British Journal of Medicine & Medical Research
16(6): 1-7, 2016, Article no.BJMMR.25760
ISSN: 2231-0614, NLM ID: 101570965

SCIENCEDOMAIN *international*
www.sciencedomain.org

Comparing Three Different Doses of Caudal Morphine for Analgesia after Salter Innominate Osteotomy

Nurgül Işikay[1], Mehmet Cesur[2], Ertuğrul Kılıc[1*] and Mehmet Murat Çelik[2]

[1]Department of Anesthesiology, Şehitkamil Government Hospital, Gaziantep, Turkey.
[2]Department of Anesthesiology, Gaziantep University, Faculty of Medicine, Gaziantep, Turkey.

Authors' contributions

This work was carried out in collaboration between all authors. Author NI designed the study, performed the statistical analysis. Author MC performed the statistical analysis, managed the analyses of the study and author EK wrote the protocol, wrote the first draft of the manuscript and managed the analyses of the study. Author MMC managed the literature searches. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/BJMMR/2016/25760
Editor(s):
(1) Rakesh Garg, Department of Anaesthesiology, Intensive Care, Pain and Palliative Care, Dr BRAIRCH, All India Institute of Medical Sciences, New Delhi, India.
(2) Toru Watanabe, Department of Pediatrics, Niigata City General Hospital, Japan.
Reviewers:
(1) Anonymous, All India Institute of Medical Sciences, Ansari Nagar, New Delhi, India.
(2) Lewis S. Coleman, Barnes Dental Surgery Center, Visalia, USA.
(3) M. Helmi, Tarumanagara Univesity, Jakarta, Indonesia.
(4) David Wels, Chris Hani Baragwanth Academic Hospital, Johannesburg, South Africa.
Complete Peer review History: http://sciencedomain.org/review-history/15075

Original Research Article

Received 18th March 2016
Accepted 14th June 2016
Published 20th June 2016

ABSTRACT

Background: Single dose caudal block application is preferred among children since it is a safe and easy method. Caudal morphine has an important advantage with its long half-life. However, caudal morphine application has some side effects such as nausea-vomiting, urinary retention, pruritus, sedation and respiratory stiffness and many of those are dose-dependent. The aim of this study was to determine the minimum morphine doses that will provide adequate analgesia and by this way to diminish the life threatening side effects such as respiratory depression as well as comfort-threatening side effects such as nausea-vomiting.
Methods: This double blind, randomized, prospective study, was performed in Gaziantep University among 60 pediatric patients aged between 1-9 years, who were planned to have Salter operation for congenital hip dislocation, with ASA classification of I-II. Premedication was not

**Corresponding author: E-mail: drertugrulkilic@yahoo.com;*

applied in any of the cases. Patients were sub-grouped randomly and for 15, 20 or 25 μg.kg^{-1} caudal morphine administration: G15, G20 and G25. Caudal injections were performed under general anesthesia just before the operations. Having total volumes of 0.75 ml.kg^{-1}, caudal injections were performed with 15, 20 or 25 μg.kg^{-1} morphine together with 0.25% bupivacaine according to the groups. The first time of analgesic requirement was recorded.

Results: The number of cases required analgesia in first 24 hours was determined as 4 (20%), 3 (15%) and 2 (10%) in Group 15, Group 20 and Group 25, respectively. There was not statistically significant difference between groups (P>0.05). In none of the patients, the pain level was as high as causing restlessness (score 2). With single dose Paracetamol, pain cured in all of these patients. Postoperative nausea and vomiting in first 24 hours was reported in 1 (5%), 2 (10%) and 8 (40%) cases in 15, 20 and 25 μg.kg^{-1} groups, respectively. Although the difference between Groups 15 and 20 was not statistically significant (p=0.548), the number of patients with nausea and vomiting in Group 25 was statistically significantly higher than that of Group 15 and Group 20 (p=0.009 and p=0.025, respectively). In first 24 hours in postoperative period, respiratory depression was not observed in any of the cases.

Conclusions: We determined that decreasing the caudal morphine dose to 15 μg.kg^{-1} in Salter osteotomy does not decrease analgesia in 24 hours but minimizes nausea-vomiting incidence.

