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Original Article

Efficacy and safety of intrathecal morphine for post cesarean section analgesia

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Abstract

Background: Government of Nepal has been conducting Cesarean section under "Safe Motherhood" program all over country. The purpose of this study was to evaluate the efficacy and safety of intrathecal morphine for post cesarean analgesia under spinal anesthesia.

Methods: A total of 300 parturients posted for Cesarean section under spinal anesthesia were divided into two groups of 150 each in this prospective randomized case-control study. Morphine group received 0.15 mg of intrathecal morphine mixed in 12 mg of 0.5% bupivacaine heavy while control group received 12 mg of 0.5% bupivacaine heavy alone, after proper preparation of spinal anesthesia. The parturients were assessed for first request of analgesic as per Visual Analog Scale, frequency of analgesics required within 24 hr, nausea, vomiting, pruritus, sedation and respiratory depression.

Results: Postoperative analgesia was significantly greater in morphine group as compare to control group (12.1 ± 7.6 vs 3.7 ± 2.9 hr). Frequency of analgesics requirements was also significantly lower in morphine group (1.7 ± 2.0 vs 3.4 ± 8.1). Visual Analog Scale was below 4 at most of time in morphine group. The incidence of nausea, vomiting and pruritus were more in morphine group as compare to control group but without any respiratory depression. There was no significant difference in APGAR score among fetus.

Conclusion: Mixing low dose of intrathecal morphine in standard dose of spinal anesthesia effectively prolongs the duration of post cesarean analgesia and decreases the frequency of analgesics requirement without any major complication in parturients or fetus.

Key words: Intrathecal morphine, post cesarean analgesia, safe motherhood.

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Introduction

Cesarean section is the most common operation in obstetrics. Now, it has been under "Safe Motherhood" program running all over country, under Government of Nepal, which is totally free to the patient. It is also a well known fact that mother has to bear severe post operative pain because of unavailability of better analgesic and modern techniques of pain control at all the centre and that too free of cost, in the current era of cost containment.

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Spinal anesthesia is the most common anesthetic technique used for cesarean section in Nepal and across the world. Intrathecal opioids are administered along with a local anesthetic during spinal anesthesia for cesarean delivery to provide postoperative analgesia.[1] The effectiveness of intrathecal morphine is well established but there has been a controversial reviews regarding its safety.[2,3,4]

This study has been conducted to review the efficacy and safety of intrathecal morphine for post cesarean section analgesia under spinal anesthesia, established in the past.

Material and Method

After IRC approval, this prospective, randomized, case-control study was conducted in 300 parturients scheduled for Cesarean section, elective or emergency, under spinal anesthesia from September to November 2013 at Nepalgunj Medical College. They were randomly divided into two groups (case and control) of 150 each by envelope method. Parturients with any contraindication to spinal anesthesia, history of hypersensitivity to morphine and chronic pain syndrome or current regular opioid use were excluded from the study.

All of parturients received Injection (Inj) Ranitidine 50 mg and Inj Metoclopromide 10 mg when decided by obstetricians for Cesarean section, preferably half an hour before. An informed consent was taken from all the parturient. All of them received one litre of Ringer lactate. They were attached to monitor for NIBP, SpO_2 and ECG. The attending obstetrician and the paediatrician were well informed about the use of intrathecal morphine, but were blinded about the case. They were allocated to receive either 0.15 mg of Morphine mixed with 12 mg of 0.5% Bupivacaine heavy (Group M) or 12 mg of 0.5% Bupivacaine heavy only (Group C) under aseptic spinal anesthesia technique. APGAR score was taken at 0 and 5 minutes of birth by pediatrician and Neonatal Intensive Care Unit (NICU) admission was noted, if required. Any patient converted to General Anesthesia or requiring supplementary analgesic intraoperatively was excluded from the study. After surgery, they were transferred to postoperative ward. The patients were monitored for vitals, first request of analgesic, frequency of analgesics required, nausea and vomiting, pruritus, respiratory depression, and sedation by nursing staffs. Observations were done at 5, 15, 30 minutes, then hourly for 12 hours then 4 hourly for next 12 hours. Patients were asked to rate their current level of pain on a Visual Analog scale (VAS) of 0 (no pain) to 10 (worst pain imaginable). A pain score >4 were given analgesia. The indwelling catheter is to remain in situ for 24 hours.

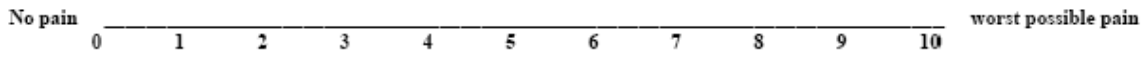

Fig.1 Visual Analog Scale

Level of sedation will be assessed by following ordinal scale.

