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Less postoperative pain after laparoscopic hysterectomy than after vaginal hysterectomy

Satu M. Pokkinen · Maija-Liisa Kalliomäki · Arvi Yli-Hankala · Kari Nieminen

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Abstract
Purpose To find out whether the severity of acute postoperative pain differs between laparoscopic (LH) or laparoscopically assisted vaginal hysterectomy (LAVH) and vaginal hysterectomy.
Methods In a prospective, powered, non-randomized trial, the consumption of oxycodone and pain scores were evaluated in 164 women up to 20 h after VH or LH/LAVH. All hysterectomies were performed under standardized general anesthesia and the pain medication was similar in both groups. The primary endpoint was the cumulative oxycodone consumed. Main secondary endpoints were pain scores (numeric rating scale NRS), operative time and hospital stay.
Results The patients in LH/LAHV group consumed less opioid than the patients in the vaginal group during the 20 h period after surgery. The difference was significant at time point 4 and 6 h. The oxycodone consumed at time point 4 h was 19.9 (95 % CI 18.1–21.7) mg in laparoscopic group and 22.8 (20.7–25.0) mg in vaginal group ($p = 0.040$) and at time point 6 h was 23.5 (21.5–25.6) mg in laparoscopic group and 27.4 (24.7–30.0) mg in vaginal group ($p = 0.026$). Pain scores were lower after laparoscopic approach and the difference was significant at time point 60 min after surgery ($p = 0.026$).
Conclusion In this study, LH was associated with reduced need of analgesics and lower acute postoperative pain scores than VH.

Keywords Postoperative pain · Hysterectomy · Vaginal · Laparoscopy · Analgesics

Introduction

Hysterectomy is one of the most common surgical operations for benign causes. Earlier studies have shown that recovery after laparoscopic (LH) or vaginal (VH) hysterectomy is faster than after the abdominal (AH) approach [1, 2]. The laparoscopic technique takes a little longer time than the vaginal technique [1, 3–6] but it offers the advantage of viewing the intra-abdominal status and alleviates performing salpingo-oophorectomy [5, 7]. Regardless of many studies comparing different routes, the choice of route still depends on the surgeon's experience and on local preferences [2, 8]. The Cochrane review of 34 trials and American College of Obstetricians and Gynecologist (ACOG) committee opinion No 444 concluded that VH should be performed in preference to AH and where VH is not possible, LH has some advantage over AH [9, 10].

The management of acute postoperative pain is still challenging despite advances in postoperative pain therapy [11]. Inadequate treatment of severe acute pain results in suffering and prolonged recovery and it has been identified as a risk factor for persistent postsurgical pain [12] thus rendering a considerable impact on the costs at society level [13].

S. M. Pokkinen (✉) · M.-L. Kalliomäki · A. Yli-Hankala
Department of Anesthesia, Tampere University Hospital, PO Box 2000, 33521 Tampere, Finland
e-mail: satu.pokkinen@pshp.fi

A. Yli-Hankala
Medical School, University of Tampere, Tampere, Finland

K. Nieminen
Department of Obstetrics and Gynecology, Tampere University Hospital, PO Box 2000, 33521 Tampere, Finland

There are only a few trials comparing postoperative pain scores or consumption of analgesics between patients who underwent LH with patients who underwent VH. In the meta-analysis published in 2011 Gendy et al. [14] concluded that total laparoscopic hysterectomy (TLH) may offer benefits compared with VH. TLH was associated with reduced postoperative pain scores and reduced length of postoperative hospital stay. Do LH and laparoscopically assisted vaginal (LAVH) hysterectomy share the same benefits over VH is unclear.

This study was designed to compare postoperative pain after VH and LH or LAVH hysterectomy for benign causes. The primary outcome was the opioid consumption. Secondary outcomes were pain intensity, operative time, hospital stay, and blood loss.

Materials and methods

The study was carried out during the period October 2008 and March 2013 and a total of 182 women enrolled into the study. We obtained the written informed consent of 99 Finnish-speaking women, who were scheduled for vaginal hysterectomy (VH) with or without salpingo-oophorectomy for non-malignant conditions at Tampere University Hospital or Valkeakoski Regional Hospital. The LH group ($N = 83$) was obtained from our other study conducted simultaneously, comparing two different techniques of anesthesia. In that study the patients, who were scheduled for laparoscopic hysterectomy, were randomized into group propofol anesthesia or sevoflurane anesthesia. The patients who were anesthetized with propofol formed the LH group to the present study. The study design was approved by the Ethics Committee (R09003) and registered with ClinicalTrials.gov (NCT01442961). The inclusion criteria were younger than 70 years, American Society of Anesthesiologists (ASA) physical status classification I/II/III and body mass index <35 kg/m^2. The exclusion criteria were diabetes, liver disease, present use of opioids, uterine prolapse and allergies to any of the study medications.

