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A descriptive study of the use of continuous morphine infusions in pediatric postoperative patients

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Background: The benefit of continuous morphine infusions for postoperative analgesia in children may be limited by the development of side effects. We performed a quality assurance study, analyzing the efficacy, side effects and dose requirements of postoperative morphine infusion in children.

Methods: Children between 4 months and 16 years of age following major thoracic, abdominal or orthopedic surgery were managed with continuous morphine infusion supplemented by nurse-administered boluses for postoperative analgesia. Pain intensity, morphine doses, and side effects were recorded every 3 hours. The Children's Hospital of Eastern Ontario Pain Scale (CHEOPS) was used for pain assessment in children up to 5 years of age, visual analog scale (VAS) was used in older patients. Side effects of interest were emetic episodes, hypoxemia (supplemental oxygen administration) and urinary retention (requiring catheterization of the bladder). Non-opioid analgesics were not used routinely during the study period.

Results: Sixty seven children were followed for a median time of 18 hours. Mean (SD) pain scores were 6.6 (0.7) for CHEOPS and 2.9 (1.4) for VAS. Emetic episodes occurred in 36.7%, hypoxemia in 26.8% and urinary retention in 5.1% of cases. The mean (SEM) morphine dose in children that experienced side effects was 41.1 (4.1) *vs*. 29.7 (2.0) $\mu g \cdot kg^{-1} \cdot h^{-1}$ in children without side effects ($p < 0.05$).

Conclusions: Continuous i.v. morphine infusions effectively reduce postoperative pain to mild and moderate levels. However, opioid-related side effects are common, especially in patients given high (close and above 40 $\mu g \cdot kg^{-1}h^{-1}$) doses of morphine. The use of additional non-opioid analgesic techniques should be encouraged in order to improve analgesia and reduce morphine requirement.

Key words: pain management, postoperative, children, morphine, continuous infusion

Continuous morphine infusions are commonly used for postoperative pain management after major surgery in children of different ages. For several years, intravenous (i.v.) morphine has been the predominant mode of postoperative pain treatment at Kaunas Medical University Clinic. Current recommendations suggest the routine use of non-opioid techniques along with opioid analgesics (1). In order to improve our present practice, we undertook a quality assurance study to analyze the efficacy and side effects of continuous i.v. morphine infusions.

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METHODS

The study was approved by the Independent Ethical Committee of Kaunas University of Medicine. Written informed consent from the parents of the patients was waived since the management was within the standard practice in the hospital. Seventy two patients, American Society of Anesthesiologists (ASA) physical status I or II, aged 4 months to 16 years, who were scheduled for major thoracic, abdominal or orthopedic surgery, were enrolled.

All children were premedicated with oral or intravenous midazolam. An anesthetic procedure with an inhalational agent, fentanyl, and a muscle relaxant was used. No regional block was used in any patient. During surgery all children were hydrated with lactated Ringer's solution according to calculated individual needs. At the end of surgery, the majority of patients were extubated and transferred to the intensive care or postoperative care unit, where pain treatment with morphine infusion was initiated.

Standard morphine dilutions were used and calculated as follows: 0.5 × patient's weight in kg as mg of morphine were diluted in 50 ml of 0.9% saline. One ml of this solution contains 10 μg · kg^{-1} of morphine. No standard loading dose was used. Instead, repeated bolus doses of 20 μg · kg^{-1} of morphine were given to ensure the analgesic effect at the start of treatment. Based on our previous experience, initial morphine infusion rates were set between 20 and 30 μg · kg^{-1} · h^{-1}. During the course of treatment, nurses were allowed to change the infusion rate in steps of 10 μg · kg^{-1} · h^{-1}, in the dose range of 10–40 μg · kg^{-1} · h^{-1}, as well as to administer additional boluses of 20 μg · kg^{-1} on demand.

Routine non-opioid supplementation was not used.

Oxygen saturation by pulse oximetry (SpO_2), the amount of morphine used, supplemental oxygen administration, sedation scores, side effects, and pain scores were recorded by the nurses every 3 h until the end of morphine infusion. Childrens' hospital of Eastern Ontario pain scale (CHEOPS), where a score of 4 indicates no pain and a score of 13 indicates the worst pain, was used for pain assessment in children up to 5 years of age (2). Six to 16 year old children were asked, if awake, to assess their pain by visual analog scale (VAS), where 0 represents no pain and 10 represents the worst pain.

Sedation was scored as follows: 0 – alert, 1 – drowsy, 2 – asleep, easy to arouse, 3 – asleep, difficult to arouse.

The side effects assessed were: emetic episodes (retching or vomiting), urinary retention (requiring insertion of catheter) and hypoxemia (supplemental oxygen at $SpO_2 < 92\%$). Hypoxemia for the first 3 postoperative hours was not considered.

Morphine infusion was discontinued after transferring the patient to the surgical ward and switching to oral, rectal or parenteral non-steroidal anti-inflammatory drugs (NSAID) or paracetamol.

