The impact of mode of anaesthesia on postoperative recovery from fast-track abdominal hysterectomy: a randomised clinical trial

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Ninnie Borendal Wodlin, Lena Nilsson and Preben Kjölhede, The impact of mode of anaesthesia on postoperative recovery from fast-track abdominal hysterectomy: a randomised clinical trial, 2011, BJOG-AN INTERNATIONAL JOURNAL OF OBSTETRICS AND GYNAECOLOGY, (118), 3, 299-308.
which has been published in final form at:
http://dx.doi.org/10.1111/j.1471-0528.2010.02697.x

Title:

Fast track abdominal hysterectomy. The impact of mode of anaesthesia on postoperative recovery - a randomised clinical trial

by

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Running title: *Fast track hysterectomy and mode of anaesthesia*

Abstract

Objective: To determine whether the duration of hospital stay after abdominal hysterectomy in a fast track setting differed between women operated under general anaesthesia or in spinal anaesthesia with intrathecal morphine.

Design: An open randomised controlled multicenter study.

Setting: Five hospitals in the south-east of Sweden.

Population: One-hundred and eighty women scheduled for benign hysterectomy were randomised; 162 completed the study, 82 were allocated to spinal and 80 to general anaesthesia.

Methods: Fast track model comprising no use of sedatives for premedication, pre-emptive antiemetic therapy, i.v. fluid restriction, analgesics based on non-opioids, early enteral nutrition and mobilisation and standard criteria for discharge. Spinal anaesthesia with 20 mg hyperbaric bupivacaine and 0.2 mg morphine. General anaesthesia with propofol, fentanyl and rocuronium, and continuous propofol and ventilation with oxygen-in-air for maintenance of anaesthesia.

Main outcome measures: hospital stay; consumption of analgesics; vomiting; pruritus and bowel function recovery.

Results: Median hospitalisation did not differ significantly between women who had hysterectomy with spinal or general anaesthesia (46 and 50 hours, respectively). Spinal anaesthesia was associated with a significantly lower use of opioids and a faster recovery of bowel function, although vomiting and pruritus were more prevalent.

Conclusions: In a fast track model the duration of hospitalisation after abdominal hysterectomy was less than 50 hours independent of the mode of anaesthesia. Spinal anaesthesia reduced the need for post-operative morphine compared with general anaesthesia.

In order to improve patient recovery after gynaecological surgery further studies based on fast track programmes are needed.

Keywords: fast-track; general anaesthesia; hysterectomy; intrathecal morphine; randomised study; spinal anaesthesia.

The study was registered in ClinicalTrial.gov Protocol Registration System (NCT00527332) with initial release 09/07/2007.

Introduction

Hysterectomy is a common gynaecological operation. It is usually performed through laparotomy under general anaesthesia as an in-hospital procedure with duration of hospitalisation between 2-11 days (1). Medical factors such as postoperative pain, nausea and paralytic ileus may affect the length of the hospital stay. In addition, time to discharge may vary because of different medical and local traditions, as well as geographic and social differences. The concept of 'fast track surgery' has developed with the aim of reducing recovery times reflected in reduced hospitalisation (2). The fast track concept comprises providing the patient with preoperative education concerning pre-, per- and postoperative care, optimizing anaesthesia, and management of pain and nausea including a minimal use of opioids, early postoperative mobilization and enteral nutrition with intravenous fluid restriction perioperatively (3-5).

Optimizing anaesthesia and pain management in order to reduce the surgical stress response facilitates post operative recovery (2). The use of peroperative regional anaesthesia during elective surgery, with or without concomitant general anaesthesia, has been shown to reduce discomfort and the need for opioids postoperatively (6,7). Intrathecally applied opioids in patients undergoing urologic, orthopaedic, haemorrhoid, gynaecologic, or obstetric surgery with spinal anaesthesia can further optimize postoperative pain management (8,9).

There are today no published randomised prospective studies with the focus on hospitalisation after gynaecological surgery in a fast track setting.

The aim of this prospective, randomised multicentre study was to determine whether the duration of hospital stay after benign abdominal hysterectomy in a fast track setting differed between those carried out under general anaesthesia and those performed under spinal anaesthesia with intrathecal morphine.

Material and Methods

An open, prospective, randomised, controlled multicentre study comparing two different anaesthetic techniques in fast track surgery of women undergoing abdominal hysterectomy for benign gynaecological diseases was undertaken. Ethical approval was obtained from the Regional Ethical Board at Linköping University. The departments of Obstetrics and Gynaecology at five hospitals in the southeast Health Region of Sweden participated in the study.

