

# The Effect of IVPCA Morphine on Post-hysterectomy Bowel Function

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**Background:** Although morphine has been shown to induce bowel dysfunction in a dose-dependent fashion, in most relevant studies it was investigated in single bolus injection. Recently, intravenous morphine via patient-controlled analgesia (IVPCA) has been widely used to provide analgesia by divided bolus doses on patients' demand with satisfactory effects. This approach, by reducing the peak serum surge, largely resembles the pharmacokinetic and pharmacodynamic advantage of continuous infusion. There is yet no report on the investigation of its effect on post-operative bowel dysfunction.

**Methods:** Fifty-one women who underwent abdominal total hysterectomy (ATH) due to uterine myoma were enrolled to investigate the association between the doses of morphine consumption by PCA and the time of first passage of flatus. In all patients morphine was administered intravenously via a PCA pump immediately after recovery from general anesthesia.

**Results:** We found that 49 out of 51 patients (96%) exhibited mild pain with IVPCA morphine. They had consumed an average dose of 16.9 mg morphine (range, 0–46 mg) upon the first passage of flatus which occurred 2036.4 min (average) post-operatively. There was no correlation between the dose of morphine and the time of first passage of flatus ( $r = 0.053$ ,  $P > 0.05$ ).

**Conclusions:** The absence of suppression of bowel movement by IVPCA morphine for post-operative pain control suggests that favorable pharmacokinetic profile of IVPCA can help reduce the morphine-induced bowel dysfunction at its therapeutic level.

**Key words:** *Analgesia, patient-controlled. Morphine. Flatulence. Hysterectomy.*

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Although the risk of abdominal surgery is greatly reduced nowadays, the post-operative pain is still a major problem during post-operative period.<sup>1-2</sup> Opioid analgesia has been demonstrated to be useful for the post-operative pain. However, it is noted that opioid analgesia for post-operative pain will decrease bowel movement<sup>3-5</sup> and delay the time of first passage of flatus and increase the days of admission. Numerous reports of human studies have shown that morphine suppresses the motility of both small and large intestines in a dose-de-

pendent manner and the suppression can be counteracted by naloxone.

PCA is widely accepted as an effective analgesic modality.<sup>6-7</sup> Unlike the conventional mode of administration, pain relief is provided through self-administration of low doses of opioids via intravenous route. Although its pharmacokinetic properties are well documented,<sup>8</sup> little is known about its association with bowel motility. This study was designed to investigate whether the post ATH bowel dysfunction is associated with PCA.

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## Materials and Methods

This study was approved by the Hospital Ethics Committee and informed consent was obtained from all patients. We studied 51 patients scheduled consecutively

for elective abdominal total hysterectomy due to leiomyoma and all of them did not receive any drugs that could possibly influence bowel motility prior to the operation.

Patients fasted appropriately before operation and enema was performed on the morning of the operation day. The day before surgery, all patients were instructed how to use the PCA (Abbott Life 4100 series PCA infuser). The content of the questionnaire which includes the time of first passage of flatus, acceptance, efficacy, and the degrees (none, mild, moderate, severe) of side effects was explained to the patients. We evaluated pain with visual analog scale (VAS). No pain means VAS 0–3; mild pain means VAS 3–5; moderate pain means VAS 5–7; severe pain means VAS 7–10. Mild nausea and vomiting: 3 episodes, (no need of treatment); moderate nausea and vomiting: 3–5 episodes, (need of treatment); severe nausea and vomiting: 5 episodes. Mild pruritus means a suffering from itching, and needs no treatment; moderate pruritus means itching that needs treatment; severe pruritus means treatment is needed, but the effect is limited. Demographic data including age, body weight, body length, previous operative history, diagnosis, the time of operation, procedure of operation and anesthetic drugs were recorded. In all patients anesthesia was induced with intravenous thiopental 5 mg/kg, succinylcholine 1.5 mg/kg and maintained with desflurane in oxygen. Nitrous oxide was not administered throughout the procedure. Rocuronium bromide was used for surgical relaxation. In all patients a standard horizontal incision was made 10 cm below the umbilicus while the wound was closed layer by layer without infiltration of local anesthetic. Upon initial return of spontaneous breathing, all patients were given intravenous atropine 0.01 mg/kg and edrophonium 0.75 mg/kg to reverse the residual muscle relaxation. PCA was applied immediately after recovery from general anesthesia. The Lifecare 4100 PCA infuser was connected to the patient's IV line, set at a minimum lockout interval of 10 min and 2-mg bolus doses of morphine "on demand". After an elapse of

