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Comparison of Morphine Given by An Intravenous Sliding Scale or by Intramuscular Route for Postoperative Pain Relief in Pediatric Patients : An Interim Analysis

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Abstract :

Objectives : **To assess the efficacy in pain relief, complication, practicality and patient's compliance of morphine given by IV sliding scale (IV) compared to that given intramuscularly (IM) in children after surgery.**

Method : **One hundred and thirty-two children were randomly allocated to receive postoperative morphine via IM route (0.1 mg/kg) on a 6-h PRN basis or IV route on a sliding scale basis. Blood pressure, heart rate, respiratory rate, SaO_2, nausea/vomiting, pain score using CHEOPS and patient's compliance were recorded. A questionnaire was used to evaluate the satisfaction with and practicality of these techniques among nurses.**

Results : **This study was terminated early and interim analysis was performed because 47% of the patients in the IM group refused treatment and only 32 patients remained for study (age 1.9-12 y, ASA 1). The proportions of patients with moderate to severe pain (IM 73.3%, IV 76.5%), median of maximum CHEOPS score (IM 9, IV10), average CHEOPS score (IM 6.01, IV 6.03), and morphine consumption (IM 0.157, IV 0.144 mg/kg/24h) of both groups were not statistically different. Neither respiratory depression**

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nor desaturation was detected. Nurses preferred using the sliding scale technique due to better patient's compliance.

Conclusions **: The IV sliding scale was superior to IM technique regarding patient's compliance and nurses' preference. The degree of pain relief obtained and complications of treatment were not different.**

Key words : Intravenous sliding scale, morphine, pediatric, postoperative pain

เรื่องย่อ : **การเปรียบเทียบผลของมอร์ฟีนที่บริหารด้วยวิธีให้เข้าหลอดเลือดดำแบบ Sliding Scale กับวิธีฉีดเข้ากล้ามในการระงับปวดหลังผ่าตัดแก่ผู้ป่วยเด็ก : Interim Analysis**

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วัตถุประสงค์ : เพื่อเปรียบเทียบผลของการบริหารยามอร์ฟีน โดยวิธีฉีดเข้าหลอดเลือดดำแบบ sliding scale กับวิธีฉีดเข้ากล้าม ต่อการระงับปวดหลังผ่าตัดในผู้ป่วยเด็ก ภาวะแทรกซ้อน และการยอมรับของผู้ป่วยและพยาบาล

วิธีการศึกษา : วางแผนศึกษาในผู้ป่วยเด็กหลังผ่าตัดที่คาดว่าจะมีอาการปวดตั้งแต่ระดับปานกลางถึงรุนแรง จำนวน 132 ราย โดยแบ่งผู้ป่วยเป็น 2 กลุ่มแบบสุ่ม กลุ่มควบคุม (IM) ได้รับการฉีดยามอร์ฟีนเข้ากล้าม (0.1 มก./กก.) เมื่อเด็กร้องขอทุก 6 ชม. กลุ่มทดลองได้รับยามอร์ฟีน ฉีดเข้าหลอดเลือดดำแบบ sliding scale (IV) บันทึกอาการปวดโดยใช้ CHEOPS score, ค่าความดันเลือด, ชีพจร, อัตราการหายใจ, SaO_2 และอาการคลื่นไส้อาเจียนทุก 1 ชม. เฝ้าสังเกต การยอมรับยาของผู้ป่วย และประเมินความพึงพอใจของพยาบาล โดยใช้แบบสอบถาม

