

# Spinal Morphine for Post-Operative Analgesia after Lumbar Laminectomy with Fusion

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## Abstract

**Background :** Intrathecal administration of preservative free morphine (spinal morphine) provides excellent post-operative analgesia. Since the dura is readily accessible by the surgeon during lumbar spinal surgery, it would be convenient and attractive to administer morphine into the spinal space to provide adequate post-operative analgesia in these patients.

**Method :** A prospective randomized controlled study evaluated the post-operative analgesic effect of spinal morphine after lumbar laminectomy with fusion. Forty patients were randomly allocated to two groups, morphine (MO) or normal saline (NSS). Morphine 0.3 mg in normal saline 0.3 ml or normal saline 0.3 ml was injected into the dural sac under direct visualization before closing the wound. An intravenous PCA morphine device was provided for post-operative pain relief.

**Results :** Median visual analog scale (VAS) pain scores were lower in the MO group at 2, 4, 24 and 48 h after surgery (1, 1, 2.75 and 1.5 cm in the MO group vs 4.25, 4.25, 5 and 4 cm in the NSS group) ( $p < 0.05$ ). The time to first patient control analgesia (PCA) demand was delayed in the MO group (131.7 min vs 29.6 min) ( $p < 0.05$ ). The cumulative doses of PCA morphine consumption were lower in the MO group in the first 24 h and 24-48 h (13.7 and 15.9 mg vs 41.3 mg and 27.1 mg) ( $p < 0.001$ ). The incidence of pruritus was higher in the MO group in 24 h and 24-48 h (45%, and 45% vs 5% and 10%) ( $p < 0.05$ ). The incidence and severity of nausea, vomiting and sedation were not different. No patient developed respiratory depression or postdural puncture headache (PDPH). The patients' satisfaction with post-operative pain management was 100 per cent in the MO group and 85 per cent in the NSS group.

**Conclusion :** Spinal morphine improved post-operative pain relief after lumbar laminectomy.

**Key word :** Spinal Morphine, Lumbar Laminectomy, Post-Operative Analgesia

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Controlling post-operative pain is now known to reduce the incidence of morbidity such as pulmonary complications and venous thrombosis(1,2).

Intrathecal administration of preservative free morphine (spinal morphine) provides excellent post-operative analgesia in a number of surgical settings(3-7). Since the introduction of the technique in 1979(8), its use has been limited by high incidences of opioid related side- effects which include nausea, vomiting, pruritus, urinary retention and respiratory depression, which may have delayed onset. In an attempt to limit major and minor opioid side effects, the use of low doses spinal opioid has been advocated(9-14).

At King Chulalongkorn Memorial Hospital, spinal morphine has been administered to patients for post-operative pain control since 1990, with small doses of 0.1 to 0.3 mg given at the same time, the local anesthetic was given during spinal block for almost all obstetrics and gynecological procedures. It is also given to higher risk old-age group; patients who came for orthopedic surgeries such as total knee replacement and hip prosthesis replacement which are known to have severe post-operative pain. The results are a better convalescent period and less post-operative complications.

There is no report of spinal morphine for lumbar laminectomy with fusion in Thailand and it is well known that post laminectomy with fusion patients are almost always faced with severe agonizing pain that does not allow them to move.

Since the dura is readily accessible by the surgeon during lumbar spinal surgery, it would be convenient and attractive to administer morphine into the spinal space to provide adequate post-operative analgesia in these patients(15-19).

The aim of this study was to evaluate the efficacy of 0.3 mg of spinal morphine for post-operative analgesia in lumbar laminectomy with fusion.

## MATERIAL AND METHOD

After obtaining approval from the ethics committee of the faculty and informed consent from each patient, this prospective, randomized, double-blind, placebo-controlled study was performed at King Chulalongkorn Memorial Hospital, a 1500-bed university hospital affiliated with the Thai Red Cross Society of Thailand. American Society of Anesthesiologist (ASA) physical status class I or II patients who had been scheduled for lumbar laminectomy with fusion under general anesthesia were recruited for

the study. Exclusion criteria were; known history of morphine allergy; past history of severe headache; narcotic dependence; inability to quantify pain by visual analog scale (VAS) pain score; inability to use a patient control analgesia (PCA) device for post-operative analgesia (rescue drug), assessed by an anesthesiologist during pre-operative visit; having accidental dura tear during the surgery.

