Comparing Low Dose Intrathecal Morphine with Femoral Nerve Block for Pain Control after Fixation of Extracapsular Hip Fracture on Top of Spinal Anesthesia: a Randomized Controlled Clinical Trial

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Abstract: **Comparing Low Dose intrathecal morphine with femoral nerve block for pain control after fixation of extracapsular hip fracture on top of spinal anesthesia: a randomized controlled clinical trial**

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Introduction: 0.1 mg intrathecal morphine can provide effective pain control after extracapsular hip fracture but must be weighed with possible complications in these fragile patients. The benefit of femoral nerve block (FNB) has yet to be conclusively proven. ***Objective:*** This study compared the effectiveness of postoperative pain control between 0.1 mg intrathecal morphine (IT-gr) and 20 ml of 0.25% bupivacaine for FNB (FNB-gr) on top of spinal anesthesia (C-gr). ***Method:*** The study was a randomized, controlled trial conducted from January 2011 through August 2012 at Siriraj Hospital. Fifty one patients were randomized into three groups (17 for each group: spinal anesthesia or controlled group (C-gr), spinal anesthesia with intrathecal morphine (IT-gr) and spinal anesthesia with femoral nerve block (FNB-gr). After operation, all patients received intravenous patient-controlled analgesia

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(IV PCA) for 48 hours. On-demand doses of PCA morphine were recorded at given times. Every patient was evaluated at 3, 6, 12, 24 and 48 hours for visual rating scale of pain, satisfaction, sensory and motor recovery, and side effects. ***Results:*** There were no significant differences between groups with respect to age, sex, body mass index, ASA physical status, site and operative time. Time to first rescue morphine was significantly longer in IT-gr than C-gr (470 vs 97 min, p = 0.003) but no significant difference between FNB-gr and C-gr. More than 50% reduction of 24 hours morphine consumption was found in IT-gr, and significantly lower than with C-gr (6.6+7.5 vs 14.2+5.5 mg, p = 0.007). The average pain scores in all groups were lower than 4 at any time after operation and these were not clinically significant. More patients in IT-gr rated "excellent" in the first 24 hours and significantly higher than the others. There was no serious complication found in the study and only a few patients had side effects. ***Conclusions:*** 0.1 mg intrathecal morphine, not FNB significantly extends the postoperative pain-free period for fixation of extracapsular hip fracture without serious complication – a key concern in elderly patients.

Keyword: *Intrathecal morphine, extracapsular hip fracture*

Introduction

Hip fracture is a common cause of morbidity and mortality in the elderly population with an increasing prevalence of osteoporosis.[1] The osteoporosis incidence in women increased from 5% at age 50 to 50% at age 85 and in men from 2.4% to 20% respectively.[2] These patients should be treated as early as possible by prompt surgery to enable early and effective rehabilitation. Regional anesthesia for surgery of the hip joint requires sufficient blockade of femoral, obturator, sciatic and lateral femoral cutaneous nerve, which can be achieved with spinal or epidural blockade.[3] It is suggested that patients with hip fracture surgery, the only proven benefit of regional anesthesia is the reduction of postoperative confusion.[4,5] Continuous epidural or peripheral nerve block, started prior to surgery, decreases intra-operative anesthetic requirement and prolongs postoperative pain-free period.[6] Femoral nerve block is one of those alternatives, though its effectiveness in surgical fixation of extracapsular hip fracture has never been proven. Intrathecal opioid even in low dose (0.1 mg morphine) can provide adequate pain-free period after hip surgery.[7] However, hip fracture usually happens in the elderly, and the risk of respiratory depression from intrathecal opioid is a matter of concern. The purpose of this study was to compare 0.1 mg intrathecal morphine and femoral nerve block with 20 ml of 0.25% bupivacaine on top of spinal anesthesia focusing postoperative pain control and side effects.

Methods

We performed a randomized, controlled

clinical trial from January 2011 to August 2012 on 51 patients with schedule of surgical fixation of extracapsular fracture hip. The study was approved by the Institutional Review Board, Siriraj Medical Center. Inclusion criteria were age 40-90 years, American Society of Anesthesiologists (ASA) physical status I-III, body weight > 30 kg, body mass index 20-35 kg/m^2, and ability to read and cooperate with evaluation techniques. Exclusion criteria were history of allergy to local anesthetic agents, analgesics and adjuvant drug preparations, inability to perform spinal block, progressive neurological deficit and severe dehydration, reoperation, pathological fractures such as severe infection and carcinogenic process.