Keywords: Caudal anesthesia; morphine; postoperative pain; child; salter osteotomy.

1. INTRODUCTION

In recent years, single dose caudal block that is performed in combination with general anesthesia for both anesthesia and postoperative analgesia is a commonly accomplished method in under diaphragmatic operations including urogenital, rectal, inguinal and lower extremity surgeries in pediatric cases. However, with the doubts due to the short half-lives and systemic toxicities of local anesthetics, some additives are combined with local anesthetics for postoperative analgesia. Among those, caudal morphine is a potent analgesic and it prominences with its long half-life. Caudal morphine has been associated with nausea-vomiting, urinary retention, pruritus, sedation and respiratory stiffness [1]. Some of these side-effects are dose-dependent [1,2]. For that reason, it is important to determine the minimal dose providing effective analgesia. Salter operation, a common operation performed in children for congenital hip dislocation (CHD), may cause severe postoperative pain in children. In literature, we could not see study about investigating the optimal dose of caudal morphine used after Salter operation for pain control.

In literature caudal morphine was used 3 different doses for circumcision [3]. In this study, we aimed to determine the analgesic affectivity and side effect incidence of 3 different morphine doses 15, 20 or 25 μg/kg^{-1}, combined with preoperative 0.25% bupivacaine in children who had Salter operation.

2. METHODS

This double blind, randomized, prospective study, was performed in Gaziantep University Medical School Sahinbey Training and Investigation Hospital, among 60 pediatric patients aged between 1-9 years, who were planned to have major congenital hip dislocation operation by orthopedics and Traumatology Department, with ASA classification of I-II. The study was approved by Gaziantep University Ethics Committee and informed consents were obtained from the parents or legal defenders of the children.

Patients with local infection on systemic or caudal region, with bleeding diathesis or under anticoagulation treatment, having CNS diseases, having any sensitivity to local anesthetics and opioids, and patients with vertebral colon deformities were excluded from the study.

Patients were sub-grouped randomly and equally with computer randomization program for 15, 20 or 25 μg.kg^{-1} caudal morphine administration for postoperative analgesia: G15 [(15 μg.kg caudal morphine) (n=20)], G20 [(20 μg.kg caudal morphine) (n=20)] and G25 [(25 μg.kg caudal morphine) (n=20)].

Before starting operation, electrocardiogram, pulse oximeter and non-invasive arterial blood pressure monitoring (Datex Ohmeda, Madison WI 53707-7550 USA) were performed to all patients, and basal values were recorded. Any premedication was not given to any of the

patients. During operation, systolic blood pressure, diastolic blood pressure, end tidal CO2, and heart rate of the patients were followed.

Anesthesia induction was obtained with sevoflurane of 6-7% concentration and 100% oxygen applied by face mask. After induction, our standart pediatric fluid infusion which is 3.33% dextrose 0.3% sodium chlorine solution 5-10 ml/kg/hour/IV (intravenous) was started. Later, 0.5 mg/kg rocuronium (Esmeron 50 mg/5 ml, MSD, N.V. Organon, Oss, Hollanda) was given via intravenous and endotracheal intubation was performed. After intubation, sevoflurane minimal alveolar concentration (MAC) was decreased to 1%. Owing to the double-blind nature, an investigator prepared the caudal injection solutions with 0,25% bupivacaine (Bustesin 0,5% VEM İdol, İstanbul) as 15, 20 or 25 $\mu g.kg^{-1}$ morphine and with 0,9% NaCl as volume replacer according to Armitage formula having total volumes of 0,75 $ml.kg^{-1}$ and coded them. Later, this investigator did not take any part in follow-up and evaluation of patients.

All caudal blocks were performed by one of the 2 experienced anesthetists. After intubation, patients were turned to lateral sims position. After skin sterilization, sacral hiatus was determined and following local anesthetic infiltration, epidural space was entered with a 22 G injector by passing sacro-coccygeal ligament and then the injector was pushed for 3-4 mm. After detecting that blood or cerebrospinal fluid was not draining passively or with aspiration; previously prepared solutions were injected in 3 doses with 1 minute intervals.