Patients

Women who were admitted to the participating units for benign hysterectomy between March 2007 and June 2009 were asked to participate. Medical inclusion criteria were women between 18 and 60 years of age, who had been admitted for abdominal subtotal or total hysterectomy due to benign gynaecological disorders. At least one ovary was to be preserved at the operation. The women had to speak Swedish fluently and understand it equally well. Exclusion criteria were American Society of Anesthesiologists (ASA) score ≥ 3, former or planned concomitant bilateral oophorectomy, postmenopausal women without hormone therapy (HT), gynaecological malignancy (cervical dysplasia not included), morphine allergy, physically disabled, severe psychiatric or mental disorder and any condition, which would exclude the women from conducting regional anaesthesia in the standardized manner of the study. After having given oral and written informed consent the included patients were randomised to receive either general anaesthesia or spinal anaesthesia including intrathecal morphine.

Randomisation

A computer generated the randomisation sequences into blocks of 10 with equal number of the two modes of anaesthesia for each of the five participating centres. The participating centres were assigned slightly different numbers of blocks corresponding to the expected number of eligible patients at the hospital. The allocated mode of anaesthesia, written on a label, was sealed in opaque consecutively numbered envelopes. At each centre the envelopes were opened in consecutive number order of patient inclusion in the study. The flow chart of the study population is shown in Figure 1. One-hundred and eighty women were randomised and 162 completed the study.

Premedication

One hour before surgery the patient received 2 g oral paracetamol. No pre-medication sedatives were given. The patient was allowed to drink clear fluids until two hours before surgery. Antibiotic- and antithrombotic prophylaxes were administered according to department routine.

General anaesthesia (GA)

General anaesthesia was induced with propofol and fentanyl. Tracheal intubation was facilitated by rocuronium. The anaesthesia was maintained with a continuous i.v. infusion of propofol and oxygen in air. Rocuronium and fentanyl were repeated during anaesthesia according to the attending anaesthetist. Twenty minutes before ending the operation 5 mg morphine was given intravenously. All patients had orogastric tubes during surgery.

Spinal anaesthesia (SA)

Spinal anaesthesia was administered with a 25-gauge needle preferably in the L3/L4 or L2/L3 intervertebral space. The anaesthetic consisted of 20 mg hyperbaric bupivacaine (5 mg/ml)

