Starting Intravenous Morphine in the Postanesthesia Care Unit Yielded Better Postoperative Analgesia†

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Abstract

The administration of morphine intravenously in the Postanesthesia Care Unit (PACU) was practiced in many parts of the world, but not routinely done in Thailand. This prospective randomized controlled trial was performed to reassure Thai personnel that this practice was safe, to find the optimum dose of morphine for administration in the PACU, and to find the pain level at which patients needed no more analgesics. Eighty gynecological patients, ASA class I or II, were randomly allocated into two groups. Group A received morphine intramuscularly on demand for pain every 6 hours as is conventional. Group B received morphine intravenously by titration (with pain) in the PACU. On the ward, they received intramuscular morphine for pain as required. No patients had respiratory depression or oversedation. The amount of morphine needed in the PACU was related to and could be calculated from the pain score at which they first needed analgesics. Time to the first requirement of intramuscular morphine on the ward in group B was significantly longer than in group A. The amount of morphine and the number of analgesic requests on the ward in group B were significantly less than in group A. We concluded that giving morphine intravenously in the PACU was safe, effective and reduced postoperative analgesic requirement. The dose of morphine in the PACU could be calculated from the pain score at patients' first request for analgesics. Most patients declined additional analgesics when their pain was acceptable and tolerable.

Key word : Postoperative Analgesia, Intravenous, Morphine, PACU

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Postoperative pain is acute, severe pain that can be relieved when appropriate analgesics are given in a suitable dose and time. When patients recover from anesthesia after operation, they are taken care of in a Postanesthesia Care Unit (PACU). There is the belief that giving opioids especially morphine in the PACU may potentiate or be synergistic with the residual effects of general anesthesia and muscle relaxants that may depress the patients' respiration and may increase the risk to the patients. This makes some personnel feel reluctant to give opioid analgesics in the PACU.

Our primary objectives were to find out whether the administration of small doses of morphine incrementally until pain was adequately relieved in the PACU was safe for reducing postoperative pain, and to find the optimum dose of morphine for administration in the PACU. The secondary objectives were to find the levels of pain and pain relief, reported as pain and pain relief scores, respectively, at which the patients needed no more analgesics.

MATERIAL AND METHOD

We performed an open prospective randomized controlled trial after approval by the Siriraj Hospital Ethical Committee and obtaining informed patient consent. We investigated 80 gynecological ASA I or II physical status patients scheduled for elective transabdominal hysterectomy and uni- or bilateral salpingectomy with or without oophorectomy *via* low midline incision. Exclusion criteria were asthma, allergy to morphine, histories of drug abuse or psychiatric problems, and the last dose of opioids in the operating room given less than 30 minutes before the end of operation. Each patient received general anesthesia with routine monitoring, including automated blood pressure monitoring, ECG, and pulse oximetry. The drugs for premedication, induction, maintenance, muscle relaxation, and reversal were at the discretion of the staff anesthesiologist.

In the PACU, 80 patients were randomly assigned into two groups, forty in each group, group A received conventional care and group B received intravenous (IV) morphine. In the conventional care group, the patients received routine care and monitoring for about 2 hours postoperatively or until vital signs were stable and there was no oversedation. Their sedation was assessed using sedation scores on a scale 0-3 (0 = no sedation at all or alert, 1 = mild sedation or drowsy, 2 = moderate sedation or asleep but responsive to verbal or physical stimulus, 3 = oversedation or unarousable). If group A patients started to feel pain and had stable vital signs and no oversedation, they would be sent back ward where they would receive their first intramuscular (IM) morphine on request and then when needed every 6 hours. When group B patients started to have pain that needed analgesics, and their sedation score was 0-1, we recorded their pain score at rest and on coughing using a verbal numerical score (VNS) (0 = no pain at all to 10 = the worst pain imaginable). This was considered time 0 and IV morphine was given by titration against pain, starting with 0.04 mg/kg, then 0.02 mg/kg every 10 minutes until they told us that they needed no more analgesics because their pain was relieved, or when a dose of 0.1 mg/kg was reached. (We limited this as the maximum dose.) The patients were asked to report their VNS at rest, VNS on coughing, and their feeling of pain relief using pain relief score (0 = not relieved at all to 100 = completely relieved) every 10 minutes after morphine administration, and at 30 minutes after each patient's last dose. On the ward, they received IM morphine on request every 6 hours.