At least 20 minutes after caudal injection, operation was started. Increase in arterial tension or heart rate by 25% above their basal levels after surgical incision was regarded as insufficient anesthesia/ analgesia. In this condition, sevoflurane (Sevorane Liquid %100, 250 ml. AbbVie, England) concentration was increased into standard inhalation doses (1-2% sevoflurane in 40% 0_2 and 60% N_2O). These patients were not evaluated in later stages of study. Following the end of surgery, after cessation of the anesthetic gases, patients were ventilated with 100% O_2 and neuromuscular blockage was reversed with intravenous 0.05 mg/kg neostigmine (Neostigmine amp. Adeka, Samsun) and 0.015 mg/kg atropine sulfate (Atropine Sülf, Galen, İdol). Patients were extubated and taken to the postoperative recovery room. Patients were evaluated in recovery room by an independent investigator who was blind for patient groups.

After operation, primary we evaluated pain degree and analgesic administration time. Saturation and heart rate were followed with pulse-oximeter (Masimo, Masimoset, USA) as well as the pain for 24 hours. In pain evaluation, our clinic pain scale was used with the measures between 0 and 2 (0: no pain, 1: crying with low voice but relax, 2: crying with high voice and restless) [3]. In patients with a pain score of 1 in first 6 hours; a salvage dose of Paracetamol and Phenobarbital (Paranox S suppozituar 120 mg, Sanofiaventis, İstanbul) usage was planned; but if the score was 1 in later periods, oral Paracetamol 20 $mg.kg^{-1}$ (Paracetamol Ped. 5 Ml 120 Mg 150 Ml suspension, Saba, İstanbul) administration was intended. The first and subsequent Paracetamol dosages and their administration times were recorded. Analgesia period was regarded as the time passed from caudal injection to the first Paracetamol requirement.

In addition for secondary outcome variables the patients were visited in every 6 hours in postoperative period and presence of urinary retention, nausea-vomiting, and pruritus were asked to the nurses and parents of the patients. Urinary retention was defined as the absence of spontaneous micturition of patients on 6^{th} hour after caudal injection.

In statistical analysis, 20% difference in pain or nausea and vomiting between groups was determined as clinically important. Statistical analyses were performed with NCSS (Number Cruncher Statistical System) 2007&PASS (Power Analysis and Sample Size) 2008 Statistical Software (Utah, USA) programs. In post hoc power analysis, the patient number of 20 in each group was determined as sufficient with 88.1% reliability, for both the first end-point of pain period and the second end-point of postoperative nausea and vomiting with a 5% of acceptable tolerance (alpha).

In distribution analysis of continuous variables, Kolmogorov Smirnov test was applied. In comparison of normally distributed groups for more than 2 independent sample comparisons, one way ANOVA analysis was used. The association of categorical variables was analyzed with chi-square test. The statistical analyses were performed with SPSS for Windows version

25 program and p <0.05 was regarded as statistically significant.

3. RESULTS

All 60 patients, included in the study, completed the study and involved in evaluation. Demographic data and operation time were similar in 3 groups (Table 1). Heart rate, respiratory rate or blood pressure did not diverge 20% from the basal values. The values of end tidal CO2 were at normally in operative period. In postoperative period, respiratory or hemodynamic complications were not observed in any of the patients.

Postoperative pain evaluation of patients is summarized in Table 2. Pain was not reported in 51(85%) of 60 included patients in first 24 hours. Additional analgesia was not required in any patients in first 12 hours. In first 18 hours, Paracetamol was required in only one patient of 15 mcg/kg morphine group. The number of cases required analgesia in first 24 hours was 4(20%), 3(15%) and 2(10%) in Group 15, Group 20 and Group 25, respectively. The number of patients requiring analgesia was not statistically significantly different between groups (P >0.05). In none of the patients, the pain level was as high as causing restlessness (score 2). With single dose Paracetamol, pain cured in all of these patients.

Postoperative nausea and vomiting in first 24 hours was reported in 1 (5%), 2 (10%) and 8 (40%) cases in 15, 20 and 25 $\mu g.kg^{-1}$groups, respectively. Although the difference between Groups 15 and 20 was not statistically significant (p=0.548), the number of patients with nausea and vomiting in Group 25 was statistically significantly higher than that of Group 15 and Group 20 (p=0.009 and p=0.025, respectively). In first 24 hours in postoperative period, pruritus, urinary retention, respiratory depression, hypotension and bradycardia were not observed in any of the cases.