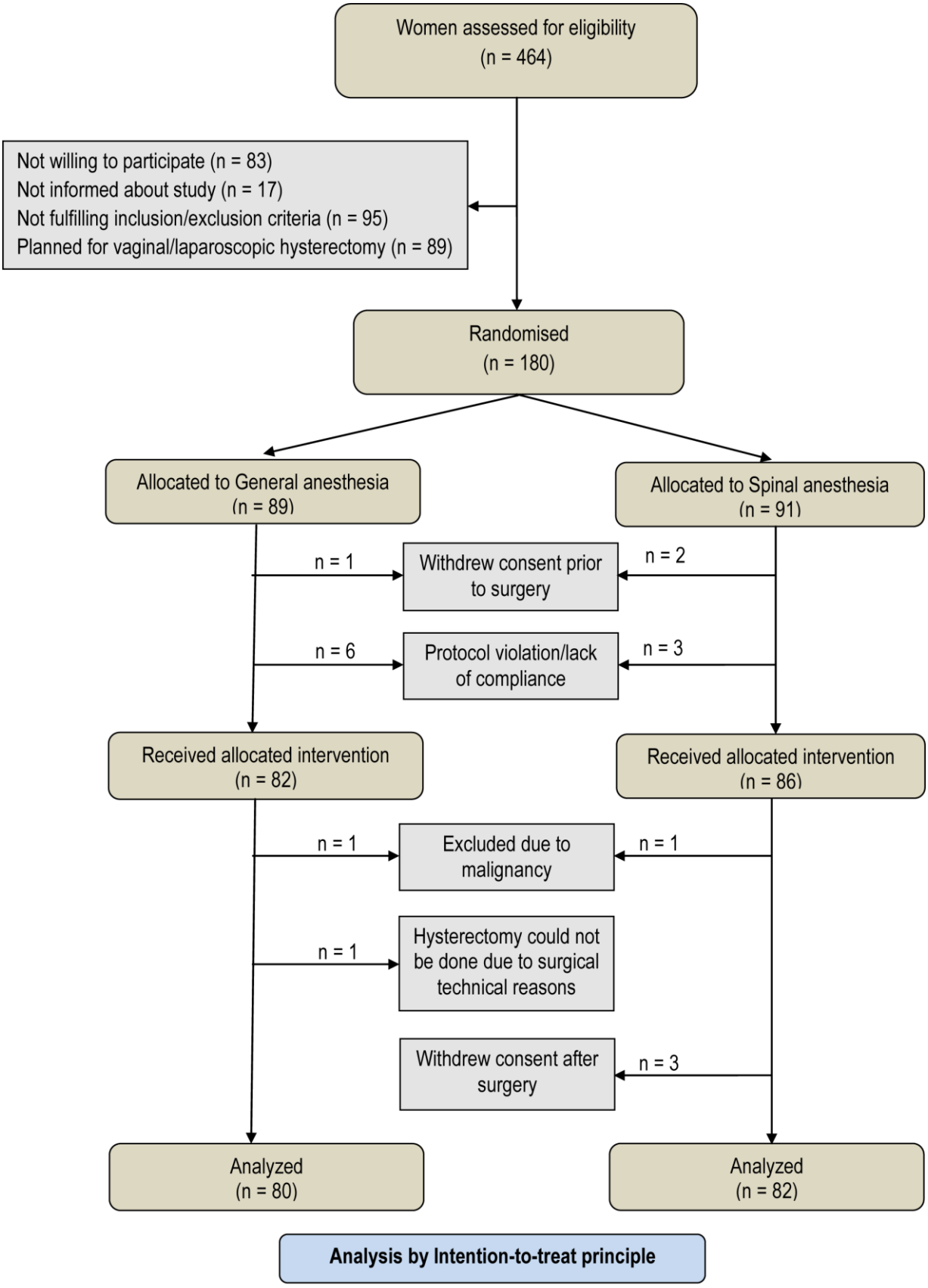

Figure 1. Flowchart of the study participants.

and 0.2 mg morphine (0.4 mg/ml). Fifteen minutes after administration of anaesthesia the level of the neural blockade was determined with a cold test and registered. Sedation was applied throughout the operation with a continuous i.v. infusion of propofol. If the spinal anaesthesia was insufficient the patient received GA according to the protocol described above.

Surgery

The decisions about mode of abdominal hysterectomy and skin incision were made prior to randomisation. The surgical technique used at the hysterectomy was left to the surgeon's discretion. It was permissible for the surgeon to plicate the sacrouterine and cardinal ligaments, but not to anchor the round ligaments to the vaginal cuff or the cervical stump; peritonealisation was not to be carried out. The surgeon injected 40 ml of bupivacaine (2.5mg/ml) subcutaneously and pre-fascially in the abdominal wall wound before ending the surgery. A transurethral urinary bladder catheter was inserted preoperatively and left until the next morning.

Perioperative parenteral fluid infusions

A restricted and similar regimen of intravenous fluids perioperatively was used in both groups. At the start of anaesthesia 5 ml/kg of lactated Ringer´s solution was administered. A continuous infusion of fenylephrine (40μg/ml) was used if the mean arterial blood pressure decreased > 30% from the baseline. Parenteral fluids composed of lactated Ringer´s solution and glucose 2.5 % were used and the target for the total amount was set at 25 ml/kg and day, provided no complications had occurred perioperatively. Parenteral infusion was terminated on the morning of the day after surgery if the postoperative surveillance was uneventful. Otherwise parenteral infusion was continued on medical indications.

Postoperative care

At the conclusion of the operation the patient was transferred to the post anaesthesia care unit (PACU) for postoperative monitoring of hemodynamic and respiratory stability, degree of sedation, pain, nausea and pruritus. The monitoring was similar after the two modes of anaesthesia. The patient was discharged from PACU to the gynaecological ward when vital signs were stable and the patient awake. The monitoring was continued in the gynaecological ward. Provided that measures were within clinically normal limits, they were registered once every hour during twelve hours, then once every third hour until 24 hours after commencing surgery. The patient was instructed to drink and eat as soon as possible after surgery. Mobilisation was initiated in the PACU and actively encouraged early in the gynaecological ward.

Postoperative pain management was obtained orally with 1,330 mg paracetamol and 50 mg diclofenac three times daily during hospitalisation. Pain intensity was measured on a visual analogue scale (VAS) ranging from 0 to10, with "0" indicating no pain and "10" indicating worst pain imaginable. The measurements were carried out in association with the monitoring of the vital signs. Additional pain relief was offered if the patient requested it or if the VAS score was greater than 3. Opioids were avoided if possible but given orally or intravenously if necessary. Pre-emptive antiemetic therapy was administered using bilateral acupressure wrist bands. These were applied preoperatively and maintained throughout hospital stay. Rescue antiemetic treatment was available with single or repeated doses, in order of use, droperidol 0.6 mg i.v. and 5-HT3 receptor antagonist, on the patient´s demand. Treatment of discomfort of pruritus comprised, in order of use, clemastine and naloxone (in low doses per orally or intravenously).