Patients were recruited before the day of surgery and written informed consent was obtained. Block of six randomization was generated by computer program. Sealed envelopes of sequential number were opened before anesthesia. Patients were allocated to three groups: Group one (Control group, C-gr) received spinal anesthesia alone; Group two (Intrathecal morphine group, IT-gr) received spinal anesthesia and 0.1mg preservation-free morphine and Group three (Femoral nerve block group, FNB-gr) received a single femoral nerve block with 20 ml of 0.25% bupivacaine before spinal anesthesia. Nerve stimulator (Stimuplex® HNS II; B Braun, Melsungen, Germany) with a 50-mm 22-gauge insulated needle (Stimuplex® A; B Braun) were used to identify femoral nerve; successful location was indicated by contraction of the quadriceps muscle at < 0.5 m Amp. Spinal block was performed with patients in lateral decubitus positioning, and hyperbaric bupivacaine (0.5% in 8.75% dextrose) 1.8-2.5 ml was injected. Successful block was assessed by loss of both cold sensation and ability to flex the knee.

Patients received balanced salt solution 80-100 ml/hr, starting in the morning of operation day. On arrival to the operating room, baseline vital monitoring, i.e. automatic non-invasive blood pressure, pulse oximeter and EKG was applied as usual. Intravenous sedation was performed using midazolam with a maximum dose of 2 mg. At PACU patients were placed on intravenous patient-controlled analgesia (IV PCA) for 48 hours with no basal rate. Patients could trigger for one mg morphine every five minutes with a dose limit of four milligrams in four hours. Additionally, patient received oral paracetamol 500-1000 mg every 8 hours for three days. Intravenous ondansetron 8 mg was started intraoperatively and continued postoperatively every 8 hours for 2 days. Chhlorpheniramine 10 mg and metoclopramide 10 mg were given on demand for treatment of pruritus and nausea and vomiting respectively.

Postoperatively at 3, 6, 12, 24 and 48 hours, all patients were evaluated by research assistants blinded to treatment groups using visual analog scale for pain assessment. Additionally recovery of sensory and locomotory function, occurrences and severity of nausea, vomiting and pruritus were recorded. The first demand for morphine was recorded. At 24 and 48 hours postoperatively, the total consumption of morphine was noted together with quality of pain control assessed by Patient Global Assessment (PGA) at four levels: 'excellencte', 'good', 'acceptable', 'bad' together with ''Patient satisfactory visual analogue scoring'' (100 millimeter).

Statistics: We considered the reduction of morphine consumption in the first 24 hours in both treatment groups should be less than 30% compared to controlled group. Using analysis of variances for comparison of continuous variables, with a two-sided α of 0.05 and an equivalence margin of β at 0.10 (power 90), the sample size of 15 patients for each group was required. Assuming a drop-out risk for FNB or spinal block failure, 17 patients on each group were designed.

Data were analyzed using SPSS version 11.5. Descriptive statistics were applied to analyze demographic variables. Chi-square test was used for categorical variables, and ANOVA for comparison of continuous variables among the groups.

Results

During the study period, 80 patients underwent surgical fixation of extracapsular hip fracture. Fifteen were operated in emergency situation; fourteen were excluded by exclusion criteria (eight cases were not suitable for spinal anesthesia, four from communication problem and two from pathological fracture). Only 51 patients consented to participate in the study. Seventeen patients were allocated in each group of spinal anesthesia alone or controlled group (C-gr), spinal anesthesia with intrathecal morphine or intrathecal group (IT-gr) and spinal anesthesia with single femoral nerve block or femoral nerve block group (FNB-gr). Three patients (one from each group) were withdrawn because of failure of spinal block and another one case in femoral nerve block group that the surgical plan was changed to total hip replacement. There were no significant differences between the groups with respect to age, sex, body mass index, ASA, operation technique and time (Table 1).

