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INTRATHECAL MORPHINE FOR POSTOPERATIVE ANALGESIA IN POSTERIOR LUMBAR SPINE DECOMPRESSION AND INSTRUMENTATION: A COMPARATIVE STUDY OF TWO DIFFERENT DOSES.

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ABSTRACT

Background: Patients undergoing lumbar spine instrumentation surgery suffer severe postoperative pain which is difficult to treat by conventional multimodal analgesic methods. In this randomized double blind study we compared the analgesic effect of two different doses of intrathecal morphine (ITM) 0.2 mg and 0.3 mg in patients undergoing posterior lumbar spine decompression and instrumentation surgery. **Materials and Methods:** Forty ASA 1 and 2 patients of either sex aged 18 years or older undergoing posterior lumbar spine decompression and instrumentation surgery between L1-L5 were randomly assigned to receive ITM either 0.2 mg (Group A, n=20) or 0.3 mg (Group B, n=20) in 2 ml saline before general anaesthesia. A morphine intravenous patient controlled analgesia (PCA) device was used for rescue analgesia in postoperative period. Assessment parameters included hemodynamics, sedation score, pain using numeric rating scale (NRS), total consumption of PCA morphine recorded for 24 hours and patient's satisfaction score. The data was analyzed using chi square test for categorical variables and student's t test for quantitative variables. **Result:** NRS score was significantly low in group B at 4, 8, 12 and 24 hours as compared to group A ($p < 0.05$). Group B also had decreased requirement for rescue analgesia ($p = 0.001$) with higher patient satisfaction. There was no significant difference between the two groups in other studied parameters. **Conclusion:** 0.3 mg ITM provided superior analgesia postoperatively in terms of NRS score and higher patient satisfaction compared with 0.2 mg with no significant difference in the incidence of side effects.

KEYWORDS: Morphine, Intrathecal, Spine surgery, Patient controlled analgesia.

KEYMESSAGE: Intrathecal morphine a safe and reliable technique for excellent postoperative analgesia in posterior lumbar spine decompression and instrumentation surgeries with minimal side effects.

INTRODUCTION

Effective pain management is an important component of postsurgical care.[1] Intrathecal opioids (ITOs) are a novel way of postoperative analgesia as they produce 'segmental analgesia' resulting in localized nociception without sensory, motor, autonomic or systemic side effects.[2] They not only allow postoperative neurological assessment in immediate postoperative period but also avoid risk of orthostatic hypotension or motor in-coordination that local anaesthetics cause.[3]

Due to its long duration of action morphine is considered a better option for intrathecal administration.

Previous studies have used 0.2 mg to 2.5 mg of ITM for postoperative pain control after lumbar spine surgery.[33-37]

DeSousa et al in a review article concluded that ITM higher than 0.3 mg has a risk of respiratory depression.[39] We studied low dose i.e. 0.2 mg and 0.3 mg of intrathecal morphine (ITM) for quality and duration of analgesia, side effects and complications in posterior lumbar spinal surgeries.

MATERIALS AND METHODS

A prospective, randomized, double bind study was carried out after approval from the ethics committee of our hospital and written informed consent from 40 patients. ASA grade I and II aged 18 years or older of either sex undergoing posterior lumbar spine decompression and instrumentation surgery between L1-L5 were included in the study. Patients with known allergies to morphine or other opioids, lumbar procedures performed in minimally invasive technique or revision lumbar spine surgery, patients with a history of severe respiratory illness including COPD, asthma,

obstructive sleep apnea, psychiatric disorders and pregnancy, patients lacking mental capacity to use PCA or on sustained release narcotics and substance abuse and patients not giving consent were excluded from the study.

A computer derived random number sequence was generated using a block randomization, forty patients were allocated to either group A (n = 20) or B (n = 20). The same was translated to sequentially numbered opaque sealed envelopes to receive ITM 0.2 mg (group A) or 0.3 mg (group B). The anaesthesiologist conducting the case as well as recording the data was unaware of the drug being administered.

After pre-anaesthetic checkup patients were acquainted with the NRS for pain scoring, use of PCA system and potential adverse drug events. Patients were kept fasting for 6-8 hours and premedicated with tab ranitidine 150 mg and tab alprazolam 0.25 mg orally, the night before surgery. On arrival in the operative room standard monitoring equipments were attached (electrocardiogram lead II and lead V5, pulse oximeter and noninvasive blood pressure) and baseline vital parameters like heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), respiratory rate (RR) and oxygen saturation (SpO_2) were noted just prior to induction of anaesthesia. Peripheral venous access was obtained.

