ORIGINAL ARTICLE

LOW-DOSE INTRATHECAL MORPHINE FOR POSTOPERATIVE ANALGESIA IN CHILDREN AFTER VARIOUS SURGICAL PROCEDURES

Sunitha K. S[1], Manukumar H[2]

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ABSTRACT: BACKGROUND: Use of Intrathecal morphine for postoperative analgesia in paediatric patients is in clinical practice[1]. The dose ranges from 2-5 mcg/kg body weight.[2, 3] The duration of analgesia depends on the type of surgery[1, 2] (12-36 hours). We evaluated the efficacy & safety profile of low-dose intrathecal morphine (3-4 mcg/kg) for postoperative pain management after various surgical procedures in children. **METHODS:** In our prospective observational clinical study, intrathecal morphine, 3-4 mcg/kg was injected at the conclusion of surgery, before extubation in 40 children undergoing various surgical procedures at VIMS & RC, Bangalore. Pain assessment was done from immediate postoperative period on an hourly basis till the patient required a rescue analgesic using FLACC Score. Vital parameters were also monitored. A FLACC Score of >5 was considered the time for initiation of rescue analgesic. All these children received 8th hourly Inj. Ondansetron, 0.1mg/kg to counteract the nausea & vomiting potential of morphine. **RESULTS:** The statistical analysis of results was done using descriptive and inferential analysis. The analgesic duration (from immediate postoperative period to rescue analgesic dose) ranged from 12-24 hours, with most patients having analgesia between 18 to 22 hours (60%). There was no incidence of side effects like nausea & vomiting, pruritus, respiratory depression, PDPH. We were unable to assess urinary retention as all children were catheterised preoperatively in view of the surgical procedure & continued till initiation of rescue analgesic. **CONCLUSION:** We conclude that low-dose intrathecal morphine (3-4 mcg/kg) for surgical procedures in paediatric patients provide intense, safe, prolonged postoperative analgesia.
KEYWORDS: Intrathecal morphine, postoperative analgesia, FLACC Score, low dose.

INTRODUCTION: Intrathecal morphine has been a widely accepted technique for providing effective postoperative pain relief even in paediatric patients, after various surgical procedures which are associated with severe pain. Table no 1 Shows the details.

	Low dose intrathecal morphine[1,2]	**High dose intrathecal morphine [4,5,6,7]**
Dose	**2 - 5 mcg/kg**	**10 – 30 mcg/kg**
Surgeries	Thoracotomies, laparotomies, orthopaedic surgeries, urological procedures, spinal fusion surgeries for scoliosis	Cardiac surgeries, frontal encephalocele repairs, spine surgeries, long term management of cancer pain

Side effects	Low incidence of side effects like nausea vomiting, pruritus, respiratory depression, urinary retention	High incidence of side effects like nausea vomiting, pruritus, respiratory depression, urinary retention

Table No 1

We evaluated the efficacy and safety of low-dose intrathecal morphine (3 – 4 mcg/kg) for postoperative analgesia following various surgical procedures in paediatric patients in our institution by a prospective observational clinical study.

METHODOLOGY: Institutional ethical committee clearance was obtained. A certain selection criteria were devised.

INCLUSION CRITERIA:

Age – 1 to 15 years.
ASA – I and II patients.

EXCLUSION CRITERIA:

- Coagulation disorders
- Infection at the site of injection
- Intracranial hypertension
- Hydrocephalus
- Parental refusal

The study population included children posted for various surgical procedures at VIMS & RC. A written informed consent was obtained from the parents of all the children. Preservative free morphine was injected intrathecally using a 21G hypodermic needle under aseptic precautions in the lowest palpable Lumbar spine interspace (in order to avoid injury to spinal cord).

The dose of intrathecal morphine given was 3-4 mcg/kg body weight and was injected at the conclusion of the surgery and before the extubation of the child. Preservative free morphine was diluted using normal saline. All the children were anaesthetised with standard GA procedure of our institution i.e. Inj. Fentanyl 2 mcg/kg IV for analgesia, sevoflurane/propofol for induction and Inj. Vecuronium, 0.1 mg/kg for muscle relaxation. Sevoflurane for maintenance of anaesthesia.