4. DISCUSSION

In this study we have determined that, among children who had Salter operation, preoperative 15, 20 or 25 $\mu.kg^{-1}$ caudal morphine applications did not show any significant difference between groups in first 24 hours regarding analgesia. However, the nausea and vomiting incidence was statistically significantly different between 15 and 25 $\mu.kg^{-1}$ morphine groups. In all 3 groups, other that nausea and vomiting, any complications including urinary retention, apnea-hypoxia, pruritus, bradycardia, or hypotension were not observed.

Currently, the treatment of acute postoperative pain is still not at intended levels and approximately more than 75% of cases complaint from moderate or severe pain in postoperative period. In a study performed with different surgical modalities, 46% of the cases were reported to have severe pain in first 24 hours after operation [2].

Table 1. Demographic features and operation times

	Group 15 (n=20)	Group 20 (n=20)	Group 25 (n=20)
Age (Year) Mean±SD	2.24±1.09	2.07±1.04	1.89±1.15
Weight (kg) Mean±SD	12.7±0.7	12.2±0.9	11.6±1.01
Gender (M/F)	4/16	4/16	5/15
Operation time (Min) Mean±SD	93.3±35.8	94.75±51.1	96.25±37.3

p≥0.005

Table 2. Evaluation of postoperative pain levels among patients

	Group 15 (n=20)	Group 20 (n=20)	Group 25 (n=20)
Number of patients without paracetamol requirement (n(%))	16 (80%)	17 (85%)	18 (90%)
Number of patients with single dose paracetamol requirement (n (%))	4 (20%)	3 (15%)	2 (10%)
Analgesia time (min) (mean±SD)	1398±491	1416±276	1428±182
Postoperative nausea and vomiting (in first 24 hours) (n(%))	1(5%)	2(10%)	8(40%)*

*p≥0.005; *p≤0.005 (when compared G25 to G15 and G25 to G20 (p=0.009 and p=0.025))*

Morphine administered with neuro-axial way is popular since it provides longer periods of analgesia with lesser doses compared with systemic administration. However, the side-effects of opioids are causing apprehension. In studies, as low as 33 μg.kg^{-1} doses of caudal morphine was determined to cause high incidences of postoperative nausea and vomiting [3].

Krane et al. [4] studied with 33-100 μg.kg^{-1} doses of caudal morphine and determined that the caudal dose of 33 μg.kg^{-1} works excellent after basic surgical interventions under diaphragm in children. In this study, the incidences of nausea-vomiting and pruritus with different doses were reported as 33-56% and 22 -57%, respectively and they did not determine any significant differences between two doses regarding nausea-vomiting and pruritus frequencies.

In the study of Cesur et al. [3] on caudal morphine with the doses of 10, 15, 30 μg.kg^{-1}, it has been determined that 10 μg.kg^{-1} caudal morphine provides sufficient dose for postoperative analgesia in circumcision operations. In this study, any respiratory complications were not reported. Nausea-vomiting was reported in rates of 13.3%, 20% and 46.7% in 10, 15 and 30 μg.kg^{-1} groups, respectively. Although there was not any statistically significant difference between 10 and 15 μg.kg^{-1} groups, the differences between 10 and 30 μg.kg^{-1} and 15 and 30 μg.kg^{-1} groups were reported to be statistically significant. Pruritus was reported in 8.9%, 11.1% and 15.6% of cases in 10, 15 and 30 μg.kg^{-1} groups, respectively. Though there was a dose-dependent upsurge tendency in postoperative pruritus incidence, there was not a significant difference between groups. This study shows that increase in caudal morphine doses does not have any effects on analgesia an10, 15 and 30 μg.kg^{-1} groups, respectively moreover, with decreasing morphine doses especially nausea-vomiting incidence may be diminished.