ผลการศึกษา : การศึกษานี้ต้องยุติก่อนเก็บข้อมูลได้ครบ เนื่องจากร้อยละ 47 ของผู้ป่วยในกลุ่ม IM ปฏิเสธการรักษา จำนวนผู้ป่วยที่ศึกษามี 32 ราย อายุ 1.6-12 ปี ASA class 1 ไม่พบความแตกต่างในอัตราส่วนของผู้ป่วยที่มีอาการปวดระดับปานกลางถึงรุนแรง (IM 73.3%, IV 76.5%), ค่า median ของ CHEOPS score สูงสุด (IM 9, IV 10), ปริมาณการใช้มอร์ฟีนใน 24 ชม. (IM 0.157, IV 0.144 มก./กก./24 ชม.) ไม่พบภาวะกดการหายใจในทั้ง 2 กลุ่ม พยาบาลชอบใช้วิธี IV ในการดูแลผู้ป่วยมากกว่าวิธี IM เพราะผู้ป่วยยอมรับวิธี IV มากกว่า

สรุป : วิธีบริหารยามอร์ฟีนเข้าหลอดเลือดดำแบบ sliding scale ดีกว่าวิธีฉีดเข้ากล้ามในด้านการยอมรับของผู้ป่วยและพยาบาล ผลการระงับปวดและภาวะแทรกซ้อนของวิธีทั้งสองไม่แตกต่างกัน

คำสำคัญ : การบริหารยามอร์ฟีนเข้าหลอดเลือดดำแบบ sliding scale, ผู้ป่วยเด็ก, อาการปวดหลังผ่าตัด

INTRODUCTION

Several studies since the 1980s have indicated that postoperative pain in children was undertreated.[1-3] They did not receive analgesic treatment to the same extent as adults did, and children often experienced postoperative pain. Since then efforts have been made to improve pain management, i.e., new analgesic substances and techniques have been introduced to children and several methods of assessing pain intensity in children have been developed.

Parenteral opioids are commonly used to treat moderate to severe pain after surgery. There are several methods that can be used for opioid administration for acute pain. Spinal or epidural opioids in children are of limited use in a hospital where anesthesiologists are available. Patient controlled analgesia (PCA) and a continuous intravenous infusion can provide a constant therapeutic blood level but the equipment for drug delivery is expensive. Moreover, PCA is only suitable for children over 7 years of age and the blood level of opioid may accumulate with an intravenous infusion technique.[4]

Children comply well with the intermittent intravenous bolus technique but the wide fluctuation in blood levels of opioids may be associated with untoward side effects and hypoanalgesia. The intramuscular route given on a PRN basis is still widely used in Thailand because of the unproven belief in its superior safety in spite of pain from the injection and the resulting fluctuation in blood levels.

Intravenous methadone given with a sliding scale technique has been recently reported as a simple, practical and inexpensive method which permits easy adjustment of the dose according to the patients' changing requirements.[5-8] A "sliding scale" adjusts the intravenous methadone dose according to the nurse's assessment of the child's pain as being either severe (0.07 mg/kg), moderate (0.05 mg/kg), or mild (0.03 mg/kg). Methadone has a much longer half-life than morphine, averaging approximately 19 hours, in children from 1 year of age through adolescence, although there is wide individual variation in the rate of clearance.[8-10] Since methadone is not available in our country, an equipotent dose of morphine and a 3-h interval assessment were used in this study.

The objectives of this study were to compare the effectiveness of intravenous (IV) sliding scale and intramuscular (IM) morphine during the first 24 hours after surgery based on 1) proportion of patients with moderate to severe pain, 2) opioid consumption, 3) untoward effects, 4) patients' compliance, and 5) nurses' satisfaction.

MATERIALS AND METHODS

After approval from our Institutional Review Board and consent from parents, children (aged 1-13 years, ASA physical status 1-2) in whom it was thought that moderate to severe postoperative pain would be experienced were enrolled in this study. Children who had respiratory, cardiovascular or neurological diseases, chronic pain, and allergy to morphine were excluded. In addition, patients who received continuous epidural analgesia were also excluded.

Patients were randomly allocated into 2 groups when they arrived to the wards. The control group (IM) received intramuscular morphine 0.1 mg/kg at 6-h interval as needed. The study group (IV) received intravenous morphine or a "sliding scale" in which morphine doses were adjusted according to the nurse's assessment of the child's pain at 3-h interval. Morphine 0.07, 0.05 and 0.03 mg/kg were given for severe, moderate and mild pain respectively. Each dose of intravenous morphine was infused over a 20-minute period.