Pain assessment was done in all children from immediate postoperative period, on an hourly basis, till the time of initiation rescue analgesic agent using FLACC Score (Table no 2)

Criteria	Score - 0	Score - 1	Score - 2
Face	No particular expression or smile	Occasional grimace or frown, withdrawn, disinterested	Frequent to constant quivering chin, clenched jaw
Legs	Normal position or relaxed	Uneasy, restless, tense	Kicking, or legs drawn up
Activity	Lying quietly, normal position, moves easily	Squirming, shifting back and forth, tense	Arched, rigid or jerking
Cry	No cry (awake or asleep)	Moans or whimpers; occasional complaint	Crying steadily, screams or sobs, frequent complaints
Consolability	Content, relaxed	Reassured by occasional touching, hugging or being talked to, distractible	Difficult to console or comfort

Table No 2

Child was monitored for stability of vital signs like HR, NIBP, SPO2 and RR. We also monitored for side effects of morphine and technique used.[3]

1. Nausea and vomiting.
2. Respiratory depression.
3. Pruritus.
4. Urinary retention.
5. PDPH.

A FLACC Score of more than 5 was considered the time for initiation of rescue analgesic agent. The Duration of analgesia (pain free period) was taken 'immediate postoperative period to time of initiation of rescue analgesic agent. Postoperatively all the children were shifted to the recovery room for 2 hours and monitored in the paediatric ward subsequently. Some children who were undergoing a major surgery were shifted directly to the paediatric intensive care unit (PICU) and monitored. All the medications for pain management were ordered only by Anaesthesiologists and not the surgeons. Routine care of all these children included continuous pulse oximetry, ECG, hourly respiratory rates, hourly NIBPs and FLACC Score assessment.

All the children received Inj. Ondansetron 0.1 mg/kg, 8th hourly, from the time of extubation till the time of initiation of rescue analgesic agent, as a prophylactic measure to counteract the nausea & vomiting potential of morphine[3,4]

Subjective assessment of analgesia was done by the surgeons and the nurse taking care of the children in the ward. Both expressed satisfaction in the analgesia provided by intrathecal morphine and requested for the same for minor procedures like circumcision, herniotomy too. But it was deferred as the pain associated with such procedures was minimal and when pain is minimal the morphine related delayed respiratory depression may happen.[1, 3]

RESULTS: It is an ongoing study in our institution. We present the results of 40 children. The mean age group of the population was 6.20+3.77 years. Of that 18 were female patients and 22 were male patients.

Age in years	No. of patients	%
1-2	12	30.0
3-5	8	20.0
6-10	16	40.0
>10	4	10.0
Total	**40**	**100.0**

Table No 3: Age distribution of the study population

Weight (kg)	No. of patients	%
10-14	12	30.0
15-19	10	25.0
20-24	8	20.0
25-30	10	25.0
Total	40	100.0

Table No 4: Weight distribution of the study population

Surgical procedures	No. of patients	%
B/L hamstrings release	4	10.0
Hypospadias repair	10	25.0
Laparotomy for ambiguous genitalia	1	2.5
Partial splenectomy for thalassemia	1	2.5
PSARP	8	20.0
Pyeloplasty	10	25.0
Post burn contracture Release & SSG (below umbilicus and lower limbs)	6	15.0
Total	**40**	**100.0**

Table No 5: Surgical procedures after which intrathecal morphine was given

Duration of analgesia i.e. FLACC score >5	No. of patients	%
<18 hours	4	10.0
18-22 hours	24	60.0
>22 hours	12	30.0
Total	40	100.0

Table No 6: Duration of analgesia i.e. FLACC Score more than 5

The least duration of analgesia obtained was 12 hours and longest duration of analgesia was 28 hours. It is important to note that all patients in the study had minimum duration of analgesia for 12 hours.