We recorded the respiratory rate, heart rate, blood pressure, and sedation score, and observed side effects and complications throughout the study. When the patients needed their first IM analgesic on the ward, they were asked when their pain had begun. Group A patients reported the pain severity at the time of injection and were asked to recall their pain severity in the PACU. The time from the end of operation to the first IM analgesic, the number of analgesic requests and the amount of opioid received during the first 24 hours postoperation were recorded. At the end of the study, the patients were questioned about their satisfaction with the previous 24 hours postoperative analgesia using a satisfaction score (0 = not satisfied at all to 100 = completely satisfied).

Statistical Analysis

The data were analyzed using chi-square test, Student's *t*-test, Mann-Whitney *U*-Wilcoxon ranked Sum *W*-test, Spearman correlation test as appropriate. Statistical package SPSS/Win 10.0 was used. The difference was considered statistically significant when $p<0.05$.

Table 1. Demographic data.

	Conventional n = 40	IV Morphine n = 40	P value
Age (yr)	40.6 ± 7.9	39.8 ± 7.6	0.634
Weight (kg)	55.3 ± 7.8	54.6 ± 9.5	0.720
Operation time (min)	133.4 ± 51.8	122.6 ± 55.0	0.371

Values are mean ± SD.
IV = intravenous.

Table 2. Verbal numerical pain scores (VNS) and pain relief score (PRS) in the intravenous morphine group at different time in the Postanesthesia Care Unit (PACU).

Time	N	VNS (0-10)		PRS (0-100)
		At rest	On coughing	
Time 0 (first analgesic request)	40	8.8 ± 1.8	9.2 ± 1.4	
At 10 min after i.v. morphine dose				
0.04 mg/kg	40	7.4 ± 2.2	8.0 ± 2.0	0.3 ± 21.5
0.06 mg/kg	39	6.2 ± 2.4	7.0 ± 2.4	31.8 ± 23.6
0.08 mg/kg	33	5.5 ± 2.4	6.3 ± 2.7	41.5 ± 27.1
0.10 mg/kg	26	5.4 ± 1.6	6.6 ± 2.0	45.8 ± 19.2
At 10 min after each patient's last dose	40	4.7 ± 2.3	5.8 ± 2.6	50.6 ± 23.9
At 30 min after each patient's last dose	40	4.2 ± 2.1	5.2 ± 2.2	54.9 ± 21.4

Values are mean ± SD.

RESULTS

The patients' age, body weight, and the operation time were not statistically different between the two groups (Table 1).

No patients in either group had respiratory depression or were oversedated. Their vital signs were within normal ranges throughout the study. After asking the patients when their pain had begun and its severity, 36 patients (90%) in group A reported their pain had started in the PACU, whereas most of the patients in group B could not recall their experience in the PACU and reported their pain had begun on the ward. Group A patients reported that their VNSs at rest and on coughing when they received their first IM analgesic were 8.9±2.1 and 9.1±1.9, respectively. The pain score they recalled in the PACU was 7.6± 3.5. In group B, after incremental IV morphine, some did not need the next dose, so the number of patients who received subsequent doses decreased (Table 2). Their pain scores in the PACU decreased gradually, whereas the pain relief score increased.