The type of hysterectomy (AH, LH or VH) was determined by the surgeon's preference before the written informed consent was obtained. The main reason for abdominal hysterectomy was enlarged uterus and these patients were not involved in this study. The route of surgery, laparoscopic or vaginal, was not strictly determined in the protocol.

All operations were performed under general anesthesia. The study patients were premedicated with peroral midazolam 7.5 mg and cetirizine 10 mg. In the operating room, standard monitoring was started. Anesthesia was induced and maintained with a target-controlled infusion of propofol [15] and remifentanil [16]. Tracheal intubation was facilitated with rocuronium, and the patients were mechanically ventilated with mixture of oxygen in air. The delivery of anesthetics was adjusted to maintain non-invasive arterial blood pressure and heart rate at $\pm$20 % of baseline, and State Entropy (Entropy, GE Healthcare, Helsinki, Finland) below 60. To prevent postoperative nausea and vomiting (PONV), all patients were medicated with IV dexamethasone 5 mg immediately after induction of anesthesia. At the end of surgery all patients were given IV paracetamol 1 g. When the surgery was completed, the remifentanil infusion was discontinued and IV bolus of fentanyl 0.05 mg was given. Neostigmine 2.5 mg with glykopyrrolate 0.5 mg IV was given to reverse neuromuscular blockade. The total amounts of infused remifentanil and propofol were recorded.

Surgical techniques

Vaginal hysterectomy (VH)

The technique for VH was briefly as follows. A local anesthetic containing lidocain and epinephrine was injected under the cervical mucosa. A circumferential incision was made and vaginal mucosa was dissected from the cervix. The peritoneal cavity was entered via posterior cul-de-sac. After that the parametrial tissue, uterine vessels, ovarian vessels and fallopian tubes or with patients undergoing salpingo-oophorectomy the infundibulopelvic ligaments were ligated with sutures and the uterus was removed. The vaginal wall was sutured with absorbable continuous suture.

Laparoscopic hysterectomy (LH)

LH group consisted of LH and LAVH. The pneumoperitoneum was created by inserting the Veress needle into the abdominal cavity through umbilicus or in the cases with suspected intra-abdominal adhesions the Hasson's technique was used for entry, a 10 mm trocar was used for camera. Additional three trocars of 5 mm were inserted laterally of both epigastric arteries and in the midline above symphysis. Bipolar forceps for electrocautery were used to create hemostasis. In LH uterine arteries were controlled laparoscopically whereas in LAVH vaginally with sutures. A local anesthetic containing lidocain and epinephrine was injected under the cervical mucosa before the vaginal incision and the uterus was removed through the vagina and the cuff was closed with vaginal continuous suture.

Both VH and LH group included hysterectomies or hysterectomies with oophorectomy.

In the post anesthesia care unit (PACU) postoperative pain was treated with patient-controlled analgesia (PCA) with oxycodone 1 mg/ml using 2 mg bolus of oxycodone

and a lock-out time of 10 min. The rescue pain medication was IV bolus of oxycodone 3 mg, if the pain was rated >3 on NRS pain scores (11-point numeric rating scale where 0 means no pain and 10 means worst pain imaginable) by the patient. During the ward stay the PCA was continued at least for 20 h after surgery and IV paracetamol 1 g was administered every 6 h. In case of nausea, the patients were given either a bolus of IV ondansetron 4 mg, and if needed IV droperidol 0.75 mg.

Data were collected up to 20 h after patients' arrival at PACU. The time the patient arrived at PACU was registered as time point 0. At time points 10 min, 20 min, 30 min, 60 min, 120 min, 4 h, 6 h, 20 h, the following data were collected: the cumulative amount of oxycodone, NRS pain scores at rest and with coughing, NRS scores for nausea, number of episodes of postoperative vomiting and sedation scores measured with a 4-point scale (0 = fully awake; 1 = awaked but still sedated; 2 = asleep but wakes to verbal command; 3 = unresponsive). The need for antiemetic medication was recorded.

Data regarding the patients' characteristics and surgical outcomes were collected from the patients' medical records.

Statistical analysis

The sample size estimation was based on the results of a previous study of laparoscopic hysterectomies, where the mean consumption of oxycodone was 0.45 (SD 0.24) mg/kg^2 during the first 24 postoperative hours [17], indicating a need of 75 patients per group to show 25 % inter-group difference with power of 0.8 and α of 0.05.