Patients were randomly allocated into 2 groups. The MO group received 0.3 mg in 0.3 ml preservative free morphine intrathecally; the NSS group received 0.3 ml of normal saline (placebo) intrathecally. The randomization sequence was selected based on a random number table. Randomly allocated coded syringe of drug, prepared by an anesthesiologist who would not be involved in post-operative visits.

All patients were premedicated with midazolam. After induction of anesthesia with thiopentone and succinylcholine, the trachea was intubated. The general anesthesia was maintained with isoflurane in a mixture of 66 per cent nitrous oxide and 34 per cent oxygen, fentanyl (1  $\mu$ g/kg/h) and vecuronium as the neuromuscular blocker. Their peri-operative monitoring included electrocardiogram, non invasive blood pressure, pulse oximetry and capnometry.

Before closure of the surgical wound, the surgeon inserted a 30-gauge needle under direct visualization into the subarachnoid space, when free flow of clear cerebrospinal fluid was obtained on aspiration, the study drug was administered. Patients in the MO group (n = 20) received 0.3 ml of 0.3 mg preservative-free morphine while those in the NSS group (n = 20) received 0.3 ml of normal saline.

After surgery, the patients were monitored for 2 h in the postanesthetic care unit (PACU). They were allowed to self-administer IV morphine via a PCA system (Abbott Pain Manager). 1 mg bolus each 6 min on demand only. The IV morphine PCA was adjusted over the next 48 h such that the pain level was kept at 3 cm on the VAS pain score.

At the ward, the patient's vital signs were recorded every 1 h for 6 h then every 4 h for 40 h. If the respiratory rate was less than 12 breaths/min, respiratory rate would be recorded every 15 min and PCA morphine would be withheld. If the respiratory rate was less than 10 breaths/min, arterial blood gas would be measured and a naloxone infusion would be used to reverse the respiratory depression.

Another anesthesiologist who was not involved in the peri-operative period visited the patient

at 2, 4, 24 and 48 h post-operatively (related to the end of surgery) to record the time to first IV PCA demand, cumulative doses of IV PCA morphine delivery and the patient was asked to quantify their pain on 10 cm VAS pain score (0 = no pain, 10 = worst imaginable pain). The patients were scored for sedation using a 4-point rating score (0 = fully awake; 1 = somnolent, responds to call; 2 = somnolent, responds to tactile stimuli; 3 = deep sedation, responds to painful stimuli), nausea and vomiting by a 4-point rating score (0 = no nausea and vomiting; 1 = mild nausea; 2 = moderate nausea; 3 = vomiting), pruritus by a 4-point rating score (0 = no pruritus; 1 = mild pruritus; 2 = moderate pruritus; treatment not requested; 3 = severe pruritus, treatment requested). Respiratory depression was defined if the respiratory rate was less than 12 breaths/min. Other complications included postdural puncture headache (PDPH) and infection. Urinary retention was not detectable since every patient received a foley catheter at the time of surgery. Patient's satisfaction with the post-operative analgesia was evaluated at 48 h post-operatively.

Power analysis was performed to determine the sample size of the groups. Allowing for the probability of a type 2 error of 0.1, type 1 error of 0.05 considering the success rate of the post-operative pain relief from the pilot study. An expected VAS pain score was in 0-3 cm range at 4 h post-operatively. Statistical analysis of the results was performed using the Student's *t*-test for demographic data, intra-operative data, time to first PCA demand and dose of PCA morphine. Pain scores were analyzed by Mann-Whitney test. Post-operative side effects and patient's satisfaction were compared by Chi-square test. All *p*-values less than 0.05 were considered significant.

## RESULTS

The two groups were not statistically different in age, sex, weight, height, the length of surgery and total fentanyl used (Table 1). The surgical pro-

**Table 1. Demographic and intra-operative data.**

	MO group (n = 20)	NSS group (n = 20)
Male/ Female (n)	9/11	10/10
Age (yr)	54.6 ± 9.9	52.8 ± 12.3
Weight (kg)	59.9 ± 8.9	64.4 ± 9.8
Height (cm)	158.6 ± 9.2	159.2 ± 9.0
Length of surgery (min)	240.5 ± 68.2	214.0 ± 66.7
Total fentanyl used (μg/kg)	2.8 ± 0.3	2.7 ± 0.2

Data are mean ± SD

cedures in the study patients and number of spinal levels operated on are summarized in Table 2.