The criteria for discharge of the patient were standardized; the patient was mobilized, tolerated normal diet, had sufficient pain relief with oral analgesics (VAS ≤ 4), had voided spontaneously with less than 150 ml residual urine (measured by a portable bladder ultrasound scan) and showed no signs of mechanical bowel obstruction. If the patient had insufficient bladder emptying at discharge the patient received a transurethral bladder catheter for another couple of days. The catheter was then removed in the out-patient clinic and the residual urine volume was subsequently controlled by means of a portable bladder ultrasound scan. The time of discharge was registered.

Time of first pass of gas and first bowel movement were registered during the hospital stay. At discharge the patient was requested to complete a diary once a day for 35 days postoperatively. The patient was instructed to record experience with pain and nausea, recovery of bowel function, time of the first pass of gas and the first bowel movement in case these had not occurred during the hospital stay.

Statistics

Data are presented as median and (range) or number and per cent. All analyses were done according to *intention-to-treat* principles. In addition, outcome measures were analyzed according to *per-protocol* principles and reported in the text. In univariate analysis Mann Whitney U-test, Yates corrected Chi-square test and Fishers´ exact test were used, when appropriate, to compare descriptive and clinical data between the two groups. Analysis of covariance (ANCOVA) was used to test differences in continuous outcome measures between the two groups and logistic regression analysis to analyze nominal effect measures. Adjustment was done simultaneously for mode of hysterectomy, skin incision, BMI, smoking habits and occurrence of change in protocol of anaesthesia in the multivariate models when appropriate. The results of the logistic regression models are presented as odds ratios and 95%

confidence intervals. Level of significance was set at 5%. Statistical analyses were carried out with the software StatView® for Windows, Copyright©, 1992-1998, Version 5.0.1 (SAS Institute Inc., SAS Campus Drive, Cary, NC 27513, USA).

Sample size calculation

With an $\alpha = 0.05$ and $1 - \beta = 0.90$ the sample size was estimated to be 180 women including a drop out of 10% given that the stay in hospital after benign abdominal hysterectomy in GA before commencing the study was 3.7 ± 2.0 days (mean ± 1 standard deviation) and based on the assumption that the duration of stay in hospital after hysterectomy would be reduced by one day after SA compared with GA.

Results

Eighty of the women randomised to GA and 82 of those randomised to SA completed the study and comprise the study population. The demographic and descriptive data of the study groups are presented in Table 1. No statistically significant differences were observed between the groups in any of these data.

In eight women (9.8%) the SA gave insufficient analgesia and the women received GA according to the study protocol. In the GA group the general anaesthesia given according to the study protocol could not maintain sufficient depth of anaesthesia in five women (6.3%) and N_2O or sevoflurane was added in these cases. The upper level of sensory blockade was median to the level of Th4 (range C3–Th10) in the 74 women who had sufficient analgesia with the SA. None of the patients in the SA group needed respiratory assistance due to high level of motor blockade. Two women in the GA group experienced severe postoperative pain in the PACU that did not respond sufficiently to i.v. opioids. The pain was controlled with a single dose of intrathecal sufentanil in one case and with continuous epidural analgesia using ropivacaine in the other case.

The ANCOVA model showed no significant difference in duration of stay in hospital from start of anaesthesia to discharge from the gynaecological ward between the two groups (GA group 50 hours (range 24 -100 hours) *vs.* SA group 46 hours (range 22 – 125 hours); p = 0.4004). However, the proportion of women who were discharged within 48 hours was significantly higher in the SA group than in the GA group (56% (46/82 women) *vs.* 39% (31/80 women); p = 0.0401 (Yates corrected Chi-square test; DF = 1)). In contrast with this, the proportion of women who stayed in hospital more than 72 hours did not differ significantly between the two groups (11.3% (9/80) in the GA group *vs.* 11.0% (9/82) in the SA group). The *per-protocol* analysis revealed similar results concerning median duration of hospital stay but the proportion of women who were discharged within 48 hours did not differ

significantly between the modes of anaesthesia. Per- and postoperative clinical data are presented in Table 2. The time in the PACU was significantly shorter for the SA group. The more rapid recovery of bowel function in the SA group was almost exclusively attributed to the amount of opioids used. When adjustment for amount of equivalent morphine and fentanyl during day 0 was included in the ANCOVA model there was no significant association between mode of anaesthesia and time to first bowel movement. A strong association was found between amount of equivalent morphine and fentanyl during day 0 and time to first bowel movement (positive correlation, $p = 0.0037$). The *per-protocol* analysis was similar in this aspect.