0 - Awake, alert.

1 - Drowsy, respond to call.

2 - Drowsy, respond to tactile stimuli.

3 - Deep Sedation, unresponsive.

Management of side effects-

1. Respiratory depression or Sedation

   If respiratory rate is < 8 or conscious state = 3

   - Give oxygen 6 l/m via Hudson mask.
   - Call the anesthetist.
   - Administer Naloxone 0.4mg IV, repeating every 2 minutes to a maximum 8 doses.
   - Intermittent ventilation with a bag and mask or mechanical ventilation, if necessary.
2. Pruritus: Itching is common across face, chest and abdomen.
   Managed with counselling, 5-hydroxytryptamine$_3$ antagonist such as Ondensetron 4mg, Inj Pheniramine, Inj Propofol 0.25mg/kg or iv/sc naloxone 50-100mcg in severe case.
3. Nausea and Vomiting: Managed with Inj Ondensetron.

4. Inadequate pain relief: Diclofenac 75mg IM, Tramadol or Pethidine IV, as required.

Statistical analysis

All values are expressed as the mean ± standard deviation. SPSS 15.0 was used for the statistical analysis. Independent "t" test was used for analyzing differences between the groups. P values less than 0.05 were considered statistically significant.

Results

The results for each group are shown in Table 1. There are no significant differences between the groups as to patient age, body weight and operative time.

Table 1 Details of the patients in morphine and control group

	Group M	Group C	p-value
Number of patients	150	150	
Mean age	25.16 ± 2.51 years (range 18-32)	24.28 ± 5.39 years (range 18-36)	0.863
Mean body weight	59.4 ± 10.73 kg	62.55 ± 9.34 kg	0.183
Mean Operative time	62 ± 3.11 minutes	70.2 ± 6.57 minutes	0.105

The VAS score at different time intervals were depicted in Fig. 1. It was significantly lower at a mean value of 2.4 ± 34 for the morphine group and a mean of 7.2 ± 11 for the control group ($p<0.001$) at 4 hours of surgery. The VAS score remained lower in the morphine group for 12 hours compared to control group ($p<0.05$). The VAS remained below 4 at most of the period in morphine group. There were up and down in VAS scoring in control group because of breakthrough pain in between analgesics. There was no significant difference between two groups after 24 hours.

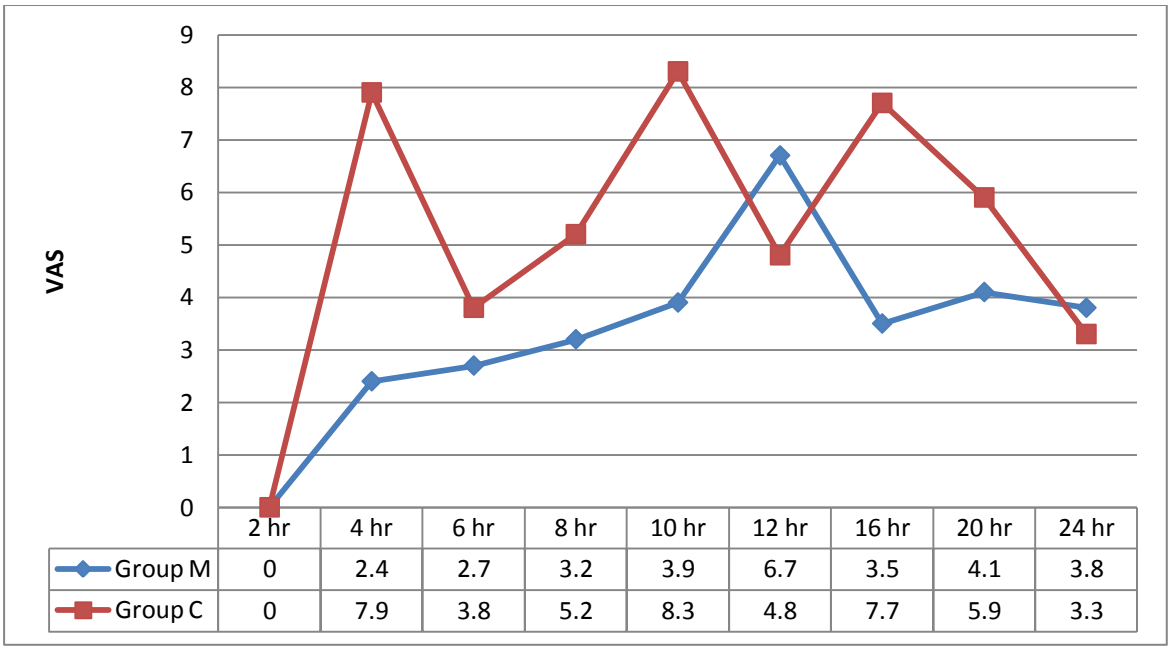

Fig. 2 Comparison of Visual Analog Scale (VAS) in morphine and control group

The time of first request of analgesic was 12.1 ± 7.6 hours for the morphine group and 3.7 ± 2.9 hours for the control group ($p<0.001$). The number of times patients required supplemental analgesics until 24 hours after surgery was 1.7 ± 2.0 in morphine group and 3.4 ± 8.1 in the control group ($p<0.05$).