Nurses were trained to score the severity of pain by using CHEOPS (Children's Hospital of Eastern Ontario Pain Scale) which has been validated in our culture.[11] They were tested for inter-observer reliability by scoring 30 pain behaviors from a videotape. Further training was performed if the intraclass correlation was less than 0.8. Children aged 5 or over reported their pain by using 5 facial expressions of pain[12] (Figure 1).

CHEOPS and Facial Expression Pain Scale scores were recorded at 3-h interval. Both pain scales were categorized according to severity of pain as follows:

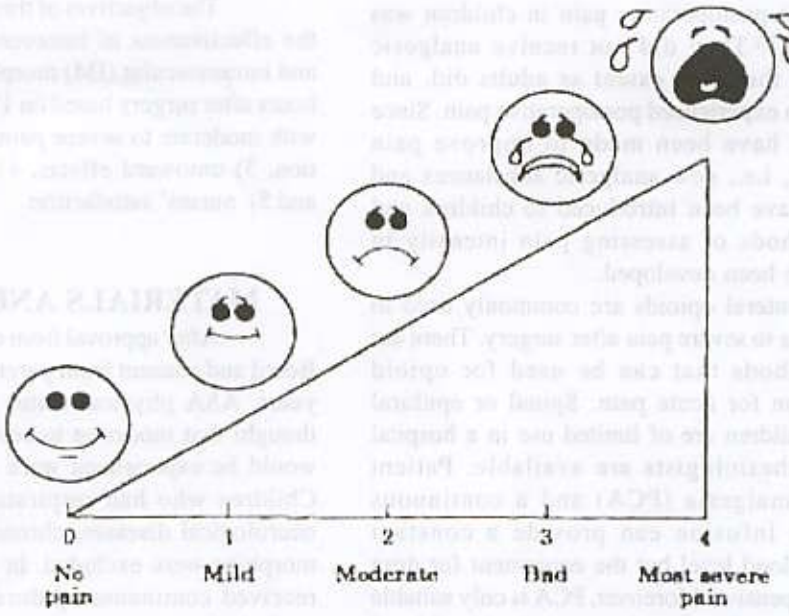

Figure 1. Facial expression pain scale

CHEOPS	Facial expression pain scale	Severity	Dose of IV morphine (mg/kg) infused in 20 min
4-5	0	No pain	0
6-8	1	Mild pain	0.03
9-10	2	Moderate pain	0.05
11-13	3-4	Severe pain	0.07

Blood pressure, heart rate, respiratory rate, and pulse oximetry were recorded every 15 minutes after morphine administration in both groups for 1 h and then recorded at hourly interval for 24 hours.

Outcome measures included CHEOPS score observed by nurses in all patients and Facial Expression Pain Scale rating in patients aged 5 years or over. In cases where CHEOPS and Facial Expression Pain Scale results indicated differences in severity, the self reported measure was selected. Morphine consumption in the first 24 hours, complications and patients' compliance with analgesic were recorded. Nurses' satisfaction was identified using a questionnaire. A systolic blood pressure of less than 70+(2× age in year) mmHg was considered hypotensive[13]; a respiratory rate of less than 16 for toddler, 14 for preschool age, and 12 for school age, were considered respiratory depression; an arterial saturation of less than 90% was considered desaturation.

Sample size was estimated based on the incidence of pain from Mather and Mackie's study which was 0.75. The sliding scale technique was assumed to reduce the incidence of pain to 0.5. Based on α error of 0.05 and power of 0.8, the sample size was 66/group.

Demographic data and nurses' satisfaction were analyzed using descriptive statistics. Differences in continuous variables were analyzed using an Unpaired t-test for parametric data and a Mann-Whitney U test for nonparametric data. Differences in categorical variables were analyzed using Chi-square or Fisher Exact test. $P < 0.05$ was considered statistically significant.