Eighteen patients in our study required supplemental analgesia immediately after extubation in the form of Inj. Fentanyl 0.5 to 1 mcg/kg. The requirement of supplemental analgesia can probably be attributed pharmacodynamics of morphine. The time of onset of action of morphine as determined after intrathecal administration is 15 to 30 minutes.

"Radiolabelled 14 C Morphine was injected intrathecally, demonstrated radioactivity in Spinal Cord within 15 to 20 minutes of injection and in the respiratory centres at 60 minutes post injection in lumbar region. Opioids access brainstem as a result of uptake of opioid into posterior radicular artery".[3, 8]

Supplemental analgesic post extubation	No. of patients	%
Nil	22	55.0
Yes	18	45.0

Table No 7: Requirement of supplemental analgesic post extubation

Twenty two patients did not require any supplemental analgesic in the immediate postoperative period, probably because they had the residual effects of general anaesthesia.

Other 18 patients who required Inj. Fentanyl in the immediate postoperative period had intrathecal morphine induced analgesia for >12 hours which cannot be attributed for fentanyl (the elimination half-life of fentanyl is 1 – 3 hours).[9]

Complications associated with morphine and technique used

1. We had no incidence of nausea and vomiting in any of our patients, probably because children in the study received Inj. Ondansetron, 0.1mg/kg, as a prophylactic measure 8th hourly till they received rescue analgesia which might have countered the nausea & vomiting potential of morphine.[3, 4]
2. We had no incidence of pruritus. According to studies previously done pruritus is a dose-dependent complication of morphine and we have used low dose of morphine (3–4 mcg/kg) intrathecally. Neurophysiological studies have identified a new class of C fibres which lead to itch response linked to centrally located receptor networks. There is an abundance of mu opioid and 5 – HT 3 receptors in these networks. And Inj. Ondansetron, which is a 5 – HT 3 receptor antagonist has known to reduce the incidence pruritus and thus Inj. Ondansetron might have countered the pruritus.[3, 10, and 11]
3. We could not assess urinary retention as most of the patients were catheterized as a part of surgical procedure. 3 patients in our study were not catheterized and we did not notice any urinary retention in them.
4. There was no incidence of respiratory depression in any of our patients. It was monitored using parameters like SpO2, RR, and consciousness of the child. The fall in SpO2 <90%,with decreased level of consciousness and tachypnoea (RR>40) if requiring supplemental oxygen, assisted ventilation or requiring naloxone administration was

considered as respiratory depression.[3,12,13] None of the children required supplemental oxygen for more than one hour. In our institution we use supplemental oxygen for one hour post extubation as a protocol in all paediatric patients post general anaesthesia. None of the children either required assisted ventilation or naloxone administration.[3, 12, 13]

5. There was no incidence of PDPH in any of our patients. PDPH is a rare complication in paediatric patients and some authors have even challenged its existence.[14]

Other hurdles encountered during the study;

1. It was a difficult task to assess FLACC score in small children as they were restless after few hours after surgery probably because of hunger, strange environment and noise from various monitors and infusion pumps. So care was taken to keep one of the parents near the child to avoid child becoming anxious in the strange atmosphere. We used a sucking gauze soaked in sugar solution as a remedial measure. If the child became quiet with that the FLACC Score when the child was restless was eliminated.
2. Ten patients in our study developed fever few hours after surgery, probably because of the surgical procedure itself. These children received paracetamol suppository in the dose of 20 – 30 mg/kg body weight once or twice at 6th hourly interval. And we could not attribute the analgesia to paracetamol because all the children were pain free even before administration of paracetamol and the half-life of paracetamol is just 1–4 hours. And the children continued to be pain free even after the half-life of paracetamol was over.

DISCUSSION: We have compared our study with two more studies where similar dosage has been used. The details have been enumerated in the table no 8 below.