The per- and postoperative use of analgesics is shown in Table 3. The consumption of opioids on day 0 and opioids and non-opioid analgesics on day 1 was significantly lower in the SA group than in the GA group. After day 2 the consumption of opioids was very low in both groups. The data are not shown for day 4 and 5. These results also held true when analyzing *per-protocol* except that consumption of non-opioid analgesics on day 1 did not differ between the two groups.

The proportions of women who used the acupressure wrist bands in the two groups and the use of rescue antiemetics did not differ significantly between the groups during the hospital stay (Table 4). When analyzing *per-protocol* a significant difference indicating a risk of vomiting on day 0 after SA occurred (OR 2.08 (95% CI: 1.08 – 4.02)). No significant difference in use of rescue antiemetics was seen in the GA group between those with and without vomiting episodes whereas a significantly higher proportion of those with vomiting episodes in the SA group received rescue antiemetics (86% *vs.* 30%; OR 4.56 (95%CI 4.56 – 44.06)). The amount of opioids used on day 0 or day 1 was not associated with occurrence of vomiting (data not shown). No vomiting episodes were observed in any of the women after day 2. The volume of i.v. crystalloids and colloid expanders (hydroxyethyl starch) given

during the time in hospital did not differ significantly between the groups (1888 ml (400 – 6000 ml) and 0 ml (0 – 1500 ml) in GA *versus* 1775 ml (1000 – 4300 ml) and 0 ml (0 – 1000 ml) in SA, respectively).

The number of complications during hospital stay was low in both groups (Table 5). None of the patients were readmitted to PACU and no untoward cardio vascular or respiratory adverse effects or other unexpected complications associated with the anaesthetic drugs were observed in the gynaecological wards during the hospital stay. Two complications were categorized as severe (life-threatening), a heavy peroperative bleeding (3000 ml) deriving from a laceration of the uterine artery from the internal iliac artery, and a pulmonary arterial embolism diagnosed on day 1. Both complications were treated according to clinical practice and the patients recovered uneventfully and were discharged on day 4 and 6, respectively. The median time to removal of transurethral catheters was 22 hours after insertion in both groups and two women in each group were discharged with the catheter in place due to urinary retention or prolonged catheterization because of bladder injury.

Discussion

This study showed that by using a fast track model it was possible to achieve a median duration of stay in hospital after abdominal hysterectomy for benign conditions of less than 50 hours. The length of stay did not differ significantly whether spinal anaesthesia including morphine intrathecally or general anaesthesia was used. The amount of opioid analgesics used postoperatively was significantly lower after spinal anaesthesia. This had a positive impact on the speed of recovery of bowel function. The negative effects of the spinal anaesthesia with morphine intrathecally compared with GA were higher prevalence of pruritus and postoperative vomiting.

The study was randomised and performed in a multicentre setting which strengthens the possibility of generalization of the results. Systematic information about all women admitted to the participating hospitals for benign hysterectomy during the study period has been obtained. More than 38% of the women who were eligible for the study participated. This is a significantly higher proportion than the 5.5-18% reported in other randomised studies of abdominal hysterectomy (10-13).

The study was primarily designed to compare duration of hospital stay and patient recovery following a standard customary procedure for abdominal hysterectomy in GA with the same measures following hysterectomy in SA. Blinding and/or placebo control was not possible in this study. The temporary paralysis of the lower extremities after SA would, for obvious reasons, be observed immediately by the patient as well as by the staff. The lack of blinding may pose a risk of bias. In order to reduce such potential bias the women were informed and monitored in a standardised fashion and the mode of incision and type of abdominal hysterectomy were decided prior to randomisation. The surgical technique of the hysterectomy had only a few limitations according to the study protocol in order to represent the daily practice of abdominal hysterectomy. The surgeon´s competence, individual surgical

technique and experience with surgery in spinal anaesthesia may theoretically influence postoperative recovery and thus be a bias. However, all surgeons were familiar with gynaecological surgery under spinal anaesthesia and the operations were performed or supervised by consultants in obstetrics and gynaecology, thus reflecting the daily practice in the clinics.

We failed to demonstrate any difference in hospital stay related to the two modes of anaesthesia, but it is striking that rapid post-operative discharge is achievable by adopting the fast track recovery ethos. In addition, it is possible that the short duration of hospitalisation post-surgery reflects the clinical trial setting and an information bias effect. All women were carefully informed preoperatively about the discharge criteria and were actively encouraged by the staff and the research nurses to achieve early mobilisation postoperatively. All staff members were well informed about the fast track concept and that discharge was possible when the criteria were met. Compared with the results in published randomised studies concerning abdominal hysterectomy this study reports a considerably shorter duration of hospital stay than do any of these studies (1,11,13-15). However, in most of these studies the criteria to define duration of hospital stay was not clear. In our study the duration of hospital stay was measured as the time from start of anaesthesia to the time of discharge from hospital. We consider this to be a useful and generalisable method for calculation of hospital stay in surgery since it eliminates preoperative practices that are often not standardized.