In a similar study, Dostbil et al. [5] investigated the quality of postoperative analgesia and someside effects such as nausea-vomiting in circumcision operations using 7.5, 10, or 15 μg.kg^{-1} morphine doses. Postoperative nausea and vomiting incidence was reported as 5%, 12.5% and 17.5% in 7.5, 19 and 15 μg.kg^{-1} groups, respectively. This is the study of literature with the minimum caudal morphine dose. At the end of this study, in the 7.5 μg.kg^{-1} morphine group, nausea-vomiting incidence was reported to be less than other groups and there was not any significant difference between groups regarding postoperative analgesia. In our study, the lowest morphine dose was 15 μg.kg^{-1}. It is clear that, since larger and deeper surgical incisionsin Salter osteotomy operations for CHD results in severe pain in a larger innervation area compared with circumcision operations, higher doses are required for pain control in this patient group. In our study, it has been determined that both 15 and 20 μg.kg^{-1} caudal morphine doses were also as effective as 25 μg.kg^{-1} dose for analgesia in Salter osteotomy operations for CHD besides with lower nausea-vomiting incidences. The operations in the study of Krane et al. [4] were major urogenital surgical operations under diaphragm. Since abdominal operations increase postoperative nausea-vomiting incidence, it is also probable that the nausea-vomiting incidences reported in that study may be affected from the performed operations. In that condition, it is clear that the results of that study cannot be compared with the results of our study group. Our study was performed on patients of Salter osteotomy operations for CHD without any abdominal interventions which defines this difference.

In our study, combined administration of peroperative bupivacaine with morphine is also compatible with the preemptive analgesia concept. Preemptive analgesia is an anti-nociceptive treatment and it may support in decreasing the postoperative pain perception by inhibiting afferent input formation. In above studies, with preoperative caudal injections, they had the advantages of intraoperative anesthetic effects. Similarly in our study, we also had the advantages of both intraoperative and postoperative analgesic effects with preoperative caudal injections.

Paracetamol that was used as salvage analgesic is commonly used in pediatric cases. Nevertheless, it is insufficient alone or quite higher doses of it are required after major surgeries. However the risk of liver toxicity of higher doses is known [6]. For that reason, it is more rational to use Paracetamol as a component of multimodal analgesia instead of alone [7]. In our study, with the addition of routine doses of Paracetamol, sufficient analgesia could be achieved in as low as 15 μg.kg^{-1} caudal morphine dose. By this way, we aimed to be protected from the side effects of high doses of opioids.

Postoperative nausea and vomiting is an important problem that deteriorates patient comfort causing prolongation of convalescent period. In first day after pediatric surgery, total nausea and/or vomiting incidence is reported between 20-30% [8]. There are many factors causing this complication. Some of those are associated with patient while some are associated with surgery [9]. These factors are not under the control of anesthetists.

The main factors under the control of anesthetists are drugs used for premedication, anesthetic agents, neuromuscular blockers and anticholin esterases used as antagonists. Moreover, postoperative pain may also upsurge the postoperative nausea and vomiting [10-12]. Therefore, it is not precise to define the presence of nausea-vomiting with only morphine. In our study, nausea-vomiting was the most common side effect of morphine and it was dose-dependent.

In literature the opioid-independent nausea-vomiting incidence that was reported higher than the nausea-vomiting incidence described in our study of 15 and 20 $\mu.kg^{-1}$ groups, also supports that nausea-vomiting cannot be directly attributed to the morphine.

Hydrophilic characteristics of caudal morphine carry both some advantages and some risk factors. Hydrophilic characteristics of morphine impede its increased levels with rostral spread, after its diffusion on subarachnoid area. For that reason, it can also be used with caudal injection for the treatment of sternal incision pain after open heart surgery [13]. However with the same reason, it may cause respiratory depression.

In literature, there is not any case reported to have respiratory depression after caudal injection. In our study, respiratory depression was not observed in any of the patients since our morphine doses were the least doses used in literature.