The time from the end of operation to the first IM analgesic in group A was significantly shorter than in group B (p=0.007) (Table 3). The amount of morphine that group B received in the PACU is shown in Table 3. The number of analgesic requests in group A (median = 3) were significantly greater than in group B (median = 1) (p=0.001). The total amount of morphine the group B patients received during the first 24 hours postoperation including the PACU and the ward was significantly less than in group A (mean difference = 4.64 mg; 95% CI 0.08-9.19). The amount of morphine that group B received on the ward only was 14.8±9.2 mg, which was less than in group A (mean difference = 9.48 mg; 95% CI 4.91-14.04). We found that when patients reported enough relief from pain that they no longer needed any analgesics, most of their pain scores were not yet zero, and their pain relief scores did not reach 100 either. This occurred in only a few (Table 4). In Table 4, the patients were categorized according to the dose of morphine they needed in the PACU. We found that the greater the pain score initially, the larger the dose of morphine needed. Among the 26 patients (65%) who received morphine incrementally to the maximum dose (0.1 mg/kg), 7 patients (17.5%)

reported they still needed an additional dose. The average morphine dose that group B received in the PACU was 0.09±0.02 mg/kg.

There was significant positive correlation between the dose of morphine needed by the patients in the PACU and VNS at rest and VNS on coughing at the time they first needed analgesics or 'time 0' (Table 4) to a fair degree (r=0.448, p=0.002, and r= 0.404, p=0.005, respectively). The regression equations were:

$$\text{Total morphine dose (mg/kg)} = 0.053 + (0.004)\ \text{VNSr}$$
$$\text{or} = 0.043 + (0.005)\ \text{VNSc}$$

Table 3. The need for analgesics during the 24 h postoperative period on the ward.

	Conventional n = 40	IV Morphine n = 40
Time to the first IM morphine request (h)*	5.2 ± 4.9	9.4 ± 7.6
The amount of morphine in the PACU (mg)	0	4.8 ± 1.2
Number of analgesic requests in 24 h†	2.7 ± 1.1	1.6 ± 1.2
0 time (n)	0	7
1 time (n)	7	15
2 times (n)	12	9
3 times (n)	13	6
4 times (n)	7	3
5 times (n)	1	0
Total dose of morphine given (mg)‡	24.3 ± 11.2	19.6 ± 9.1

Values are mean ± SD.
IV = intravenous, IM = intramuscular, n = number of patients.
* p = 0.007
† p = 0.001
‡ mean difference = 4.64 mg; 95% CI 0.08-9.19

Table 4. The verbal numerical pain scores (VNS, 0-10) and pain relief scores (PRS, 0-100) of the intravenous morphine group categorized according to the total dose of morphine needed in the Postanesthesia Care Unit (PACU).

	Total dose of morphine patients needed (mg/kg)			
	0.04 (n=1)	0.06 (n=6)	0.08 (n=7)	0.10 (n=26)
At time 0				
VNS at rest	7.0 ± 0	7.3 ± 2.9	8.3 ± 2.4	9.4 ± 1.1
VNS on coughing	8.0 ± 0	8.2 ± 2.3	8.9 ± 1.7	9.6 ± 0.9
At 10 min after the last dose				
VNS at rest	4.0 ± 0	4.7 ± 3.3	2.4 ± 2.4	5.4 ± 1.6
VNS on coughing	6.0 ± 0	5.5 ± 2.7	3.0 ± 2.6	6.6 ± 2.0
PRS	50.0 ± 0	41.7 ± 30.6	76.4 ± 21.4	45.8 ± 19.2
At 30 min after the last dose				
VNS at rest	3.0 ± 0	4.5 ± 3.3	2.0 ± 1.6	4.7 ± 1.6
VNS on coughing	5.0 ± 0	4.8 ± 1.9	2.7 ± 2.0	6.0 ± 1.9
PRS	50.0 ± 0	46.7 ± 26.6	79.3 ± 18.4	50.4 ± 17.0

Values are mean ± SD.

where VNSr and VNSc are VNS at rest and VNS on coughing at time 0, respectively, and the maximum dose is 0.1 mg/kg (Fig. 1).