The median VAS pain scores ranged between 1-2.75 cm 48 h post-operatively in the group receiving spinal morphine. VAS scores were significantly lower compared with the group that received spinal saline: at 2 h (1 cm in the MO group and 4.25 cm in the NSS group; *p* < 0.001), 4 h (1 and 4.25 cm; *p* < 0.001), 24 h (2.75 and 5 cm; *p* < 0.05) and 48 h (1.5 and 4 cm; *p* < 0.05), (Fig. 1).

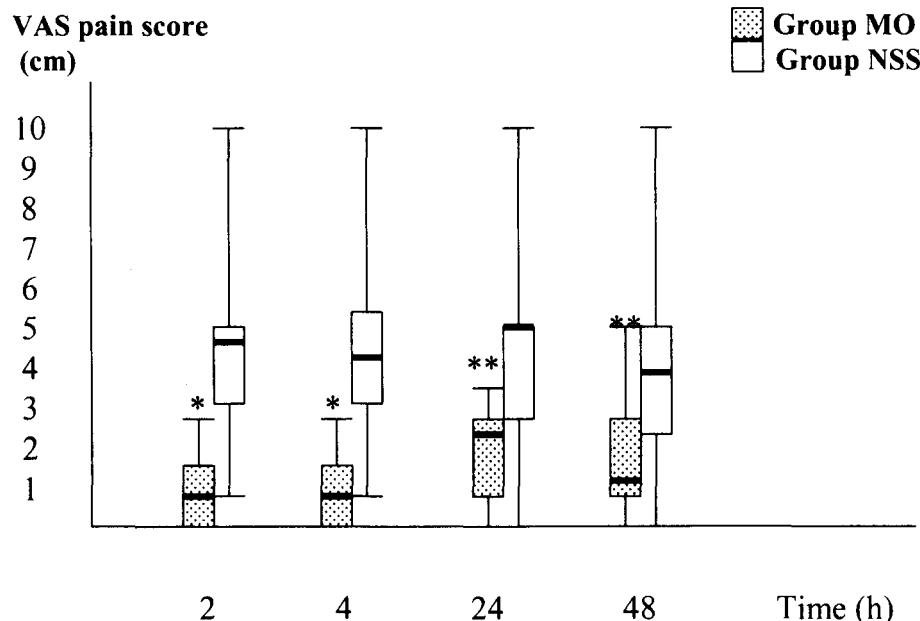
The mean time to first IV PCA morphine demand was significantly delayed in the MO group, compared to the NSS group (131.7 ± 213.8 min and 29.6 ± 15.5 min; *p* < 0.05). Cumulative doses of post-operative IV PCA morphine consumption were also significantly lower; *p* < 0.001 in the MO group, compared to the NSS group in the first 24 h (13.7 ± 7.5 and 41.3 ± 13.9; *p* < 0.001) and 24-48 h (15.9 ± 12.3 mg and 27.1 ± 11.7 mg; *p* < 0.001), (Table 3).

There was no difference in post-operative complications with regard to sedation or nausea/vomiting between the two groups in the first 24 and 24-48 h (Table 4). Nausea with or without vomiting occurred in 7 patients (35%) in the MO group and 10 patients (50%) in the NSS group in the first 24 h.; 7 patients (35%) in the MO group and 12 patients (60%) in the NSS group in 24-48 h. There were 2 patients in the MO group and 3 patients in the NSS group who

**Table 2. Type and level of surgery.**

Patients	Laminectomy and fusion		Levels of surgery	
	bone graft	bone graft + instrument	2 level	> 2 level
MO group (n = 20)	8	12	10	10
NSS group (n = 20)	7	13	11	9

Data are number of the patients



**Fig. 1.** Box plot of VAS pain scores at 2, 4, 24 and 48 h after surgery. Boxes represent interquartile range, horizontal lines in the boxes represent median values, and error bars are the range. The VAS pain scores were significantly reduced at 2 h, 4 h ( $p < 0.01$ ; \*), 24 h and 48 h ( $p < 0.05$ ; \*\*) in the MO group when compared with the NSS group.