24 h since the end of operation menthol packing and 10 mg bisacodyl suppository (Ducolax) were routinely used every four hours until flatus had occurred.

Statistical analysis were performed using linear regression analysis of variance and Spearman rank correlation as appropriate and  $P < 0.05$  was considered to be statistically significant.

## Results

The age of patients ranged from 32 to 76 years, with an average of 45.6 years. Average weight was 57.2 kg (42.5–99.9 kg) and average height 156.9 cm (144–175 cm). Previous abdominal surgeries are summarized in Table 1. There was no close correlation between previous history of abdominal surgery, the time of operation and the time of first passage of flatus.

The operative procedures were decided based on the age of patient and gross picture of ovaries. The time of operation, time of first passage of flatus and total dose of morphine consumed were recorded (Table 2). There was no correlation between TFF and the time of operation (correlation coefficient: 0.127,  $P > 0.05$ , Fig. 1). There was also no correlation between the dose of morphine and the time of first passage of flatus ( $r = 0.053$ ,  $P > 0.05$ ) (Fig. 2).

**Table 1. Previous Abdominal Surgery**

Procedure	Number of patients	Time of operation (min)
None	33	89 ± 21.8
Tubal ligation	5	105 ± 28.8
Cesarean section	4	103 ± 23.0
Appendectomy	6	91 ± 18.4
Myomectomy	2	91 ± 13.5
Salpingectomy	1	85 ± 0
Total	51	92 ± 23

**Table 2. Association between Operative Procedure, Time of Operation, Time of First Flatus and Morphine Consumption Dose**

Procedure	Number	PCA (mg)	Time of operation (min)	Time of first flatus (min)
TAH only	15	17.2 ± 9.1	84 ± 17	2,042 ± 406
TAH + BSO	16	16.1 ± 10.2	96 ± 27	2,099 ± 295
TAH + RSO	9	17.6 ± 7.8	94 ± 24	2,230 ± 368
TAH + LSO	11	17.1 ± 8.6	93 ± 17	1,886 ± 259
Total (mean ± SD)	51	16.9 ± 11.0	92.2 ± 22.9	2,036.5 ± 410.1

TAH = Total abdominal hysterectomy; BSO = Bilateral salpingo-oophorectomy; RSO = Right salpingo-oophorectomy; LSO = Left salpingo-oophorectomy.

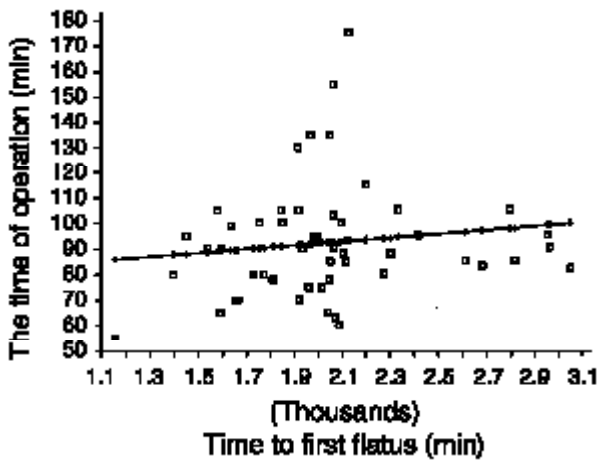


Fig. 1. The correlation between time to first flatus and time of operation.

Pain relief score and satisfactory score were agreeable and there was no patient who needed other analgesic. The severity of side effects such as nausea, vomiting and pruritus is shown in Table 3. Only one patient suffered from severe vomiting with the use of IVPCA for post-op pain relief.