Data on patientś age, weight, height, and cumulative oxycodone consumption were analyzed using independent sample *t* test. NRS scores for pain, doses of antiemetic drugs, sedation, duration of surgery, weight of uterus and blood loss were compared using Mann–Whitney test. χ^2-test was used to analyze smoking habits, ASA, NRS scores for nausea, type of surgery, indication of surgery and hospital stay. Probability (p) values <0.05 were considered significant. The statistical analysis was performed using Statistical Package for Social Sciences (SPSS^{TM}), Windows version 20.0 (SPSS Inc.; Chicago, IL., USA).

Results

In the final analysis, there were 90 patients in the VH group and 74 patients in the LH group. The flow of the patients is presented in Fig. 1. One patient in the VH group was given IV ketoprofen 100 mg on the ward and one patient in the LH group underwent relaparoscopy 14 h after the first operation. These patients were included in the final analysis but the second one only up to six postoperative hours. Demographic data of patients are presented in Table 1.

The patients in the LH group consumed less oxycodone after surgery than the patients in the VH group. The difference was significant at time point 4 h ($p = 0.040$) and at time point 6 h ($p = 0.026$) after surgery (Fig. 2). NRS pain scores at rest were significantly lower in the LH group at time point 60 min ($p = 0.026$) after surgery (Fig. 3) as were the NRS scores for nausea. At the time point 60 min 97 % of patients had no nausea in the LH group compared with 84 % of patients in the VH group ($p = 0.002$), however, no difference in the need for antiemetic medication was found ($p = 0.098$). The difference in NRS pain scores with coughing was not significant at any observed time. The recovery from anesthesia was similar in both groups.

The indications of surgery differed partly in VH and LH groups. The most common main indication of surgery in both groups was uterine leiomyoma. In the LH group there were more salpingo-oophorectomies compared with the VH group, the duration of surgery was longer and the patients stayed for a longer time in hospital (Table 2).

Discussion

In our study the laparoscopic technique for hysterectomy was associated with reduced consumption of analgesics in the acute postoperative period compared with the vaginal technique. However, the intensity of pain and the need of analgesics varied considerably between patients.

Most of the studies comparing vaginal and laparoscopic approach have focused on the incidence of perioperative complications, the operative time and the length of hospital stay. To our knowledge only Ghezzi et al. [18] have shown in a randomized prospective trial having postoperative pain as the primary outcome that TLH is associated with lower postoperative pain scores and a reduced need for rescue analgesia compared with the vaginal approach. The findings of our study comparing VH with LH or LAVH are similar with those by Ghezzi et al. despite the difference in technique. In Finland the main technique for laparoscopic hysterectomy is either LH or LAVH and THL is performed rarely [19]. Other studies in the field have discussed pain measurement and management, but it has not been the primary focus of these studies. In the eVALuate trial by Garry et al. [2] a higher proportion of patients undergoing VH used opioids than patients undergoing LH and Soriano et al. [4] reported that the use of analgesics did not differ between LAVH and VH groups.

In our study the consumption of opioids was chosen as for the primary outcome and pain scores as secondary outcome, since ethically both of the groups should be allocated a similar level of analgesia, i.e. adequate pain