There was no significant difference in APGAR score at 0 and 5 minutes of birth among the group Table 2. The rate of NICU admission among the group was too non-significant. None of the fetus required naloxone for the resuscitation.

Table 2. Details of fetus in morphine and control group

	Group M	Group C	p-value
APGAR score at 0 min	(7.15 ± 2.2)/ 10	(6.81 ± 9.33)/ 10	>0.05
APGAR score at 5 min	(8.01 ± 5.1)/ 10	(8.67 ± 3.81)/ 10	>0.05
NICU admission	56 (37.33%)	49 (32.67%)	>0.05

The side effects were observed more in morphine group than control group and were managed with medication and counselling. No major side effect like respiratory depression occurred in either group. Sedation scores were 0 and 1 in all cases in both the groups.

Table 3. Details of side effects in morphine and control group

	Group M	Group C
Nausea	49 (32.67%)	31 (20.67%)
Vomiting	36 (24%)	24 (16%)
Pruritus	39 (26%)	4 (2.67%)
Respiratory Depression	0	0

The level of satisfaction among parturients, obstetricians, pediatricians and nursing staffs was very good.

Discussion

The purpose of this study was to investigate the efficacy of intrathecal morphine along with standard dose of spinal anesthesia in terms of postoperative analgesia, supplemental analgesic drugs required and side effects observed, among parturients undergoing cesarean section. The study shows that intrathecal morphine adds a further analgesic effect postoperatively but with some minor side effects. Morphine was chosen for the study because of its wide availability at most of the centres of Nepal.

Behar et al[5] and Wang et al[6] in 1979 reported that the intrathecal and epidural opioids were effective for acute and severe pain in human. Despite the early reports regarding the analgesic efficacy of intrathecal morphine,[7,8,9] it failed to gain widespread use due to high incidence of respiratory depression, related to the use of large dose of morphine. Wang et al[6] with 0.5 and 1.0 mg of intrathecal morphine had 15-22 hour of analgesia without respiratory depression whereas others[10,11,12] reported high frequency of delayed respiratory depression with dose of 2-15 mg. Subsequently, mini-dose concept of intrathecal morphine had promising results.[13,14,15,16]

In 1994, Blitt et al[17] coated "avoidance of subarachnoid opiates" as a strategy to improve perioperative safety. Responding to it, Abouleish[18] challenged theses guidelines as being unsubstantiated by the scientific evidence, and warned of the legal consequences of making avoidance the standard of care. In 1999, Gwirtz et al[19] published high patient satisfaction and low incidence of side effects in over 6000 patients.

Baraka et al[1] had effective labour analgesia with 1mg of intrathecal morphine but with high incidence of pruritus, somnolence and nausea/vomiting (85-100%). Intrathecal morphine acts by binding to dorsal horn receptors. In 1988, Abboud et al[13] reported that 0.25 and 1.0 mg doses of intrathecal morphine reduced VAS pain scores by 50% or more for a mean of 27.7 and 18.6 hour respectively. In this study, 12.1 hour of analgesia was found with low dose of 0.15 mg of intrathecal morphine whereas Abouleish et al[18] found 27 hour of analgesia but with 0.2 mg of intrathecal morphine. It clearly signifies that increasing the dose of intrathecal morphine, increases the duration of analgesia but at a cost of higher incidence of side effects. In this study, major side effect such as respiratory depression was not observed in any of case, probably because of use of low dose of morphine. We do noticed more of minor side effects like nausea and vomiting, pruritus especially around the trunk and face in morphine group than in control group, which is similar to others finding. These

side effects are caused by the drug gaining access to the spinal cord and brain stem from the cerebrospinal fluid.[20,21] Hence, intrathecal morphine requires appropriate postoperative care.