Nausea and vomiting were significantly more common in group A than in group B (p=0.04). Twenty-one patients (52.5%) in group A had nausea and vomiting which started in the PACU in 3 patients (two continued to the ward) and started on the ward in 18 patients. Twelve patients (30%) in group B had nausea and vomiting. Three of them had symptoms only in the PACU. In 4 patients the symptoms started in the PACU and continued to the ward. Symptoms started on the ward in 5 patients. When group B patients who developed nausea and vomiting in the PACU received metoclopramide 10 mg IV, they felt better and were able to receive the next IV morphine dose.

Satisfaction score for pain treatment in group A was 70.3±21.8, and in group B was 71.3± 20.4, which showed no statistical difference. Satisfaction scores in both groups showed no relationship to the presence or absence of nausea and vomiting although some patients commented that they were not satisfied because of nausea and vomiting. However, we found a low degree of positive correlation between the satisfaction score and pain relief score at 30 minutes after each patient's last dose of morphine (Spearman correlation=0.38, p=0.015).

DISCUSSION

Patients receiving conventional pain treatment in the PACU suffered from pain needlessly before getting IM analgesic just because the belief that opioids might do them harm during the immediate postoperative period and during transfer to the ward.

Morphine can be given to patients *via* many routes. Morphine given intramuscularly has a slow onset and yields an unsteady blood level. Continuous intravenous (IV) and patient-controlled analgesia (PCA) methods are very effective[1,2] and yield a steady analgesic blood level[3], but both methods

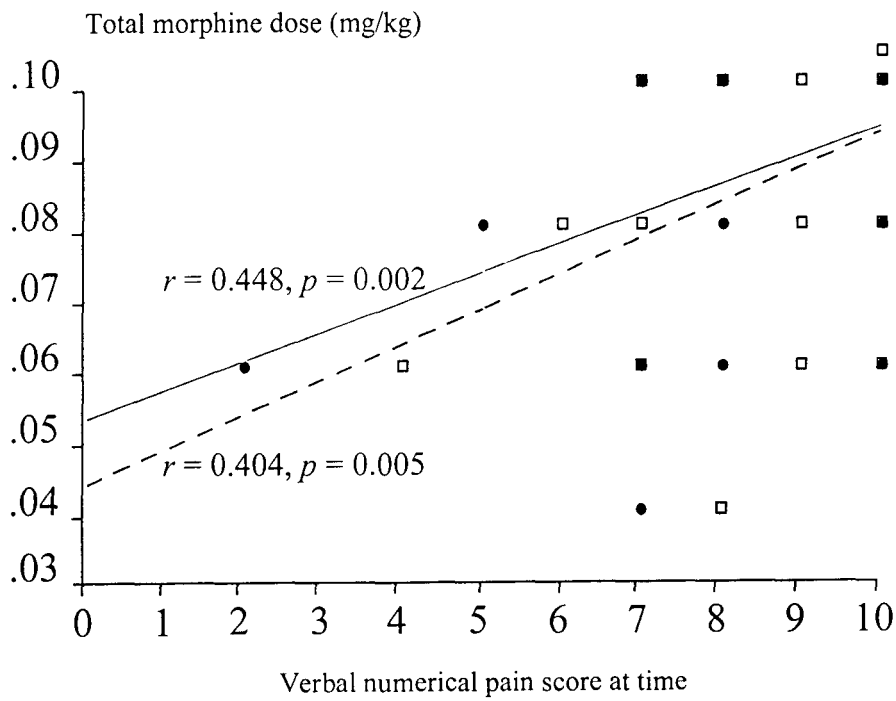

Fig. 1. Correlation between the dosage of morphine administered in the Postanesthesia Care Unit (Total morphine dose, mg/kg) and verbal numerical pain scores (0-10) at time 0. —— , • = total morphine dose and verbal numerical pain score at time 0 at rest (VNSr). ----- , □ = total morphine dose and verbal numerical pain score at time 0 on coughing (VNSc).

need either special apparatus or personnel to control drug administration, so it might be impracticable in some hospitals. Morphine given intravenously and intermittently has a fast onset and does not need any sophisticated apparatus but it should be given in an appropriate dose so patients will not develop respiratory depression or oversedation[4,5].