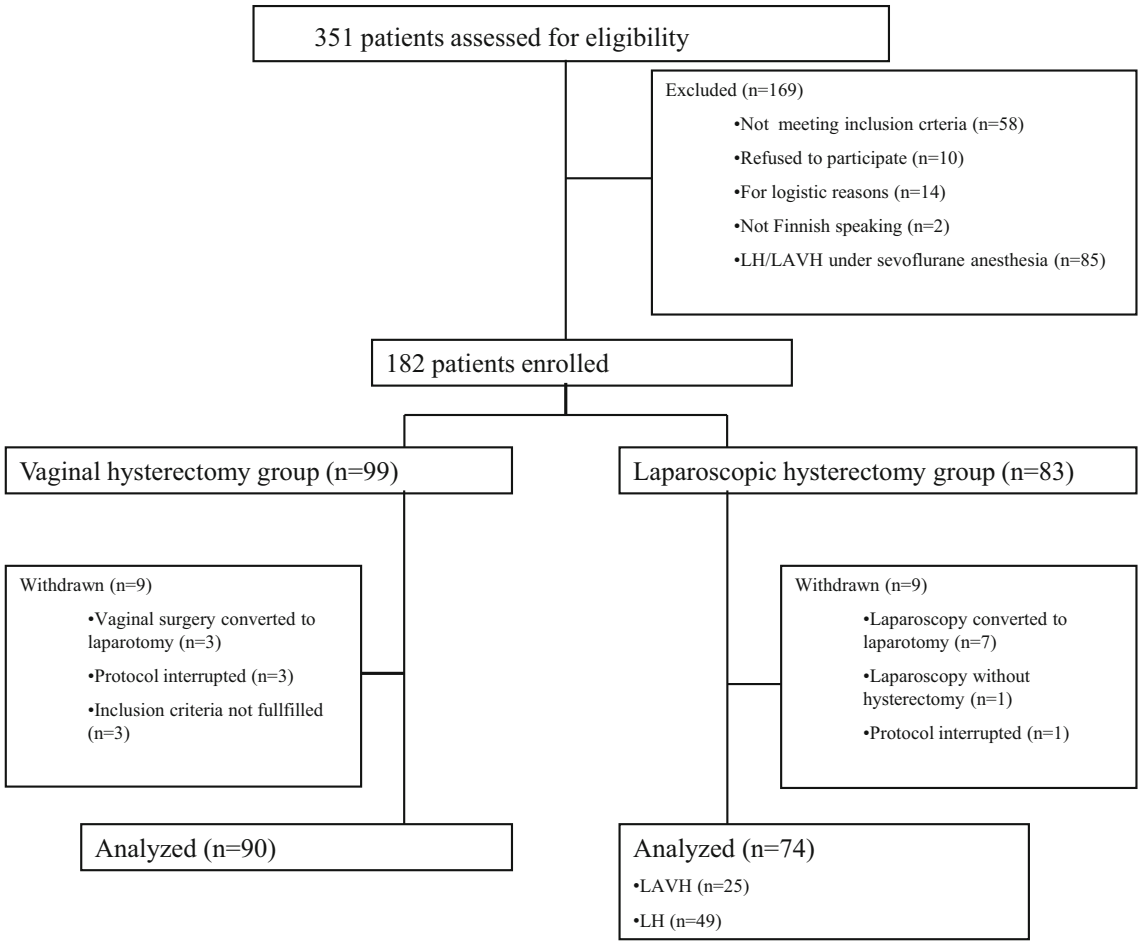

Fig. 1 Flowchart of the patients

Table 1 Demographic data of patients

	VH ($n = 90$)	LH ($n = 74$)	p value
Age (year)	47.5 (6.3)	50.2 (7.2)	0.013
Weight (kg)	71.1 (10.4)	70.7 (12.2)	0.841
Height (cm)	165.9 (4.9)	165.8 (6.0)	0.940
Smoking	24 (26.7 %)	10 (13.5 %)	0.043
Physical status			0.269
ASA 1–2	90 (100.0 %)	73 (98.6 %)	
ASA 3	0 (0.0 %)	1 (1.4 %)	

Values are mean (SD), *n* (%)

VH vaginal hysterectomy, *LH* laparoscopic hysterectomy, *ASA* American Society of Anesthesiologist physical status classification

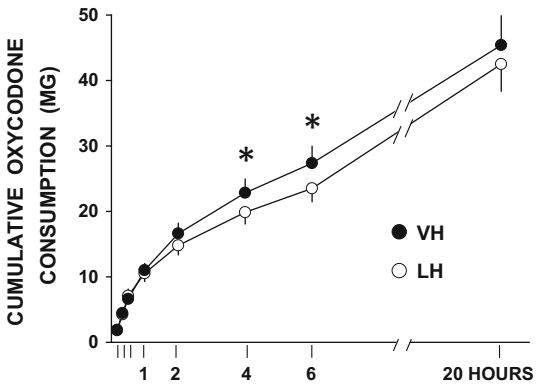

Fig. 2 Cumulative consumption of oxycodone (mean, 95 % CI) in patients who underwent laparoscopic hysterectomy (LH) or vaginal hysterectomy (VH) during the 20 h after surgery. The difference was significant at time point 4 h ($p = 0.040$) and at time point 6 h ($p = 0.026$)

treatment. The patients announced significantly higher pain scores in the postanesthesia care unit 1 h after vaginal surgery than after laparoscopic surgery. The cumulative consumption of oxycodone was increased thereafter in the VH group compared with the LH group although the statistical significance was found only at time points four and 6 h after surgery.