The consumption of opioids was significantly lower in the SA group during the first two days postoperatively, indicating a sustained postoperative analgesic effect of the intrathecal morphine. This is in accordance with the results presented by Massicotte *et al* (16). Due to lower requirement of opioids by the women in the SA group, they had a faster recovery of bowel function. However, this did not affect the need for treatment of nausea nor did it affect the duration of hospital stay. These results seem to be in accordance with those of Hansen *et*

al. who investigated oral osmotic laxatives as a means of hastening the bowel recovery after abdominal hysterectomy (17).

Since the risks of postoperative nausea and vomiting, according to the Cochrane Review by Lee *et al* (18), are reported to be similar after acupoint P6 stimulation and antiemetic drugs we selected to use the acupressure wrist bands as the preventive measure in order to avoid undesired side effects of antiemetic drugs, which potentially could influence the duration of hospitalisation (19). Both groups also received propofol either for induction and maintenance of the general anaesthesia or as sedation in association with spinal anaesthesia. Propofol possesses direct antiemetic effects (20). The need for rescue antiemetics did not differ between the groups, irrespective of the amount of consumed opioids in the present study. Significantly more women vomited postoperatively in the group who received SA solely even though there was no significant difference in overall use of rescue antiemetics between the groups. It is a clinical observation that vomiting is not always preceded or accompanied by nausea. Such vomiting might be triggered by the gastric paralysis after intra abdominal surgery. Only the women who had general anaesthesia received an orogastric tube and gastric emptying during the hysterectomy. This might contribute to explaining why the prevalence of women who vomited was higher in the group that had SA and did not need conversion to GA.

Pruritus is a known and common adverse effect of intrathecal morphine occurring in about 37% (21). In our study 38% in the SA group received antipruretics which was significantly higher than the 2.5% in the GA group. This significant difference in use of antipruretics was only seen on the day of surgery.

The advantages with the SA compared with GA in a fast track hysterectomy model were that significantly less opioids were needed postoperatively and consequently there was faster recovery of the gastrointestinal function. However, the clinical significance of this may be limited given that the median reduction in time to pass flatus and first bowel movement was

just two and seven hours respectively in favour of SA. Despite these advantages no difference was found in hospital stay between the modes of anaesthesia. This may reflect the disadvantages of SA, namely increased risks of vomiting and pruritus needing treatment.

Hysterectomy is encumbered with a substantial number of annoying postoperative side effects, which, if not life-threatening, do affect the patient's comfort and consequently the character of postoperative care. However, adoption of a fast track concept of recovery encompassing education of staff and patients in conjunction with a supportive infrastructure of the health care can result in rapid post-operative recovery and discharge from hospital regardless of mode of anaesthesia. Future studies of fast-track programmes in gynaecological surgery encompassing improved anaesthesia, with emphasis on patient comfort and safety are needed in order to further enhance postoperative recovery.

Acknowledgements

We are indebted to Associate Professor Sigga Kalman, MD, PhD, for valuable discussions in the prelude of the study. The physicians and research nurses in the multicentre study group are thanked for their invaluable work and support in the study.

Disclosure of Interests

None of the authors or "GASPI" study group members has any conflicts of interest to declare.

Ethics approval

The Regional Ethical Board at Linköping University (registration nr: M159-06, approval date 15 November 2006; amendment 1: registration nr T83-07, approval date 3 October 2007; amendment 2: registration nr T19-08, approval date 4 March 2008); and the Swedish Medical Products Agency (registration nr: EudraCT nr 2006-002520-41) approved the study.

Funding

The study was supported financially by grants from the Medical Research Council of South East Sweden; Linköping University and the County Council of Östergötland.

Contribution to authorship

NBW, LN and PK planned and conducted the study. The data were processed and analysed by NBW, LN and PK. NBW was the primary author of the manuscript. All authors contributed to the elaboration of the manuscript, revised the paper and approved the final version.