The index anaesthesiologist prepared the aforementioned injection taking all aseptic precautions and delivered it to the operating room to ensure all parties were blinded. Patients were placed in sitting position and the spinal puncture was performed at L3–L4 interspace using a 25-gauge whitacre pencil-point spinal needle. Once free flow of CSF had been recognized, the intrathecal morphine (0.2 mg or 0.3 mg) in 2 ml normal saline 0.9 % was injected.

Patient was made supine. Anaesthesia was induced with inj. propofol 2 mg/kg, inj. midazolam 1 mg and inj. morphine 0.1 mg/kg i.v. Endotracheal intubation was facilitated with inj. vecuronium bromide 0.1 mg/kg i.v. Anaesthesia was maintained with 50% N_2O in O_2 with sevoflurane 2%. Neuromuscular relaxation was maintained with inj. vecuronium top ups of 1 mg i.v. every hourly. The lungs were mechanically ventilated to keep end tidal CO_2 ($EtCO_2$) within normal range. Temperature probe was inserted and temperature was recorded. Patient was catheterized and urine output was recorded. Patient was made prone for surgery. 30 mins before completion of surgery all patients were given inj. ondensetron 0.15 mg/kg body wt. for prevention of postoperative nausea and vomiting (PONV).

At the end of the surgery patients were made supine, residual neuromuscular block was reversed with inj. neostigmine (0.05 mg/kg) and inj. glycopyrolate (0.008 mg/kg). Endotracheal tube removed and patients were transferred to the post anesthesia care unit (PACU). All patients had PCA morphine in postoperative period up to 24 hrs. PCA was programmed to deliver a 0.5 mg morphine bolus with a 20 minutes lockout time via a dedicated intravenous cannula.

In postoperative period following parameters were recorded at 1, 2, 4, 8, 12 and 24 hours after the surgery : pain score by NRS, noninvasive blood pressure, heart rate, respiratory rate, oxygen saturation, nausea, vomiting, pruritus, sedation score, total morphine consumption in 24 hours and patient satisfaction score. Rescue analgesia was provided with injection morphine using PCA in incremental doses till NRS score was less than 3.

Pain was assessed by NRS 0- 10 cm long scale on which 0 is taken as no pain and 10 being worst possible pain. NRS < 3 was taken as satisfactory pain relief. Side effects including nausea, vomiting, respiratory depression (RR < 8 breaths/min), sedation and pruritus were also recorded. For sedation, Ramsey Sedation Score was used - if awake- 1- anxious, agitated, restless, 2- cooperative, oriented, tranquil, 3- responsive to commands only, If asleep- 4- brisk response to light glabellar tap or loud auditory stimulus, 5- sluggish response to light glabellar tap or loud auditory stimulus and 6- no response to light glabellar tap or loud auditory stimulus. Side effects if any were treated as in table shown below.

Side Effects	**Treatment**
Respiratory Depression (RR<8)	Oxygenation Call the anaesthetist on duty Intermittent bag and mask ventilation Inj. Naloxone 0.4 mg iv, repeating it every 2 mins to a maximum of 8 doses.
Nausea & Vomiting	Inj. Ondensetron 0.15mg/kg
Sedation Score of 6	Call the anaesthetist on duty Observe SpO2, airway If there is fall in SpO2 < 90% and airway compromise, administer inj. Naloxone 0.4mg iv, repeating every 2mins to a maximum of 8 doses.
Bradycardia (HR< 50/min)	Inj. Atropine 0.05 mg/kg to be repeated if required
Pruritis	Mild- Inj. Ondensetron 0.15mg/kg Moderate to severe- Inj. Naloxone 0.1 mg iv

At the end of 24 hours, patients were asked to rank the quality of pain relief on a four point pain satisfaction scale with - 1 – Excellent, 2 – Very good, 3 – Satisfactory and 4 – Poor.

Statistical Methods

The sample size calculation was based on estimating a 30% decreased in postoperative morphine requirement as observed in the previous studies. A calculated sample size of 20 patients would be required to attain the power of at least 80% and 5% significance level with 90% confidence interval. Therefore, we enrolled 20 patients in each group. Statistical analysis was performed using Statistical Package for Social Sciences (SPSS) version 15.0. Statistical significance of categorical variables between the groups were compared by chi square test and that of quantitative variables were compared by using Student's t test and non-parametric Mann Whitney U-test in case data does not follow normal distribution. Quantitative variables are presented as mean (± SD), while ordinal data are presented as number (%). A value of $P < 0.05$ was considered statistically significant.