Minimal invasive surgical techniques have been indicated to reduce acute postoperative pain as has been shown in trials comparing abdominal hysterectomies with

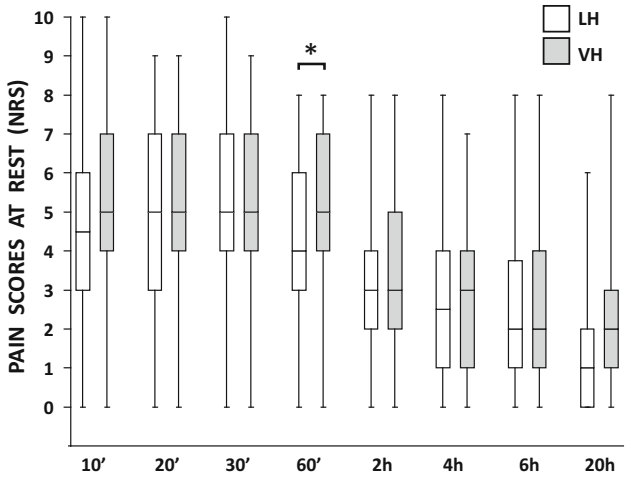

Fig. 3 NRS pain scores (median, 25th and 75th percentile range, minimum, maximum) at rest in patients who underwent laparoscopic hysterectomy (LH) or vaginal hysterectomy (VH) during the 20 h after surgery. The difference was significant at time point 60 min ($p = 0.026$)

laparoscopic hysterectomies [2, 7, 20]. Vaginal hysterectomy has been regarded as the most minimally invasive technique of hysterectomy whereas laparoscopic hysterectomy moderately invasive [21]. Yet, in our study, regardless of more salpingo-oophorectomies and a longer operation time, the patients in laparoscopic group experienced less postoperative pain. The management of bleeding differs between VH and LH and also this might affect the pain intensity. In the laparoscopic route electrocautery is used to create hemostasis whereas vessels are ligated with sutures in the vaginal approach. Even though there are many arguments supporting VH over LH, these findings of pain should not be ignored. In contrast to the findings of meta-analysis by Gendy et al. [14], in our study laparoscopy was associated with a longer hospital stay compared with vaginal hysterectomy. The reason for this is unclear, and could not be found in a retrospective analysis of the medical notes of the patients.

The first limitation of this study is the unexpectedly long enrollment period; the study was a one-site study carried out in Pirkanmaa Hospital District including Tampere University Hospital and Valkeakoski Regional Hospital. In the university hospital setting most of the gynecological patients are cancer patients or otherwise severely ill and the number of patients to be operated for benign causes is minor. The data were collected by the primary investigator, which also made challenges for the enrollment. The technique of surgery was not changed during the study enrollment. Thus, in our consideration the long enrollment period does not influence the results. The second limitation is lack of randomization. Randomization of patients into the study groups would be difficult because of

Table 2 Characteristics of surgery

	VH ($n = 90$)		LH ($n = 74$)		p value
	n	%	n	%	
Main indication of surgery					
Uterine leiomyoma	68	75.6	50	67.6	0.257
Menstrual disorders	15	16.7	13	17.6	0.879
Pelvic pain	6	6.7	3	4.1	0.465
Other	1	1.1	8	10.8	0.007
Type of surgery					
Hysterectomy with SO	6	6.7	42	56.8	<0.001
Hospital stay					<0.001
1 day	81	90	43	59[n]	
2–4 days	9	10	30	41[n]	

	VH ($n = 90$)		LH ($n = 74$)		p value
	Median	Q1–Q3	Median	Q1–Q3	
Duration of surgery (min)	64	46–78	131	104–167	<0.001
Estimated blood loss (ml)	109	50–200	143	50–350	0.338
Uterus weight (g)	216	150–330	200	135–334	0.486

VH vaginal hysterectomy, *LH* laparoscopic hysterectomy, *SO* salpingo-oophorectomy, *Q1* lower quartile, *Q3* upper quartile

[n] $n = 73$ one patient is not included because of relaparoscopy 14 h after the first operation

gynecologists own preferences to surgical routes. To make the groups comparable we excluded all patients with uterine descent. The uterine prolapse is one of the most common cause to choose the vaginal route, whereas the other causes are more dependent on gynecologists own preferences. Although there were some differences in the proportions of indications, the main indication of surgery was uterine leiomyoma in both groups and the weight of uterus was similar between groups.

In conclusion, we found that the LH is associated with less oxycodone use and lower NRS pain scores postoperatively than VH. The intensity of pain and the need of analgesics varied considerably between patients.

Conflict of interest The authors declare that they have no conflict of interest and they have full control of all primary data and agree to allow the journal to review the data if requested. No study sponsors have been involved.

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