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Table 1. Perioperative demographic and descriptive data

Characteristics		General anaesthesia (n = 80)	Spinal-morphine anaesthesia (n = 82)
Age (years)		45 (33 – 58)	46 (35 – 58)
Body mass index (kg/m^2)		25.3 (19.0 – 41.5)	25.4 (18.9 – 38.0)
BMI ≤ 25		39 (48.8%)	35 (42.7%)
BMI > 25 and < 30		24 (30.0%)	31 (37.8%)
BMI ≥ 30		17 (21.2%)	16 (19.5%)
Parity		2.0 (0 – 5)	2.0 (0 – 8)
Smokers		16 (20.0%)	13 (15.9%)
Previous laparotomy		29 (36.3%)	29 (35.4%)
Previous anaesthesia**	General anaesthesia	21 (72%)	21 (70%)
	Spinal/epidural anaesthesia	8 (28%)	9 (30%)
Concomitant diseases	Psychiatric	8 (10.0%)	6 (7.3%)
	Musculoskeletal	11 (13.8%)	6 (7.3%)
	Cardiovascular	8 (10.0%)	9 (11.0%)
	Chronic pulmonary	3 (3.8%)	7 (8.5%)
Concomitant medication	Analgesics	21 (26.3%)	11 (13.4%)
	Antidepressants	8 (10.0%)	5 (6.1%)
Indication of hysterectomy	Bleeding disturbances	46 (57.5%)	46 (56.1%)
	Mechanical symptoms	27 (33.7%)	29 (35.4%)
	Cervical dysplasia/endometrial hyperplasia	4 (5.0%)	5 (6.1%)
	Endometriosis/dysmenorrhoea	3 (3.8%)	2 (2.4%)
ASA*	Class I	59 (73.7%)	55 (67.1%)
	Class II	21 (26.3%)	27 (32.9%)
Mode of hysterectomy	Total abdominal	55 (68.8%)	51 (62.2%)
	Subtotal abdominal	25 (31.2%)	31 (37.8%)
Mode of skin incision	Midline	6 (7.5%)	7 (8.5%)
	Low transverse	74 (92.5%)	75 (91.5%)

Figures denote median and (range) or number and (%).
* ASA the American Society of Anesthesiologist classification of physical status.
** A women may have had more laparotomies.
No statistically significant differences were observed between the groups in any of the variables (univariate analyses).

Table 2. Peroperative data

Characteristics	General anaesthesia (n = 80)	Spinal-morphine anaesthesia (n = 82)	Analysis of covariance *p* - value*
Operating time (minutes) **	75 (40 – 225)	70 (40 – 173)	0.1478
Estimated peroperative bleeding volume (ml)	150 (10 – 3000)	100 (10 – 1100)	0.3340
Uterus weight (g)	298 (41 – 1655)	302 (58 -2784)	0.2205
Time of anaesthesia (minutes)***	124 (86 – 266)	115 (60 – 210)	0.1651
Time in PACU (hours)	4.3 (1.8 – 23.0)	3.6 (1.5 – 14.2)	0.0328
Time with urinary catheter (hours) ****	22 (7 – 145)	22 (9 – 236)	0.8770
Time to first pass of gas (hours) ****	29 (10 – 100)	27 (5 – 90)	0.0187
Time to first bowel movement (hours) ****	57 (22 – 124)	50 (11 – 153)	0.0394

Figures denote median and (range).
PACU = post anaesthesia care unit.
* Analysis of covariance with adjustments simultaneously for mode of hysterectomy, skin incision, BMI, smoking habits and change of mode of anaesthesia.
** Time from skin incision to skin closure.
*** Time from start of anaesthesia to extubation (GA) or leaving the operating room (SA).
**** Time from start of anaesthesia to event occurs postoperatively.

Table 3. Peroperative anaesthetic drugs and postoperative analgesics during hospital stay.

Characteristics	General anaesthesia	Spinal-morphine anaesthesia	Analysis of covariance* *p* -value
Peroperatively	(n = 80)	(n = 82)	
Propofol (mg)	1150 (101 – 3050)	384 (54 – 1494)	<0.0001
Fentanyl (mg)	0.3 (0.0 – 0.7)	0.0 (0.0 – 0.5)	<0.0001
Fenylephrine (µg)	0 (0 – 1500)	625 (0 – 3400)	<0.0001
Morphine (mg)	5.0 (0 – 10)	0 (0 – 7.5)	<0.0001
Day 0 (= day of surgery)	(n = 80)	(n = 82)	
Equivalent morphine dose (mg) **, #	18.5 (5.0 – 49.5)	0.4 (0.0 – 35.8)	<0.0001
Non-opioid analgesics (RDD)	2.1 (1.1 – 2.8)	1.8 (1.2 – 2.8)	0.8074
Day 1	(n = 80)	(n = 82)	
Equivalent morphine dose (mg)	0.0 (0.0 – 42.7)	0.0 (0.0 – 40.8)	0.0462
Non-opioid analgesics (RDD)	2.0 (0.0 – 2.7)	1.2 (0.0 – 2.7)	0.0400
Day 2	(n= 56)	(n=47)	
Equivalent morphine dose (mg)	0.0 (0.0 – 15.0)	0.0 (0.0 – 26.7)	0.6913
Non-opioid analgesics (RDD)	0.0 (0.0 – 2.0)	0.0 (0.0 – 2.3)	0.6407
Day 3	(n= 12)	(n= 9)	
Equivalent morphine dose (mg)	0.0 (0.0 – 6.7)	0.0 (0.0 -16.6)	0.2918
Non-opioid analgesics (RDD)	0.5 (0.0 – 2.0)	0.7 (0.0 -2.2)	0.8834