Seventy $\mu g.kg^{-1}$ caudal morphine was given to 138 children in the study of Valley and Bailey [13]. Clinically significant respiratory depression was reported in 11(<8%) children. However, in 11 children, intravenous morphine was also administered together with caudal dose. In the study of Krane et al. [4] on children aged between 1-16 years, any delayed respiratory depression was not reported with 100 $\mu g.kg^{-1}$ caudal morphine doses [4]. With the short half-life of Bupivacaine, it is clear that it does not affect the postoperative analgesia levels of our morphine study. Arora et al. [14] performed caudal anesthesia before operationson patients that will have lower extremity operations. They gave 30 $\mu g.kg^{-1}$ morphine by caudal way to half of the cases and 0.25% bupivacaine to the other half. In bupivacaine group, maximum analgesia time was 8 hours while in morphine group it was reaching 26 hours. This study also shows that, in our study, the bupivacaine ratio in bupivacaine-morphine combination will not affect in elongation of postoperative analgesia period to 24 hours.

One of the main limitations of this study is the lack of placebo group. This limits us to know the nausea-vomiting ratio among patients who had Salter osteotomy under only general anesthesia. Another limitation is the performing caudal analgesia with blind technique without using an imaging technique to show it was an optimal injection or not. However, we believe that, this limitation was overcome partially with the clinical observation of effective caudal anesthesia as with low doses of inhalation anesthesia without analgesia, any increase in pulse or blood pressure was not observed.

5. CONCLUSION

In conclusion, decreasing the caudal morphine doseto 15 $\mu g.kg^{-1}$ in Salter osteotomy does not decrease analgesia in 24 hours but minimizes nausea-vomiting incidence.

FINANCIAL DISCLOSURE

The authors declared that this study has received no financial support.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Navil F, Michael F. Pediatric postoperative pain management. Churchill Livingstone. 1993;485-518.
2. Bonnet F, Marret E. Postoperative pain management and outcome after surgery. Best Practice & Research Clinical Anaesthesiology. 2007;21:99-107.
3. Cesur M, Alıcı HA, Erdem AF. Effects of reduction of the caudal morphine dose in

paediatric circumcision on quality of postoperative analgesia and morphine-related side-effects. Anaesth Intensive Care. 2007;35:743-7.
4. Krane EJ, Tyler DC, Jacobson LE. The dose response of caudal morphine in children. Anesthesiology. 1989;71:48-52.
5. Dostbil A, Gursac Celik M, Aksoy M, Ahiskalioglu A, Celik EC, Alici HA, Ozbey I. The effects of different doses of caudal morphine with levobupivacaine on postoperative vomiting and quality of analgesia after circumcision. Anaesth Intensive Care. 2014;42:234-8.
6. Jöhr M. Postoperative pain management in infants and children: New developments. Curr Opin Anaesthesiologi. 2000;13:285-289.
7. Byers GF, Doyle E, Best CJ, Morton NS. Postoperative nausea and vomiting in paediatric surgical inpatients. Paediatr Anaesth. 1995;5:253-256.
8. Martinić R, Sošić H, Turčić P, Konjevoda P. Hepatoprotective effects of met-enkephalin on acetaminophen-induced liver lesions in male. CBA Mice. 2014;7:1.
9. Kotiniemi LH. Outcome after minor surgery in children. Curr Opin Anaesthesiol. 2001;14:325-329.
10. Olutoye O, Watcha MF. Management of postoperative vomit- ing in pediatric patients. Int Anesthesiol Clin. 2003;4:99-117.
11. Kotiniemi LH, Ryhanen PT, Valanne J, Jokela R, Mustonen A. Postoperative symptoms at home following day-case surgery in children: A multicentre survey of 551 children. Anaesthesia. 1997;52:963-969.
12. Romsing J, Ostergaard D, Drozdziewicz D, Schultz P, Ravn G. Diclofenac or acetaminophen for analgesia in paediatric tonsil-lectomy outpatients. Acta Anaesthesiol Scand. 2000;44:291-295.
13. Valley RD, Bailey AG. Caudal morphine for postoperative analgesia infants and children: A report of 138 cases. Anesth Analg. 1991;72:120-124.
14. Arora MK, Rajeshwarı S. Comparison of caudal bupivacaine and morphine for relief of postoperative pain in children. J ındıan Assoc Pedıatr Surgvol. 2004;9:8-14.

Peer-review history:
The peer review history for this paper can be accessed here:
http://sciencedomain.org/review-history/15075