**Table 3.** Post-operative analgesic requirements.

	MO group (n = 20)	NSS group (n = 20)	P-value
The time to first PCA demand (min)	$131.7 \pm 213.8^*$ (20-333)	$29.6 \pm 15.5$ (5-54)	0.001
Cumulative PCA morphine consumption (mg)			
0-24 h	$13.7 \pm 7.5^*$ (3-29)	$41.3 \pm 13.9$ (12-71)	0.000
24-48 h	$15.9 \pm 12.3^*$ (0-50)	$27.1 \pm 11.7$ (7-54)	0.003

Data are mean  $\pm$  SD (minimum to maximum value)

\*  $p < 0.05$ : see text for explanation

had vomiting and required antiemetic treatment. Symptoms were easily managed with conventional antiemetic therapy using metoclopramide, except 1 patient in the NSS group. The incidences of sedation were 10 patients (50%) in the MO group and 14 patients (70%) in the NSS group in the first 24 h; 7 patients (35%) in the MO group and 7 patients (35%) in the NSS group in 24-48 h. The sedation effect was most imminent 2 hours post-operatively (Table 5). No patient in either group had deep sedation. Pruritus was found signifi-

cantly more often in the morphine group at 24 h and 24-48 h ( $p < 0.05$ ) (45% vs 5% and 45% vs 10%). Mostly, the pruritus was mild to moderate degree. Only 1 patient in the MO group had severe pruritus and was easily managed with conventional therapy using nalbuphine. The symptom was seldom found at 48 h.

No patient developed respiratory depression (respiratory rate  $< 12$  breaths/min). There were no postdural puncture headaches. Two patients in both

Table 4. Post-operative complications.

Complications	Time and group									
	0-24 h		24-48 h		P-value	0-24 h		24-48 h		P-value
	MO group	NSS group	MO group	NSS group		Case	%	Case	%	
Nausea/Vomiting	7 <sup>a</sup>	35 <sup>b</sup>	10	50	0.522	7	35	12	60	0.205
Sedation	10	50	14	70	0.333	7	35	7	35	1.000
Pruritus	9*	45	1	5	0.011	9*	45	2	10	0.034
RR < 12	0	0	0	0		0	0	0	0	
PDPH	0	0	0	0		0	0	0	0	
Dizziness	1	5	0	0	1.000	1	5	0	0	1.000

<sup>a</sup> number of patients with clinical symptoms<sup>b</sup> % of patients with clinical symptoms

\* p &lt; 0.05: see text for explanation

Table 5. Severity of complications at 2 h, 4 h, 24 h and 48 h post-operatively.

Time	Nausea and vomiting		Sedation		Pruritus	
	MO group	NSS group	MO group	NSS group	MO group	NSS group
2 h	0 <sup>a</sup> , 1 <sup>b</sup> , 1 <sup>c</sup>	3, 2, 0	9, 0, 0	13, 0, 0	2, 2, 0	0, 0, 0
4 h	2, 2, 2	5, 1, 2	8, 0, 0	11, 0, 0	6, 2, 0	1, 0, 0
24 h	3, 3, 0	8, 1, 2	5, 0, 0	3, 2, 0	6, 2, 1	2, 0, 0
48 h	1, 2, 0	2, 2, 0	2, 0, 0	3, 0, 0	3, 0, 0	2, 0, 0

data are number of patients who had clinical symptoms

<sup>a</sup> number with mild symptoms,<sup>b</sup> number with moderate symptoms,<sup>c</sup> number with severe symptoms and required treatment

Table 6. Patients' satisfaction of post-operative pain management.

Patients satisfaction	MO group (n = 20)	%	NSS group (n = 20)	%
Satisfied	20	100	17	85
Dissatisfied	0		3	15

groups complained of mild dizziness, not related to position. There was no statistically significant difference in patient satisfaction between the two groups. All patients in the MO group were satisfied with the pain treatment. Three patients in the NSS group were dissatisfied because of inadequate analgesia (2 patients) and severe vomiting (1 patient), (Table 6).

## DISCUSSION

There is clear evidence that spinal morphine was able to alleviate post-operative pain after multi-level laminectomy with spinal fusion in most of the

patients. All patients in the MO group had a VAS pain score of 0-3 cm at 2 and 4 h; and 80 per cent and 85 per cent of the patients at 24 and 48 h, respectively. This compared to 20 per cent, 25 per cent, 30 per cent and 35 per cent of the patients in the NSS group. It was also found that some patients in the MO group did not experience any pain at all (0 cm VAS pain score) and the percentage was 40, 45, 5 and 90 at 2, 4, 24 and 48 h respectively.