Figures denote median and (range).
RDD sum of recommended daily dosage
*Analysis of covariance with adjustments for mode of hysterectomy, skin incision, BMI, smoking habits and change of mode of anaesthesia.
** The dosage given peroperatively is not included.
# Opioids given postoperatively has been converted into the equivalent intravenous dose of morphine

Table 4. Vomiting and use of antiemetics and antipruritics postoperatively.

Characteristics		General anaesthesia	Spinal-morphine anaesthesia	OR (95% CI)*
Day 0 (= day of surgery)		(n = 80)	(n = 82)	
Vomiting (no. of women)		24 (30.4%)	36 (43.9%)	1.90 (0.98 – 3.59)
Antiemetics (no. of women):	Acupressure wrist bands only	33 (41.2%)	36 (43.9%)	Reference
	Acupressure wrist bands + antiemetics	40 (50.0%)	42 (51.3%)	1.02 (0.52 – 1.98)
	Antiemetics only	5 (6.3%)	2 (2.4%)	0.41 (0.07 – 2.28)
	No acupressure wrist bands or antiemetics	2 (2.5%)	2 (2.4%)	1.03 (0.13 – 7.98)
Antipruritics (no. of women)		2 (2.5%)	31 (37.8%)	25.26 (5.75 – 111.04)
Day 1		(n = 80)	(n = 82)	
Vomiting (no. of women)		11 (13.9%)	10 (12.2%)	0.76 (0.28 – 2.12)
Antiemetics (no. of women):	Acupressure wrist bands only	45 (56.3%)	44 (53.7%)	Reference
	Acupressure wrist bands + antiemetics	15 (18.7%)	11 (13.3%)	0.70 (0.28 – 1.79)
	Antiemetics only	4 (5.0%)	3 (3.7%)	0.74 (0.15 – 3.75)
	No acupressure wrist bands or antiemetics	16 (20.0%)	24 (29.3%)	1.59 (0.74 – 3.41)
Antipruritics (no. of women)		3 (3.8%)	8 (9.8%)	3.16 (0.79 – 12.64)
Day 2		(n = 56)	(n = 47)	
Vomiting (no. of women)		1 (1.8%)	1 (2.1%)	NA
Antiemetics (no. of women):	Acupressure wrist bands only	32 (57.1%)	24 (51.1%)	Reference
	Acupressure wrist bands + antiemetics	3 (5.4%)	2 (4.2%)	0.63 (0.05 – 7.92)
	Antiemetics only	1 (1.8%)	0 (0%)	NA
	No acupressure wrist bands or antiemetics	20 (35.7%)	21 (44.7%)	1.18 (0.49 – 2.85)
Antipruritics (no. of women)		1 (1.8%)	2 (4.2%)	2.30 (0.19 – 27.32)

Figures indicate number and (%).

* Logistic regression analysis with adjustments for mode of hysterectomy, skin incision, BMI, smoking habits and change of mode of anaesthesia.

Table 5. Per- and postoperative complications during hospital stay.

Complications	General anaesthesia (n = 80)	Spinal-morphine anaesthesia (n = 82)
Heavy bleeding, exceeding ≥ 1000 ml	2 (2.5%)	2 (2.4%)
Blood transfusion (no. of women)	3 (3.8%)	0 (0%)
Bladder injury	1 (1.3%)	2 (2.4%)
Reoperation due to bladder injury	0 (0%)	1 (1.2%)
Reoperation due to retained surgical towels	1 (1.3%)	0 (0%)
Retroperitoneal and subcutaneous emphysema	1 (1.3%)	0 (0%)
Pulmonary embolism	0 (0%)	1 (1.2%)
UTI	1 (1.3%)	1 (1.2%)
Cholecystolithiasis	1 (1.3%)	0 (0%)
Post-dural puncture headache	0 (0%)	1 (1.2%)
Urticaria	1 (1.3%)	1 (1.2%)
Urinary catheter at discharge (no. of women)	2 (2.5%)	2 (2.4%)

Figures denote number and (%).
No statistically significant differences were observed in any of the variables between the groups (univariate analysis. Fisher´s exact tests).