Table 1 Participants' demographic data, all continuous data were displayed in mean ± SD

	Control group N = 16	IT-gr N=16	FNB gr N=15	p-value
Age (years)	78 ± 5.2	70.8 ± 13.6	72.7 ± 12	0.16
Sex (male:female)	7:9	6:10	7:8	0.14
BMI (kg/m^2)	21 ± 2.7	22.2 ± 2.2	22.2 ± 2.7	0.24
ASA (1:2:3)	0:7:9	3:9:4	1:8:6	0.06
Operative time (min)	89.7 ± 23.3	103.8 ± 16	97.7 ± 13.4	0.29
Side (Rt:Lt)	7:9	6:10	9:6	0.09

Time to first rescue morphine was longest in patients with intrathecal morphine, IT-gr (median 470 min), much shorter in patients with femoral block, FNB-gr (120 min) and shortest in C-gr (97.5 min), the difference between IT-gr and C-gr was significant (p = 0.003, Table 2). Total morphine consumption in 24 hours postoperatively was lowest in IT-gr and more than 50 % reduction when compared

with C-gr. (6.6 + 7.5 mg vs. 14.2 + 5.5 mg, p = 0.007; Table 2). Patients in FNB-gr needed less morphine compared to C-gr, but the difference was not significant (10.5 + 3.6 mg, p = 0.3). Between > 24-48 hr, the total morphine consumption was still lowest in IT-gr, but the differences between the three groups were not significant (Table 2)

Table 2 Time to first dose morphine and morphine consumption 24 and 48 hours

	Control group N=16	IT-gr* N=16	FNB gr** N=15	p-value
Latency (min)				
Minimum	15	30	10	*p = 0.003
Maximum	312	> 24 Hr	525	**p = 0.77
Median	97.5	470	120	
Morphine (mg, mean and range)				
24 hours	14.2 ± 5.5	6.6 ± 7.5	10.5 ± 3.6	*p = 0.007
	4-21	0-24	5-16	**p = 0.29
> 24- 48 hours	18.8 ± 7.9	13.0 ± 10.7	19.1 ± 18.2	*0.53
	5-30	0-39	6-80	**p = 0.99

*Comparing between control and It-group, ** Comparing between control and FNB group

The average postoperative pain scores in all groups were generally below 3.5 at any time. The pain score in IT-gr was consistently lower than C-gr until the end of the investigation period and also lower than FNB-gr until 24 hr postoperatively (Figure 1)

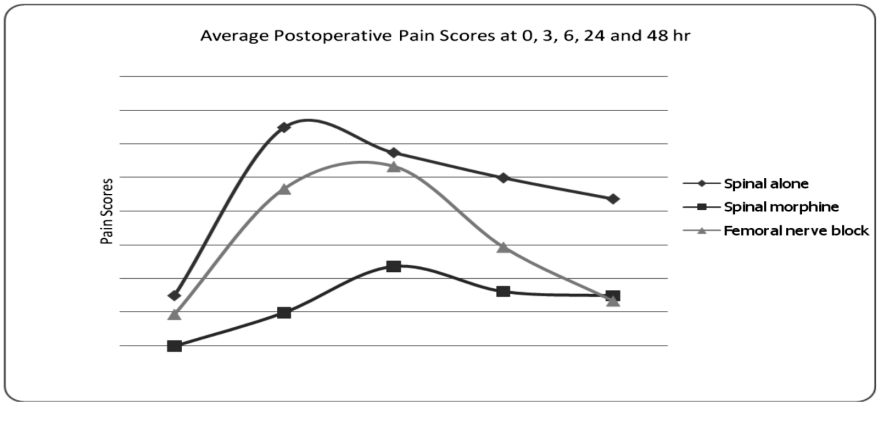

Figure 1 Comparison of Mean visual rating scores at 0, 3, 6, 24 and 48 hours postoperation

The greatest difference was observed 3-6 hours after operation. None of the differences in pain score reached statistical significance.