Epidural opioid has established its popularity in this present era of analgesia. Advantages for the intrathecal opioids in comparison to epidural analgesia include technical ease of administration, simplicity of postoperative management and low cost. The failure rate of spinal injection is much lower than that of epidural placement.[22] Recent changes in healthcare economics have placed cost control at the forefront of medical care and patient management. Gwirtz and associates reported that intrathecal opioids cost less than one third as much as epidural opioids.[19]

Government of Nepal has been conducting Cesarean section under "Safe Motherhood" program with limited resources and expertise. A better modern pain control techniques such as epidural analgesia and patient-controlled-analgesia or even strong opioids at regular supply are poorly available at most of the centres. Anesthetic assistant are allowed to perform Cesarean section under Obstetrician or MD General Practice but they fail to provide a better pain free post operative periods. Hence, in this study 0.15 mg of intrathecal morphine was added to standard dose of 12 mg bupivacaine in spinal anesthesia so that it can do justice to the parturients for the control of their postoperative pain, cost effectively.

Conclusion

This study establishes that 0.15 mg of intrathecal morphine safely prolongs the postoperative analgesia in the parturients undergoing Cesarean section under spinal anesthesia, despite higher incidence minor side effects like nausea, vomiting and pruritus but without any major complication to parturient or fetus. This cost effective technique also decreases the frequency of further analgesic requirements.

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References

1. Baraka A, Noueihid R, Hajj S. Intrathecal injection of morphine for obstetric analgesia. Anesthesiology 1981;54:136-40.
2. Gustafsson LL, Schildt B, Jacobsen K. Adverse effects of extradural and intrathecal opiates: report of a nationwide survey in Sweden. Br J Anaesthiol 1982;54:479-86.
3. Gjessing J, Tomlin PJ. Postoperative pain control with intrathecal morphine. Anesthesia 1981;36:268-76.
4. Chaney M. Side effects of intrathecal and epidural opioids. Can J Anesth 1995;42:891-903.
5. Behar M, Magora F, Olshwang D, Davidson JT. Epidural morphine in the treatment of pain. Lancet 1979;1:527-9.
6. Wang JK, Nauss LA, Thomas JE. Pain relief by intrathecally applied morphine in man. Anaesthesiology 1979;50:149-151.
7. Kalso E. Effects of intrathecal morphine injected with bupivacaine on pain after orthopaedic surgery. Br J Anesthiol 1983;55:415-22.
8. Nordberg G, Hedner T, Mellstrand T, Dalistrom B. Pharmacokinetic aspects of intrathecal morphine analgesia. Anesthesiology 1984;60:448-54.
9. Chadwick HS, Ready LB. Intrathecal and epidural morphine sulphate for postcesarean analgesia: a clinical comparison. Anesthesiology 1988;67:137-43.
10. Odoom JA, Sih IL. Respiratory depression after intrathecal morphine. Anesth Analg 1982;61:70.
11. Davies GK, Tolhurst-Cleaver CL, James TL. Respiratory depression after intrathecal narcotics. Anesthesia 1980;35:1080-3.
12. Glynn CJ, Mather LE, Cousin LE, Wilson PR, Graham JR. Spinal narcotics and respiratory depression. Lancet 1979;2:356-7.
13. Abboud TK, Dror A, Mosaad P, Zhu J, Mantilla M, Swart F. Mini-dose intrathecal morphine for the relief of post-cesarean section pain. Anesth Analg 1988;67:137-43.
14. Abouleish E, Rawal N, Fallon K. Combined intrathecal morphine and bupivacaine for cesarean section. Anesth Analg 1988;67:370-4.
15. Kirson LE, Goldman JM, Slover RB. Low-dose intrathecal morphine for postoperative pain control in patients undergoing transurethral resection of prostate. Anesthesiology 1989;71:192-5.
16. Allano C. Low dose spinal morphine for postop analgesia on surgical wards. Br J Anesthesiol 1999;82:189.
17. Blitt CD, Kaufer-Bratt C, Ashby J, Caillett JR. QA program reveals safety issues, promotes development of guidelines: AZ practice model. APSF Newsletter 1994;9:17-9.
18. Abouleish EI. No need to avoid spinal narcotics [letter] APSF Newsletter 1994;9:50.
19. Gwirtz KH, Young JV, Byers RS. The safety and efficacy of intrathecal opioid analgesia for acute postoperative pain: seven years' experience with 5969 surgical patients at Indiana University hospital. Anesth Analg 1999;88:599-604.
20. Abouleish E. Apnoea associated with intrathecal administration of morphine in obstetrics. Br J Anaesth 1988;60:592-4.
21. Scott PV, Fisher HB. Intraspinal opiates and itching: A new reflex? BMJ 1982:284:1015-6.
22. Gerig HJ, Kern F. Success and failure rate in peridural anesthesia. A 1-year study. Reg Anaesth 1985;8:25-32.