	OUR STUDY	**THE CHILDREN'S HOSPITAL, PHILADELPHIA[1]**	**INNSBURK MEDICAL UNIVERSITY, AUSTRIA[4]**
Type of study	Prospective observational study	Retrospective study	Prospective randomized single blinded
Score adopted	FLACC Score	Numeric verbal rating scale (0 – 10) for children > 7 years FLACC Score for children < 7 years	No of times the PCA was used
Age group	6.20 + 3.77 years	5.6 + 5.1 years	12 – 17 years
Type of surgeries	From laparotomies to tendo-achilles release	Thoracotomies, orthopaedic, urological, laparotomies and laparoscopies	Dorsal spinal fusion for idiopathic scoliosis
No. of patients	40	187	28

Dose of intrathecal morphine	3 – 4 mcg/kg	4 – 5 mcg/kg	5 mcg/kg + sufentanyl 1mcg/kg (14 children) Other 14 children were control group & did not receive intrathecal morphine
Duration of analgesia	12 – 28 hrs.	8 – 36 hrs.	Determined that IV opioid requirement was nil or less compared to control group in first 24 hours
Complications	PONV – Nil Pruritus – Nil Urinary retention – could not be assessed Respiratory depression – Nil PDPH – Nil	PONV – 32 % Pruritus – 37 % Urinary retention – 6% Respiratory depression – only 2 patients → supplemental oxygen beyond 60 post op minutes. No need of assisted ventilation or naloxone PDPH – 1 patient transient PDPH	PONV – high incidence in both ITM & Control group. Therefore attributed to surgical procedure Pruritus - < 30 % Respiratory depression – used Ramsay sedation score (2-3) & none required assisted ventilation or naloxone
Conclusion	Effective and safe analgesia with minimum monitoring	Useful and safe adjunct for postoperative analgesia	ITM significantly reduced postoperative opioid requirement with minimum side effects

Table No 8

The 3rd column in the above table shows the study done at The Children's Hospital, Philadelphia. The age group of the study population in their study is similar to that of our study and the type of surgeries are also similar. The study population is 187 patients. The duration of analgesia does not vary much in both the studies. Incidence of complications are higher in their study, probably because the study population is more. But it is a retrospective study and may have associated biases.

The other study at Innsburk Medical University, Austria has used similar dosage but along with sufentanyl probably to cover the lag period between intrathecal morphine injection and onset of morphine analgesia (20 – 30 minutes). It has been used only for spinal fusion surgeries in scoliosis and their age group is also higher. They have not noted the total analgesic period, but the requirement of IV narcotic analgesics in the first 24 hours of postoperative period. They conclude that requirement of IV opioid in the first 24 hours after intrathecal morphine was nil or

less. The only morphine related complication noted by them was pruritus. They observed high incidence of PONV in both morphine and control group and hence it was attributed to surgery.

SUMMARY & CONCLUSION: Intrathecal preservative free morphine in the doses of 3 - 4 mcg/kg provided an effective, safe postoperative analgesia without any major complications. It was easily accomplished with no discomfort to the child as it was done under GA at the conclusion of surgery. It was accomplished with a simple 21 G hypodermic needle and a 1 ml syringe and hence it is highly cost effective method of providing postoperative analgesia. Addition of Ondansetron in the postoperative period helps to counteract nausea, vomiting & pruritus potential of morphine. Safe analgesia with minimum and lesser degree of postoperative monitoring can be achieved. An active, cheerful, comfortable child after a major surgical procedure which is the goal of all Anaesthesiologists and Surgeons was achieved.