Patients' global assessment and satisfactory score was best in IT-gr (Table 3)

Table 3 Satisfaction scores

	Patient global assessment at	Control group N=16	IT-gr N=16	FNB gr N=15	p-value
24 hr	- Excellent	19%	69%	40%	0.04
	- Good	56%	25%	60%	
	- Acceptable	12%	6%	0%	
	- Bad	12%	0%	0%	
48 hr	- Excellent	31%	56%	47%	0.7
	- Good	50%	38%	40%	
	- Acceptable	13%	6%	13%	
	- Bad	6%	0%	0%	
Satisfaction score at					
24 hr (100 mm)		68.7 ± 17.4	84.3 ± 17.8*	83.3 ± 14.9**	*p = 0.04
		30 - 100	50 - 100	60 - 100	**p = 0.07
48 hr (100 mm)		73.1 ± 16.2	86.8 ± 14.9*	84.0 ± 15.4**	*p = 0.05
		40 - 100	50 - 100	60 - 100	**p = 0.16

*Comparing between control and It-group, ** Comparing between control and FNB group

Patients with C-gr had the worst results at any time; only in this group pain therapy was judged as 'bad' (12% after 24 and still 6% after 48 hr). Regarding the overall satisfactory score, IT-gr and FNB-gr were similar, both being better than C-gr.

As demonstrated in Table 4, no serious complications occurred during this study and only some side effects were recorded without differences between the groups (Table 4)

Table 4 Side effects

Number of patients	Control group N=16	IT-gr N=16	FNB gr N=15	p-value
Sedation score >1	None	None	None	0.6
Nausea/vomiting	1	1	None	0.5
Pruritus	None	1	None	0.09

One patient each from C-gr and IT-gr needed treatment for severe nausea, vomiting and pruritus.

Discussion

Regional anesthesia, both spinal and epidural has been considered an alternative to general anesthesia in hip joint surgery especially for the elderly, as it may decrease the incidence of postoperative confusion[4, 5], especially if morphine was added intrathecally for effective postoperative pain control. However, using spinal morphine in these patients has raised a serious concern about potential side effects, such as sedation, respiratory depression, nausea and vomiting (PONV). Those worries led to the question of the lowest effective dose of intrathecal morphine. In this study we used the lowest dose of spinal morphine (0.1 mg), and found it effective for pain control, being significantly superior to spinal anesthesia without morphine, and even better compared to femoral block. Importantly, no relevant side effects occurred and even PONV incident was rare.

Effective and early preoperative pain therapy after hip fracture both with continuous epidural[8, 9] or regional block 10-12 have been proven not only to increase patients' comfort but also to reduce the incidence of peri-operative myocardial ischemia.[8] However, the effectiveness of these methods on patients' outcome is unclear. In our study, the effectiveness of postoperative pain control using femoral nerve block with 20 ml 0.25% bupivacaine on top of spinal anesthesia was poor, especially when compared with intrathecal morphine. This result is different from the conclusions of Parker and coworkers (Cochrane review)[6] in 2002, reviewing four studies with different anesthetic techniques. Only in studies with general anesthesia, additional triple nerve block could prolong postoperative pain-free period and reduce analgesic requirement postoperatively.[13, 14] In patients with spinal anesthesia for surgical fixation of hip fracture, the effect of femoral nerve block was not satisfying[15, 16] whereas low dose intrathecal morphine was more effective. However, it has to be noted that femoral blockade is not the number one method of choice for peripheral block of the hip. The psoas compartment block provides better analgesia, but its application is sophisticated and time-consuming compared to intrathecal morphine that can be performed easily and fast. Other types of peripheral nerve block need more studies for comparing to intrathecal morphine for postoperative pain control.

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การศึกษาเปรียบเทียบประสิทธิภาพการระงับปวดภายหลังการผ่าตัดกระดูกสะโพกหักด้วยเหล็กดามระหว่างการทำ Femoral nerve block และการให้มอร์ฟีน 0.1 มก ในช่องไขสันหลัง