RESULTS

An interim analysis of this study was performed because 47% of patients in the IM group refused the treatment since they were afraid of an injection. Only 32 patients were enrolled. Forty five nurses from 3 pediatric surgical wards were tested for inter-observer reliability which yielded a very high agreement, ICC (95% CI) = 0.85 (0.77-0.91). Five children (16%) reported moderate to severe pain in spite of a mild pain on the CHEOPS score as observed by nurses.

Age, sex, anesthetic technique, and type of surgery were not different between the groups (Table 1). The proportion of patients with moderate to severe pain after surgery, morphine consumption, maximum and average pain scores including episodes of moderate to severe pain were not different. Only 53% of patients in the IM group accepted the injection whereas all patients in the IV group accepted the treatment (Table 2).

Regarding complication, there was no episode of respiratory depression according to age groups. One patient in the IV group developed mild hypotension (1 mmHg less than 70+(2× age) mmHg[13]) which resolved spontaneously within 5 minutes. No episodes of desaturation were detected. The lowest recorded oxygen saturation values were not different between the groups (Table 3).

According to the nurses' opinion, the IV sliding scale group took more time, caused more safety concerns, required close monitoring of vital signs and arterial oxygen saturation than did the IM group. However, nurses were more reluctant to give an IM injection to the children. The quality of analgesia was not different between the 2 groups. Patients refused IM injection much more than did patients in the IV groups. Therefore, the IV groups yielded higher patients' and nurses' satisfaction. Nurses reported IV as a preferred technique in routine practice (Table 4).

DISCUSSION

Due to ethical concerns, this study had to be terminated early because 47% of the patients in the IM group refused pain treatment. They preferred to tolerate persistent postoperative pain to the acute, sharp pain of an intramuscular injection. This study

Table 1. Demographic data.

	IM group (n = 15)	IV group (n = 17)	p-value
Age (y)	7.33 ± 3.52	7.88 ± 3.37	0.945[$]
Sex (male: female)	10:5	7:10	0.149*
Anesthetic technique			
- General : General + regional	8:7	10:7	0.755*
Type of surgery			
- Head-neck	1	4	0.447*
- Abdomen	3	5	
- Groin-perineum	7	5	
- Extremity	4	3	

* Chi-square test, [$] Unpaired t- test.

Table 2. Pain outcomes, morphine consumption and patients' compliance.

	IM group (n = 15)	IV group (n = 17)	p-value
Proportion of patients with an episode of moderate to severe pain, n (%)	11 (73.3)	13 (76.5)	0.838*
Average episode of moderate to severe pain (mean ± SD)	2.80 ± 3.03	3.17 ± 2.74	0.974[$]
CHEOPS			
- Maximum CHEOPS, median (IQR)	9 (5-11)	10 (8-11)	0.358[#]
- Average CHEOPS (mean ± SD)	6.013 ± 1.094	6.028 ± 0.957	0.793[$]
Morphine consumption (mg/kg/24h)	0.157 ± 0.169	0.144 ± 0.124	0.233[$]
Patient's compliance, n (%)	8 (53)	17 (100)	0.001*

* Chi-square, # Mann Whitney U test, $ Unpaired t- test.

Table 3. Untoward effects.

	IM group (n = 15)	IV group (n = 17)
Respiratory depression, n (%)	0 (0)	0 (0)
Respiratory rate (/min, mean ± SD)	20.53 ± 1.40	19.53 ± 1.12
Hypotension, n (%)	0 (0)	1 (7.14)
Lowest SBP (mmHg, mean ± SD)	101.13 ± 9.53	96.53 ± 7.95
Nausea/vomiting, n (%)	2 (13.3)	3 (17.6)
Desaturation, n (%)	0 (0)	0 (0)
Lowest SaO_2 (%, mean ± SD)	96.27 ± 2.43	96.38 ± 1.93

Table 4. Nurses' satisfaction (n = 28).