This study has shown that by starting the administration of optimum small doses of IV morphine incrementally in the PACU, pain could be alleviated promptly. Although this method was laborious compared with IV-PCA, it is suitable for a developing country. This method could be practical for postoperative pain relief because there was no respiratory depression or oversedation in any patients. It was easy to administer and needed no expensive equipment.

The administration of IV morphine in titrated doses every 10 minutes until the patients felt comfortable or the dose reached 0.1 mg/kg in 30 minutes in the PACU relieved postoperative pain safely. It was able to decrease the frequency and the amount of IM morphine required on the ward because the patients could rest and felt comfortable for a longer period of time.

The total amount of morphine the patients needed in the PACU was positively correlated with the level of pain at which they first needed analgesics, and could be calculated from their pain score at the first analgesic request. The total dose of morphine given in this study did not relieve pain completely, but to such a level that most patients needed no more analgesics, or to the maximum dose we had limited as a safe level for the study. The pain levels and the pain relief scores at 10 and 30 minutes after a dose of 0.1 mg/kg of morphine received by the group of 26 patients did not represent the state of pain relief for the whole group because seven of these wanted to receive more analgesic beyond the limited dose. Thus, for some patients, the maximum dose of morphine given incrementally in 30 minutes would be larger than 0.1 mg/kg but care should be exercised because side effects would also increase with a larger dose[6].

The patients' need for analgesics varied according to their pain threshold although they were undergoing the same type of operation and are in the same ethnic group and culture. In general, analgesia is achieved when the plasma opioid concentration reaches a particular level, the minimum effective analgesic concentration (MEAC), depending on an individual patient[7]. It could be implied that the initial and the following doses of morphine in this study should be larger or the interval should be shorter so the MEAC would be reached faster. Practically, we can adjust the administration of IV morphine in the PACU by increasing an incremental dose or decreasing an interval according to an individual need of analgesic. By increasing an incremental dose, we can calculate the total morphine dose that should be given, using the patient's pain score, then give half or three-fourths of the dose calculated initially (which may be more than the 0.04 mg/kg). After patient evaluation at intervals of 10 minutes, give another half or one-fourth of the dose calculated incrementally until their pain is adequately relieved. Using this technique, the total dose of morphine that relieves pain adequately may be lower than the calculated dose because the MEAC is reached more rapidly. An alternative is to give morphine at intervals of less than 10 minutes. This alternative may add more workload to personnel because patients need to be evaluated more frequently. In patients with an ASA class higher than I-II, IV morphine should be given cautiously although patients in the PACU are usually under close observation.

It was interesting to find that when most patients refused additional analgesics, they were not absolutely pain free (their pain score would have been zero), but their pain scores had reduced to between approximately 2 and 5. This corresponded to their pain relief reported as pain relief scores around 50 and 80, showing that most patients did not need complete pain relief. These levels of pain and pain relief scores could represent the level of pain that was acceptable and tolerable to the patients.

Although more patients in group A than in group B complained of pain during their stay on the ward (data not shown), the satisfaction scores showed no difference between the groups. The reasons could be due to the design of the study, the method used for measuring satisfaction, and the patient's attitude towards pain. This was not a cross-over design where the patients could compare which method was more satisfactory. A structured questionnaire instead of a satisfaction score based on a direct question might be a better method to use for measuring patients' satisfaction. Some patients commented that they

accepted pain as an unavoidable symptom and their expectation for pain relief was not high. What they expected was care from doctors and nurses. Nevertheless, pain relief score could determine satisfaction, as the satisfaction score in group B was positively correlated with pain relief score at 30 minutes after each patient's last dose.

SUMMARY

In conclusion, the administration of IV morphine by titrated doses, at the time they requested analgesia in the PACU, was safe, effective, and reduced the postoperative analgesic requirement. We propose equations for calculating the total dose of morphine for administration using the pain scores at the patients' first request for analgesics. When most patients felt enough relief from pain and declined additional analgesics, their pain scores did not reach zero, neither did their pain relief scores reach 100, but were at a level they could accept and tolerate.