REFERENCES:

1. Ganesh A, Kim A, Casale P. et al. Low-dose intrathecal morphine for postoperative analgesia in children. International Anaesthesia Research Society. Anaesthesia Analgesia February 2007; 104(2):271- 276.
2. Duman A, Apiliogullari S.Letters to the editor, International Anaesthesia Research Society, Anaesthesia Analgesia, Oct 2007; 105(4):1170-1171.
3. Hindle A. Continuing Education in Anaesthesia, Critical Care & Pain, May 2008;8(3):81-85.
4. Galloway K, Staats PS, Bowers DC. Intrathecal analgesia for children with cancer via implanted infusion pumps. Med Pediatr Oncol 2000; 34: 265–7.
5. Meignier M, Ganansia MF, Lejus C, Testa S. Intrathecal morphine therapy in children with cancer. Cah Anesthesiol 1992; 40:487–90.
6. Tobias JD, Mateo C, Ferrer MJ, et al. Intrathecal morphine for postoperative analgesia following repair of frontal encephaloceles in children: comparison with intermittent, on-demand dosing of nalbuphine. J Clin Anesth 1997; 9: 280–4.
7. Peterson KL, DeCampli WM, Pike NA, et al. A report of two hundred twenty cases of regional anesthesia in pediatric cardiac surgery. Anesth Analg 2000; 90: 1014 –19.
8. Ummenhofer WC, Arends RH, Shen D, Bernards CM. Comparative spinal distribution and clearance kinetics of intrathecally administered morphine, fentanyl, alfentanil, and sufentanil. Anesthesiology 2000; 92: 739–53.
9. Ronald. D. Miller et al, Miller's anaesthesia, 7th ed, chapters 27, 81, 83, 86, 87.
10. Charuluxananan S, Somboonviboon W, Kyokong O, Nimcharoendee K. Ondansetron for treatment of intrathecal morphine-induced pruritus after cesarean delivery. Reg Anesth Pain Med 2000; 25: 535–9.
11. Yeh HM, Chen LK, Lin CJ, et al. Prophylactic intravenous ondansetron reduces the incidence of intrathecal morphine induced pruritus in patients undergoing cesarean delivery. Anesth Analg 2000; 91: 172–5.
12. Bujedo B M. A clinical approach to neuraxial morphine for the treatment of postoperative pain, Pain Research and Treatment, Vol 2012, Article ID 612145.

13. Jones SE, Beasley JM, Macfarlane DW, Davis JM, Hall-Davies G. Intrathecal morphine for postoperative pain relief in children. Br JAnaesth 1984; 56: 137–40.
14. Goyal R, Jinjil K, Baj BB, Singh S, Kumar S. Paediatric Spinal Anesthesia, Indian Journal of Anaesthesia 2008; 52 (3): 264-270.

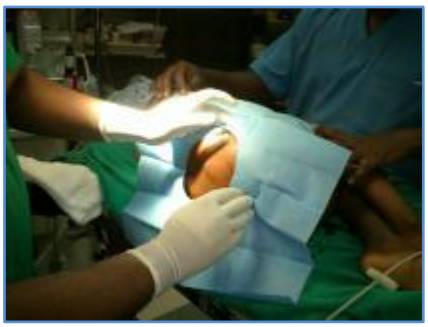

Figure 1

Figure 2

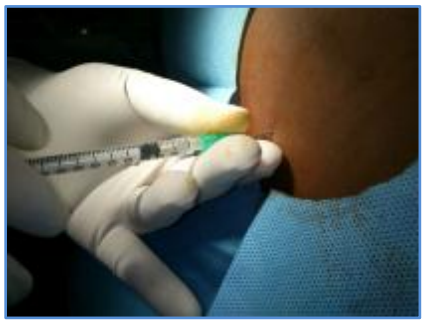

Figure 3

AUTHORS:

1. Sunitha K. S.
2. Manukumar H.

PARTICULARS OF CONTRIBUTORS:

1. Professor, Department of Anaesthesiology, Vydehi Institute of Medical Sciences, Whitefield, Bangalore.
2. Post Graduate Student, Department of Anaesthesiology, Vydehi Institute of Medical Sciences, Whitefield, Bangalore.

NAME ADDRESS EMAIL ID OF THE CORRESPONDING AUTHOR:

Dr. K. S. Sunitha,
A-904, Mantri Greens, Sampige Road,
Malleswaram, Bangalore – 560003.
E-mail: relaxreverse@yahoo.co.in

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