Statistics

Simple means of all observations were used for sedation and pain scores for each patient. The mean used morphine dose in μg · kg^{-1} · h^{-1} was calculated for the study period. Analysis of variance with repeated measures was used for the comparison of morphine doses within the 18 hours (median duration of morphine treatment) of the study. The tukey honest significance test was used for *post-hoc* comparisons. *T* test for independent samples, χ^2 and one-way ANOVA were used where appropriate. A p value of 0.05 was considered statistically significant. The results are presented as means with standard error (SEM) or standard deviation (SD) or as medians with ranges.

RESULTS

Sixty-seven patients (22 patients aged 4 months to 5 years and 45 patients aged 6 to 16 years) completed the study. Five patients were excluded because of incomplete protocols.

Demographic data are shown in Table 1.

The median (range) duration of morphine infusion was 18 (6–93) hours. On the first postoperative day, the mean (SEM) morphine dose was 39 (3.6) μg · kg^{-1} · h^{-1}. Twenty patients continued treatment on the second postoperative day, and the mean (SEM) morphine dose used during this period was 24.2 (0.7) μg · kg^{-1} · h^{-1}.

The mean (SD) sedation score was 1.1 (0.5).

The mean (SD) pain scores were 2.9 (1.4) for VAS and 6.6 (0.7) for CHEOPS. The mean (SD) VAS scores were significantly higher in girls than in boys 9 hours after starting morphine infusion (4.4 (1.6) *vs*. 3.0 (1.6) with $p < 0.05$), and 3.3 (1.5) *vs*. 2.6 (1.2) with $p > 0.05$ at 18 h).

Side effects occurred in 56.4% of patients. The incidence of hypoxemia was 26.8% and predominated in patients after thoracic surgery. The inci-

Table 1. **Demographic data on patients treated with morphine infusion**

1. Age, median (range)		9 (0.4–16) yr
2. Weight, mean (SD)		31.0 (17.2) kg
3. Gender:	female	23 (34.3%)
	male	44 (65.7%)
4. Type of surgery:	thoracic	33 (49.3%)
	abdominal	22 (32.8%)
	orthopedic	12 (17.9%)
5. Length of surgery, mean (SD)		149.3 (50.8) min [a]
6. Intraoperative fentanyl dose, mean (SD)		6.4 (2.0) μg/kg [a]

[a] Length of surgery and intraoperative fentanyl dose did not differ between surgical procedures.

dence of emetic episodes was 36.7%. A significantly higher incidence of emetic episodes was found in girls compared to boys. Morphine was stopped in 2 patients because of persistent retching and vomiting. The incidence of urinary retention was 5.1% of 59 patients without urinary catheters postoperatively.

The doses of morphine and the incidence of side effects according to patients' age, gender and surgical procedure are shown in Table 2. There were significant differences in mean morphine doses between the different surgical procedures. Patients after thoracic procedures required significantly more morphine compared to the patients after abdominal or orthopedic surgery.

Patients who experienced side effects had a significantly higher morphine consumption compared to those without, 41.1 (4.1) and 29.7 (2.0) $\mu g \cdot kg^{-1} \cdot h^{-1}$ respectively, ($p < 0.05$). There were no differences in length of surgery, intraoperative fentanyl dose or pain scores between these two groups.

DISCUSSION

This study describes morphine requirement and the incidence of side effects using morphine infusion supplemented by nurse-administered boluses for postoperative analgesia. The mean morphine dose at 18 h after surgery was almost 40 $\mu g \cdot kg^{-1} \cdot h^{-1}$. According to the pain scores, this dose appeared to reduce pain to mild or moderate levels and is similar to the dose reported earlier by Bray et al. (3). However, this dose is at the upper limit of what is currently recommended for postoperative pain management by continuous infusion in children (4). Additional non-opioid analgesics may significantly reduce morphine requirements postoperatively (5–7). Our patients were not given regular non-opioid supplementation, as this was not routine practice at the time the study was conducted.

Hypoxemia was defined as SpO_2 less than 92% in room air. Then, supplemental oxygen was routinely administered to the patients to maintain adequate oxygenation. The incidence of hypoxemia in our study was higher than that reported by other investigators. Z. Esmail et al. reported only 4.5% incidence when oxygen was administered to maintain SpO_2 above 94% (8). A direct comparison with the latter study, however, cannot be made due to methodological differences. Predominance of thoracic surgery might have contributed to the high incidence of hypoxemia in our patients by several mechanisms. The majority (87% (29/33)) of performed thoracic procedures were corrections of thoracic deformities (pectus excavatus or pectus carinatus). Preoperative respiratory function in these patients is usually not affected (9). Surgical trauma, however, involves tissues participating in respiratory mechanics and may cause a restrictive decrease in lung function postoperatively, if pain is not adequately treated. In accordance to previous findings (10), our thoracic patients required higher doses of morphine compared with other types of surgery (Table 2). Morphine, like other opioids, changes the pattern of breathing and may lead to arterial desaturation in postoperative patients (11). Thus, high morphine doses might have additionally contributed to the development of hypoxemia in our patients after thoracic procedures.