Spinal morphine given to patients who had lumbar spine surgery for relief of post-operative pain was first reported in 1985(15). The advantage of this technique includes easy administration, simple post-operative pain management, and rapid onset of action. Easing of post-operative pain and earlier discharge from the hospital was the outcome.

Blacklock in 1986(16), used 1 mg of spinal morphine for laminectomy. No analgesic was used for the first 24 h post-operatively. All patients in the spinal morphine group required twice the amount of narcotic analgesics during the 2nd through 5th days

after the operation compared to the control group. All patients developed urinary retention for 24-36 h. In a previous study, the authors found no increase in requirement for narcotic analgesics after 24 h in the MO group. Urinary retention was not detectable since the bladder was catheterized for 3 days.

Johnson in 1989(17), abandoned the use of 1.5 to 2.5 mg of spinal morphine for lumbar fusion, as it afforded no better pain relief than IV PCA morphine alone and side effects of nausea and pruritus were common.

Spinal morphine is known to have complications that include nausea, vomiting, pruritus, urinary retention, sedation and respiratory depression. The incidences of these complications are proportional to the amount of morphine given. Respiratory depression usually occurs between 3.5-7.5 h after the spinal morphine is given. It is the result of the distribution of morphine in the CSF circulated to the 4<sup>th</sup> ventricle which is the suppression respiratory center. It is recommended to give low doses of spinal morphine, not more than 0.4 mg to avoid respiratory depression(9-14).

Ross in 1991(18), used 0, 0.125, 0.25 and 0.5 mg of spinal morphine after lumbar spine operation. 0.25 and 0.5 mg provided superior analgesia with a decreased length of hospitalization. The side effect was not different between the treated patients and the control group.

Boenzaart in 1999(19), used 0.2, 0.3 and 0.4 mg of spinal morphine for post-operative pain management after lumbar spine fusion with or without decompression. 0.2 mg was found to be inadequate and some patients who were given 0.4 mg of morphine were hypercapneic with  $\text{PaCO}_2$  up to 7.1 kPa (53 mmHg). So, authors selected 0.3 mg of spinal morphine for the study to avoid side effects including respiratory depression.

To monitor respiratory depression, the respiratory rate was monitored every 15 minutes during the first 2 h after the surgery and every one-hour for the next 6 h. No respiratory depression (respiratory rate less than 12 breaths/min) was found.

The authors deliberately chose to combine spinal and systemic opioid administration, because the post-operative pain of major spinal surgery is expected to last longer than 24 h, and it is not possible to cover the entire period with a single-shot intrathecal injection. Additionally, PCA therapy was con-

tinuous after the beneficial effects of spinal analgesia wore off. There is ample experimental evidence that spinal and systemic opioid act synergistically(20). Spinal morphine provided highly satisfactory post-operative analgesia and was rated by the patients as being > 80 per cent successful in controlling post-operative pain during 48 h after surgery.

In spite of the large amount of morphine administered, the patients in the NSS group were relatively experienced the lumbar laminectomy pain, compared to the patients in the MO group. The possible reason is the narcotic side-effect itself including the sedative effect which might limit the self-administered IV PCA morphine(21). On the contrary, patients in the morphine group who were relatively pain-free administered much smaller amounts of IV PCA morphine. In spite of their higher level of pain perception, 85 per cent of the patients in the NSS group were satisfied, which might have resulted from the satisfaction of being able to administer the opioid by themselves.

Incidence and severity of side effects were acceptable and easily controlled except 1 patient in the NSS group who had vomiting. There was no significant difference of incidence of nausea/vomiting and sedation between the saline and the spinal morphine groups. Nausea and vomiting in patients who have received spinal morphine is considered to be a side effect of the morphine; the mechanism is alleged to be activation of opioid receptors in the fourth ventricle caused by cephalad migration of the morphine. Because the severity of nausea and vomiting observed was not different between the control and treatment groups, however, a different mechanism is likely in most patients. For this reason, the treatment of nausea and vomiting with an antiemetic, rather than an opioid antagonist, may be more effective in patients who have received spinal morphine. The sedation effect in both groups was most imminent at 2 h post-operatively which can probably be explained by the residue anesthetics effect. Pruritus was found significantly more often in the morphine group compared to the NSS group. The incidence and severity of pruritus effect in patients who have received spinal morphine was found to be decreased at 48 h post-operatively, it is possible that the morphine had been removed from the fourth ventricle at that time. Headache was not a complaint. There were no serious or life-threatening complications.

