in their study, but the quantities of these medications were not reported. Their laparoscopic technique was quite similar to ours in all other respects, except the suturing of the vaginal cuff. They sutured the vagina and the uterosacral ligaments laparoscopic ally, whereas we did it vaginally. The operative time was longer in our study, possibly because of the teaching role of our hospital. A team consisting of an expert surgeons and a trainee assistant performed all procedures. VAS scores were low in both studies despite the methodological differences. Vaginal local anesthesia in our study increased the number of patients with VAS scores less than 3 during the first 24 postoperative hours without adverse effects. Vaginal cuff anesthesia does not significantly lengthen operative time and as far as costs are concern, it is cheap.

Ropivacaine was used because of its safety profile, which is superior to bupivacaine. Ropivacaine exhibits fewer cardiovascular and central nervous system toxicities than bupivacaine in healthy volunteers. Ropivacaine exhibits efficacy that is generally similar to the same dose of bupivacaine in postoperative pain relief [19, 20]compared pre-incision infiltration of extended-release liposomal bupivacaine with 0.25% bupivacaine for port-site analgesia in traditional and robotic laparoscopic hysterectomy. Pain in the liposomal bupivacaine group was slightly lower, but they found no difference in opioid use or measures of function.

The strengths of our study were the randomized nature of the trial, the standardized protocols of the anaesthesia and surgical technique, the strict follow-up, documentation of pain and medication use and data of pain during 24 hours after surgery.

However, there are some limitations to our study. The first limitation is the estimation of the amount of oxycodone needed for postoperative pain. A re-calculation of the power analysis showed that a new study would need thousands of women in order to show a statistical difference in the need of oxycodone, if there is any. However, the unexpectedly low need for oxycodone could not be predicted. The use of oxycodone was lower than expected compared to earlier studies performed in our clinic [16, 17]. Our current use of concomitant local anaesthesia at abdominal trocar incision sites may partially explain the lower need for postoperative oxycodone in this study, in contrast to earlier studies in the same department. The similar and low use of oxycodone is likely to limit the conclusions that may be drawn. Another limitation is the frequency of eliciting VAS scores for pain, which were collected at 1, 3, 6, 12 and 24 hours postoperatively. These scores could have been recorded more

frequently. The time intervals of pain intensity reporting reflect normal clinical practice. However, no complications were related to the use of vaginal cuff infiltration.

7. Conclusion

The present single-centre randomized study demonstrated that vaginal cuff infiltration with local anesthetic, concurrently with abdominal trocar incision analgesia, was feasible and safe for postoperative pain relief. All women in this study required low quantities of postoperative oxycodone. Vaginal injection of ropivacaine at the end of laparoscopic hysterectomy increased the amount of women who experienced only minimal postoperative pain for the first 24 hours after surgery, with no impairments in surgical outcome.

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