The overall incidence of emetic episodes and urinary retention in our population was similar to previously reported findings (8, 12). However, we observed striking gender differences in the incidence of emesis: in spite of similar mean morphine doses, girls were affected more than twice as often as the boys. In earlier studies, only morphine, but not gender was related to nausea/ vomiting (13–15). Since girls and boys in our study also differed in VAS scores, the higher incidence of emesis might have been related to the experience of more pain (16, 17).

When all side effects were considered, we observed that the children who experienced at least one of them had received significantly higher doses of morphine compared with those who did not. In

Table 2. **Morphine doses ($\mu g\ kg^{-1}\ h^{-1}$) and incidence of side effects according to age, gender and surgical procedure. Results are presented as means (SEM) and proportions in %**

Variable	Age, years		Gender		Type of surgery		
	0.4–5	6–16	Male	Female	Thoracic	Abdominal	Orthopedic
Morphine dose	37.6 (3.5)	39.8 (3.7)	39.7 (3.5)	37.6 (3.8)	46.9 (4.7)[a]	34.6 (3.0)	27.1 (2.0)
Incidence of hypoxemia	29.4	25.6	29.7	21.1	42.9 [a]	11.8	9.1
Incidence of emetic episodes	23.8	43.6	28.6	63.6 [b]	46.2	31.8	25.0
Incidence of urinary retention	5.9	4.8	2.4	11.8	6.3	–	8.3

[a] $p < 0.05$, compared to abdominal and orthopedic surgery. [b] $p < 0.05$, compared to male gender.

earlier studies an increased incidence of hypoxemia and emesis was associated with a higher morphine dose in children treated by patient-controlled morphine analgesia (18, 19). Although lower morphine consumption with the addition of non-opioids can be achieved, studies remain inconclusive concerning side effects. The addition of a NSAID resulted in a lower incidence of hypoxemia in adult patients after thoracotomies as well as a lower incidence of urinary retention in children after orthopedic surgery (20, 21). However, other studies indicate that despite lower morphine doses with the addition of non-opioid analgesics, there are no differences in the incidence of side effects (6, 22).

In conclusion, we observed that continuous i.v. morphine infusions effectively reduced the postoperative pain to mild and moderate levels as assessed by validated pain measurement tools in children. However, opioid-related side effects are common, especially in patients given high (close and above $40\ \mu g \cdot kg^{-1} \cdot h^{-1}$) doses of morphine. The use of additional non-opioid analgesic techniques should be encouraged in order to improve analgesia and reduce morphine requirement.

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VAIKŲ POOPERACINIO SKAUSMO GYDYMAS MORFINO INFUZIJOMIS

S a n t r a u k a

Gydant pooperacinį skausmą morfino infuzijomis, atsiradęs šalutinis poveikis gali sumažinti šio analgezijos būdo efektyvumą. Mes atlikome prospektyvinį tyrimą, norėdami išsiaiškinti analgezijos kokybę, pašalinio poveikio dažnį ir morfino poreikį gydant vaikų pooperacinį skausmą.

Metodika. Tyrėme vaikus, operuotus dėl krūtinės ląstos, pilvo organų ar ortopedinių ligų, nuo skaumo po operacijų gydytus morfino infuzijomis. Vaikų amžius svyravo tarp 4 mėn. ir 16 metų. Kas tris valandas gydymo metu stebėta analgezija, sunaudotas morfino kiekis ir šalutinis poveikis. Vaikų iki 5 metų amžiaus analgezijai įvertinti naudota CHEOPS (Children's Hospital of Eastern Ontario Pain Scale), o 6–16 metų amžiaus – vizualinė analoginė skalė (VAS). Mus dominantis šalutinis poveikis buvo vėmimas, hipoksemija (papildoma deguonies terapija), šlapimo susilaikymas (būtina šlapimo pūslės kateterizacija). Papildomos analgezijos priemonės vaikams netaikytos.

Rezultatai. Ištirti 67 ligoniai. Gydymo trukmė morfinu siekė 18 (6–93) val. (mediana ribos). Vidutinė (SD) analgezija vertinant CHEOPS buvo 6,6 (0,7) balo bei 2,9 (1,4) balo vertinant VAS. Vėmė 36,7%, hipoksemija buvo 26,8%, o šlapimas susilaikė 5,1% ligonių. Vaikams, kuriems išsivystė šalutinis poveikis, vidutinė (SEM) morfino dozė sudarė 41,1 (4,1) $\mu g \cdot kg^{-1} \cdot h^{-1}$, tuo tarpu be šalutinio poveikio – 29,7 (2,0) $\mu g \cdot kg^{-1} \cdot h^{-1}$ ($p < 0.05$).

Išvada. Morfino infuzijos yra efektyvi priemonė gydant vaikų pooperacinį skausmą, tačiau esant didelėms dozėmis šalutinis poveikis gana dažnas. Tai turėtų paskatinti gydytojus naudoti papildomus analgezijos būdus ir sumažinti morfino poreikį po operacijų.

Raktažodžiai: skausmo gydymas, pooperacinis, morfinas, vaikas