บทคัดย่อ

บทนำ: มอร์ฟีน 0.1 มก. ที่ฉีดเข้าช่องน้ำไขสันหลังมีผลการระงับปวดที่ดีสำหรับการผ่าตัดใส่เหล็กดามที่ข้อสะโพกหักนอกแคปซูลแต่ต้องพิจารณาถึงภาวะแทรกซ้อนที่อาจเกิดขึ้นได้โดยเฉพาะในผู้ป่วยเปราะบาง ประโยชน์ของการฉีดยาชารอบๆ เส้นประสาทฟีมอรัลสำหรับการผ่าตัดนี้ยังไม่สามารถสรุปได้ชัดเจน ***วัตถุประสงค์:*** การศึกษานี้เปรียบเทียบผลการระงับปวดหลังผ่าตัด ระหว่างการให้มอร์ฟีน 0.1 มก. ฉีดเข้าช่องน้ำไขสันหลัง หรือ การฉีดยาบิวพิวาเคน 0.25 % จำนวน 20 มล. รอบๆเส้นประสาทฟีมอรัล ในผู้ป่วยที่ได้รับการระงับความรู้สึกด้วยวิธี spinal block ***วิธีการศึกษา:*** การศึกษาเป็นการศึกษาควบคุมแบบสุ่มทำที่โรงพยาบาลศิริราชในช่วงเดือนมกราคม พศ. 2554 ถึงเดือนสิงหาคม พ.ศ. 2555 ผู้ป่วย 51 คน ได้รับการแบ่งกลุ่มโดยการสุ่มเป็น 3 กลุ่มๆ ละ 17 คน กลุ่มควบคุม (C-gr) ผู้ป่วยจะได้รับการฉีดยาชาเข้าไขสันหลังอย่างเดียว กลุ่มที่สอง (IT-gr) ผู้ป่วยจะได้รับมอร์ฟีน 0.1 มก. พร้อมการฉีดยาชาเข้าไขสันหลัง และกลุ่มที่สาม (FNB-gr) ผู้ป่วยจะได้รับยาบิวพิวาเคน 0.25 % จำนวน 20 มล. รอบๆ เส้นประสาทฟีมอรัล ร่วมกับการฉีดยาชาเข้าไขสันหลัง ผู้ป่วยทุกคนหลังการผ่าตัดจะได้รับยามอร์ฟีนเข้าทางหลอดเลือดดำแก้ปวด ผ่านเครื่องที่ควบคุมโดยตัวผู้ป่วยเอง (patient-controlled analgesia (PCA)) มีการประเมินค่าความปวดเมื่อ 3, 6, 12 และ 24 ชั่วโมงหลังการผ่าตัด และมีการประเมินความพึงพอใจต่อวิธีการระงับปวดที่ได้รับ ภาวะแทรกซ้อน อาการชาหรือขาอ่อนแรง ***ผลการศึกษา:*** ไม่พบความแตกต่างระหว่างกลุ่มในแง่ของอายุ เพศ ดัชนีมวลกาย สมรรถภาพร่างกายแบ่งตาม ASA ตำแหน่งและระยะเวลาการผ่าตัด ในกลุ่มที่ได้รับมอร์ฟีนทางช่องน้ำไขสันหลัง มีระยะเวลาการระงับปวดนานกว่าโดยได้ยามอร์ฟีนทางหลอดเลือดดำครั้งแรกเมื่อเวลา 470 นาทีเปรียบเทียบกับ 97 นาทีในกลุ่มควบคุม ($p = 0.003$) และใช้ยามอร์ฟีนใน 24 ชั่วโมงแรกน้อยกว่า (6.6+7.5 มก. เทียบกับ 14.2+5.5 มก., $p = 0.007$) แต่ไม่มีความแตกต่างทางนัยสำคัญทางสถิติระหว่างกลุ่ม FNB กับกลุ่มควบคุม ผู้ป่วยทุกคนได้ค่าคะแนนความปวดที่น้อยกว่า 4 ตลอดระยะเวลาของการศึกษา กลุ่ม IT ให้คะแนนความพึงพอใจในเกณฑ์ดีมากสูงกว่ากลุ่มอื่นๆ ภาวะแทรกซ้อนพบน้อยมากในผู้ป่วยทุกกลุ่ม ***สรุป:*** มอร์ฟีนขนาด 0.1 มิลลิกรัมที่ฉีดเข้าช่องน้ำไขสันหลัง เพิ่มระยะเวลาที่ผู้ป่วยไม่รู้สึกปวดหลังการผ่าตัดใส่เหล็กดามในผู้ป่วยที่กระดูกสะโพกหักแบบนอกแคปซูล โดยมีภาวะแทรกซ้อนน้อยมาก ซึ่งเป็นประเด็นที่สำคัญ ในการดูแลรักษากลุ่มผู้ป่วยสูงอายุ

คำสำคัญ : *มอร์ฟีนทางไขสันหลัง, กระดูกฟีเมอร์หัก*