In conclusion, 0.3 mg spinal morphine given to patients with additional IV PCA morphine is better than PCA morphine alone to alleviate post-operative

lumbar laminectomy with fusion pain, and besides pruritus there was no difference in other side effects including nausea, vomiting and sedation.

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## การฉีดมอร์ฟีนเข้าช่องไขสันหลังเพื่อลดความปวดหลังการผ่าตัด lumbar laminectomy with fusion

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การศึกษานี้เปรียบเทียบผลลดความปวดหลังการผ่าตัด lumbar laminectomy with fusion ในผู้ป่วย 2 กลุ่ม กลุ่มละ 20 ราย คือ กลุ่ม MO ได้รับการฉีด มอร์ฟีน 0.3 มก (ในน้ำเกลือ 0.3 มล) เข้าทางช่องไขสันหลัง เทียบกับในกลุ่ม NSS ซึ่งได้รับการฉีดน้ำเกลือ 0.3 มล เข้าทางช่องไขสันหลัง โดยทั้งสองกลุ่มจะได้รับการดมยาสลบตามแบบมาตรฐานและได้รับยาแก้ปวดเท่ากันคือ fentanyl 1 มก/ครั้ง/กก/ชม ก่อนการยืนปิดแผลผ่าตัดศัลยแพทย์จะเป็นผู้ฉีดยาเข้าทางช่องไขสันหลัง หลังผ่าตัดได้รับยาเม็ดมอร์ฟีนข้าหลอดเลือดดำเพื่อแก้ปวดเพิ่มเติมโดยวิธี patient control analgesia (IV PCA) การประเมินการแก้ปวด และภาวะแทรกซ้อนต่าง ๆ ทำโดยวิสัญญีแพทย์ผู้ซึ่งไม่ทราบว่าผู้ป่วยอยู่ในกลุ่มใดที่เวลา 2, 4, 24 และ 48 ชม หลังเข้าบีบแผล

พบว่ากลุ่ม MO เริ่มกด IV PCA เพื่อขอยาแก้ปวดครั้งแรกช้ากว่าในกลุ่ม NSS อย่างมีนัยสำคัญทางสถิติ ( $p$ -value < 0.05) (131.7 และ 29.6 นาที) กลุ่ม MO ขอยาแก้ปวดโดยวิธี IV PCA น้อยกว่าในกลุ่ม NSS อย่างมีนัยสำคัญทางสถิติ ทั้งที่เวลา 0-24 และ 24-48 ชม ( $p$ -value < 0.05) (13.7, 15.9 มก ในกลุ่ม MO และ 41.3, 27.1 มก ใน กลุ่ม NSS) ในขณะที่ผู้ป่วยในกลุ่ม MO พบรีระดับความปวดประมีนโดยวิธี visual analog scale (VAS) ต่ำกว่าในกลุ่ม NSS อย่างมีนัยสำคัญทางสถิติทั้งที่เวลา 2, 4, 24 และ 48 ชม. ( $p$ -value < 0.05) (1, 1, 2.75, 1.5 ชม ในกลุ่ม MO และ 4.25, 4.25, 5, 4 ชม ในกลุ่ม NSS)

อาการข้างเคียงได้แก่ คลื่นไส้, อาเจียน ง่วงซึม พบร้าไม่แตกต่าง อาการคันพูนในกลุ่ม MO มากกว่าในกลุ่ม NSS อย่างมีนัยสำคัญทางสถิติ ( $p$ -value < 0.05) และพบคันมาก 1 ราย ในกลุ่ม MO ไม่พบอาการปวดศีรษะหรือการกดการหายใจ นอกจากนี้มีผู้ป่วยจำนวน 3 ราย คิดเป็นร้อยละ 15 ในกลุ่ม NSS รู้สึกไม่พอใจกับการให้ยาและบัดเป็นจำนวนมากจากยังรู้สึกปวดมากและอาเจียนมาก

**คำสำคัญ :** มอร์ฟีนเข้าช่องไขสันหลัง, ผ่าตัดกระดูกสันหลังส่วนเอว, แก้ปวดหลังผ่าตัด

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