	Proportion of nurses who rated high score, n (%)	
	IM technique	IV sliding scale technique
Waste time	13 (46)	17 (61)
Reluctant to give drug	18 (64)	11 (39)
Anxious of complication	15 (54)	20 (71)
Frequent vital sign monitoring	21 (75)	27 (96)
Pulse oximetry requirement	18 (64)	23 (82)
Quality in pain relief	28 (100)	28 (100)
Patients' refusal	28 (100)	5 (6)
Nurses' preference	18 (64)	28 (100)
Patients' preference	9 (32)	28 (100)
Selection for routine practice	15 (54)	27 (96)

therefore included only a limited sample of 32 patients. This might have decreased the power of the study, particularly with regard to the negative findings.

However, some of the information obtained through this study should be considered. First, the proportion of patients with at least one episode of moderate to severe pain after surgery was 73.3-76.5%, which corresponded to the results of Mather and Mackie's study in 1980 (75%).[2] This high incidence of undertreated pain indicates a need to further improve efforts to control postoperative pain in pediatric patients..

Second, morphine consumption was not different between both groups. However, 7 patients in the IM group refused morphine injection and requested oral paracetamol instead, which would indicate that the actual morphine requirement was probably higher than what was recorded.

Third, the average and maximum CHEOPS scores were not different between the groups in spite of the fact that 47% of patients in the IM group refused treatment. The reason for this is that analgesic was given by oral or intravenous route when patients refused IM injection.

Fourth, the intravenous, sliding scale pain management originally used methadone with a 4-h interval assessment. Methadone has a longer half-life of 19 h,[8-10] which can adequately cover the assessment interval. Morphine, however has a shorter half-life. Morphine has a serum half-life in adults of 2.9 ± 0.5 hours when administered intravenously and 4.5 ± 0.3 hours when administered intramuscularly. The clearance of intravenous morphine tends to be slightly faster in children ranging from 79-133 minutes.[14] The analgesic effect of morphine might be not long enough to cover the 3-h interval assessment. Moreover, some nurses were reluctant to give IV morphine 0.03 mg/kg for mild pain, but were accustomed to giving analgesic only for moderate and severe pain. Therefore therapeutic blood levels of the morphine might have fluctuated, causing the analgesic effects of the IV sliding scale administration to show no apparent benefit.

Fifth, nurses preferred using the IV sliding scale technique to the IM technique despite the awareness of possible complications and the burden of more frequent and intensive monitoring. Their misconceptions concerning analgesia for fear of complications has changed as a result of regular education about pain and its management in children. In this study, giving a slow infusion of morphine over 20 minutes, with close monitoring for the following 30 minutes and the availability of an opioid antagonist seemed to effectively alleviate the nurses' fear of complications.

Sixth, pain assessment from using CHEOPS and the Face Scale seemed to be technically difficult and time consuming in clinical use. However, after training and testing for inter - rater reliability, including assessment for this study, the nurses became accustomed to these scales and continued to use them in routine practice.

Finallly, almost half of the pediatric patients were willing to tolerate surgical pain due to fear of IM injection. This is probably the most significant result drawn from this study and firmly reiterates the results of previous studies.

There were several limitations of this study regarding difficulty in blinding the route of morphine administration. The use of unblinded caregivers and patients might have created a bias and resulted in low compliance and co-intervention. Measurement bias was not avoidable in the IM group when using both the behavioral assessment scale (CHEOPS) and the self report scale (Facial Expression Scale) because children might not accurately express their true feelings, either verbally or behaviorally.

In summary, the IV sliding scale technique was superior to the IM technique in both patient's compliance and nurses' preference. The degree of pain relief obtained and complications of treatment were not different. The appropriate patient assessment interval when using a morphine IV sliding scale technique should be studied further.

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