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การให้มอร์ฟีนเข้าหลอดเลือดดำตั้งแต่ในห้องพักฟื้นทำให้ผลการระงับปวดหลังผ่าตัดดีขึ้น†

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การให้มอร์ฟีนทางหลอดเลือดดำเพื่อระงับปวดตั้งแต่ในห้องพักฟื้น มีการปฏิบัติน้อยมากในประเทศไทยทั้งที่เป็นที่ปฏิบัติกันโดยทั่วไปในหลายประเทศ ผู้วิจัยได้ทำการศึกษานี้เพื่อยืนยันว่าการให้มอร์ฟีนทางหลอดเลือดดำเพื่อระงับปวดตั้งแต่ในห้องพักฟื้นมีความปลอดภัย เพื่อหาขนาดมอร์ฟีนที่เหมาะสมที่จะให้ในห้องพักฟื้นและ หาระดับความปวดที่ผู้ป่วยไม่ต้องการยาเพิ่มอีก โดยศึกษาในผู้ป่วย 80 รายที่มารับการผ่าตัดทางนรีเวช แบ่งเป็น 2 กลุ่มเท่ากันโดยวิธีสุ่ม กลุ่มควบคุมได้รับมอร์ฟีนฉีดเข้ากล้ามเมื่อปวด โดยเริ่มที่หอผู้ป่วยตามแบบการรักษาเดิมที่เคยปฏิบัติ กลุ่มศึกษาได้รับมอร์ฟีนเข้าหลอดเลือดดำครั้งละน้อยจนกว่าจะเพียงพอในห้องพักฟื้น ผู้ป่วยได้รับการประเมินคะแนนความปวด คะแนนการลดปวด การง่วงซึม และสัญญาณชีพทุกครั้งหลังได้รับยา เมื่อกลับหอผู้ป่วย จะได้มอร์ฟีนฉีดเข้ากล้ามเมื่อต้องการ พบว่าปริมาณมอร์ฟีนที่ผู้ป่วยต้องการในห้องพักฟื้นมีความสัมพันธ์ทางบวกอย่างมีนัยสำคัญกับคะแนนความปวดขณะต้องการยาระงับปวด ระยะเวลาตั้งแต่เสร็จผ่าตัดถึงเวลาที่ได้มอร์ฟีนครั้งแรกที่หอผู้ป่วย ของกลุ่มศึกษานานกว่ากลุ่มควบคุมอย่างมีนัยสำคัญทางสถิติ ปริมาณมอร์ฟีนและจำนวนครั้งของการขอยาน้อยกว่ากลุ่มควบคุมอย่างมีนัยสำคัญทางสถิติ ไม่มีรายใดเกิดการกดการหายใจหรือง่วงซึมมากเกินไป โดยสรุป การให้มอร์ฟีนทางหลอดเลือดดำครั้งละน้อยเพื่อระงับปวดในห้องพักฟื้น ทำให้ผู้ป่วยต้องการยาระงับปวดที่หอผู้ป่วยช้ากว่า ปริมาณยาระงับปวดที่ต้องการที่หอผู้ป่วยน้อยกว่าผู้ป่วยที่ไม่ได้รับมอร์ฟีนในห้องพักฟื้น โดยที่ปริมาณมอร์ฟีนทั้งหมดที่ทยอยให้ในห้องพักฟื้นสามารถคำนวณได้จากคะแนนความปวดขณะเริ่มต้องการยาระงับปวด เมื่อผู้ป่วยปฏิเสธยาเพิ่ม พบว่าความปวดไม่ได้หายไปหมดแต่อยู่ในระดับที่ผู้ป่วยยอมรับได้

คำสำคัญ : การระงับปวดหลังผ่าตัด, มอร์ฟีน, ห้องพักฟื้นหลังผ่าตัด

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