### Discussion

Many factors such as anemia, nutrition, previous operative history, infection, electrolyte imbalance, anesthesia, operative procedure and opioids have been considered as the possible causes of the delayed recovery of bowel function after abdominal surgery. It is well known that opioid drugs delay gastric emptying and intestinal motility. PCA with limitation of the size of individual

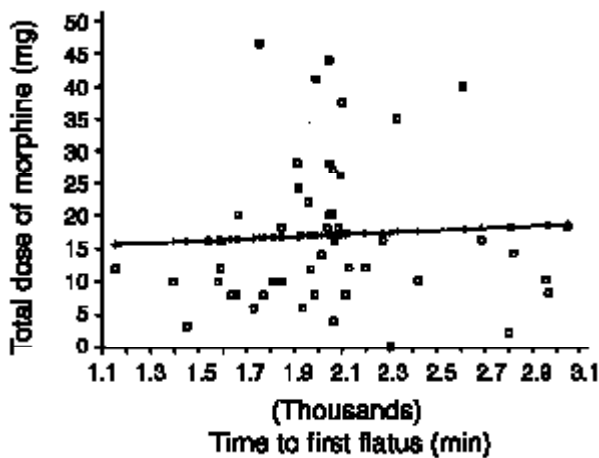


Fig. 2. The correlation between time to first flatus and total dose of morphine consumption.

Table 3. Score of Pain Relief, Satisfactory and Side Effects

	1	2	3	4	Total
Pain	10	39	2	0	51
Nausea	28	18	5	0	51
Vomiting	32	12	6	1	51
Pruritus	46	4	1	0	51

1 = None; 2 = Mildp; 3 = Moderate; 4 = Severe.

boluses and total dose by predetermined lock-out intervals to avoid inadvertent overdose allows the patient to deliver smaller intravenous dosage of opioid on demand safely. We studied the association between the TFF and total doses of morphine in patients with myoma uteri, because the operative procedure selected and the time of operation for this disease were almost uniform.

The time of flatus as recorded by patients and nursing staff is a good clinical evidence to indicate the return of bowel motility.<sup>9</sup> Abdominal total hysterectomy with or without salpingo-oophorectomy due to leiomyoma is an operative procedure without much variation. When taking the patients with leiomyoma as our study model, we could reduce the effect of operation on the time of flatus as much as possible.

Morphine will depress the recovery of bowel function after abdominal surgery and this effect appears to be dose-dependent and occurs at doses greater than 8 mg given intramuscularly.<sup>10</sup> Our result concludes that morphine will not delay the recovery of bowel function after abdominal surgery if given in smaller intravenous doses by PCA.

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## 病患自控式止痛嗎啡對於子宮切除後腸蠕動的影響

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背景：嗎啡會引起腸蠕動失調，而且是以劑量效應的方式來表現，只是之前這類的研究是以單次劑量的給予來探討。近年來，經靜脈病患自控式止痛提供了一個非常滿意的止痛效果。這樣的給藥方式減少了巔峰的血中藥物濃度，在藥物動力學方面的作用類似持續靜脈給藥的方式。目前還沒有報告研究經靜脈病患自控式止痛對腸蠕動的影響。

方法：我們收集了五十一位接受子宮切除手術的病人來研究經由病患自控式止痛所使用的嗎啡量和排氣時間的關係，而嗎啡是在手術後立即利用經靜脈病患自控式止痛幫浦來給予。

結果：我們發現其中四十九個病人可以有效的解除疼痛或只表現輕微的疼痛，嗎啡平均使用量為 16.9 mg，而平均排氣時間為 2036.4 分鐘，結果顯示此類手術病患使用自控式止痛裝置時，嗎啡的使用量和排氣時間之間並無關聯性。

結論：在有效治療劑量下使用經靜脈病患自控式止痛的嗎啡給予方式可以減少嗎啡所引起的腸蠕動失調。

關鍵詞：病患自控式止痛。嗎啡。氣脹。子宮切除。