RESULTS

The demographic profile in relation to age, weight, gender, ASA grade and duration of surgery in the two groups were comparable (Table I). The extend of the surgical procedure was similar in both the groups involving two or three levels of lumbar vertebrae.

TABLE I: DEMOGRAPHIC DATA

	GROUP A (0.2 mg intrathecal morphine)	GROUP B (0.3 mg intrathecal morphine)	P – Value
AGE (years)	54.10 ± 10.25	57.10 ± 13.30	0.429
GENDER (M/F)	10/10	12/8	0.525
WEIGHT (kgs)	77.05 ± 15.49	79.55 ± 19.05	0.651
DURATION OF SURGERY (hrs)	3.111 ± 0.51926	3.226 ± 0.51626	0.434
ASA GRADE (1/2)	9/11	8/12	0.749

The NRS score at 1 hour and 2 hours postoperative was comparable in both the groups (p value 0.714 and 0.721 respectively). In group B, there was a statistically significant decrease in the NRS score at 4, 8, 12 and 24 hours postoperative. On the other hand in group A, NRS score was slightly more than the value at 2 hours. When comparing the two groups, in group B, none of the patient had pain score greater than 2. The difference in NRS score was statistically significant at 4, 8, 12 and 24 hours postoperative between the two groups ($p < 0.05$) (Table II).

TABLE II: NUMERIC RATING SCALE

NRS SCORE	Group A (0.2 mg Intrathecal Morphine)		Group B (0.3 mg Intrathecal Morphine)		P value
	n	Mean ± SD	n	Mean ± SD	
1 hr	9	2.22 ± 1.20	5	2.00 ± 0.71	0.714
2 hrs	6	1.83 ± 0.41	1	2.00 ± 0	0.721
4 hrs	11	2.18 ± 0.60	6	1.50 ± 0.55	0.037
8 hrs	18	2.56 ± 0.70	8	1.38 ± 0.74	0.001
12 hrs	16	2.81 ± 0.54	10	1.90 ± 0.74	0.001
24 hrs	15	2.07 ± 0.46	2	1.00 ± 0.00	0.006

The morphine consumption as rescue analgesia over 24 hours was much higher in group A as compared to group B. The difference was found to be statistically significant (p value 0.001) (Table III). The patient satisfaction in group B was much higher than in group A ($p = 0.001$) (Table IV). However, the exact time of first use of rescue analgesia could not be recorded as it was administered by the patient himself / herself.

TABLE III: MEAN 24 HOUR MORPHINE REQUIREMENT

GROUP	Mean 24 hour morphine requirement in mg (Mean ± SD)
GROUP A (0.2 mg Intrathecal Morphine)	2.8 ± 1.22
GROUP B (0.3 mg Intrathecal Morphine)	0.5 ± 0.487
P VALUE	0.001

TABLE IV: PATIENT SATISFACTION SCORE

PATIENT SATISFACTION SCORE	Group A (0.2 mg Intrathecal Morphine)		Group B (0.3 mg Intrathecal Morphine)		P value
	Frequency	%	Frequency	%	
1	2	10%	13	65%	0.001

2	10	50%	5	25%	
3	8	40%	2	10%	
Total	20	100%	20	100%	

The mean sedation score at 1 hour, 2 hours and 12 hours postoperative was comparable in both the groups (p value 0.061, 0.370 and 0.119 respectively). The difference between the two groups was statistically significant at 4 hours, 8 hours and 24 hours ($p < 0.05$). But it was not clinically significant as none of the patient had score > 4 at any occasion.

Hemo dynamic parameters (HR, SBP, DBP, RR and SpO_2) were within the normal limit during the entire 24 hour postoperative period (Table V). There was no occasion when the RR was < 10/min or oxygen saturation < 93% in either group. The number of patients complaining of vomiting and pruritus in the postoperative period were comparable between the two groups (Table VI).

TABLE V: HEMODYNAMIC PARAMETERS

Hemodynamic Parameters	Group A (0.2 mg Intrathecal Morphine)	Group B (0.3 mg Intrathecal Morphine)	P value
	Mean ± SD	Mean ± SD	
Heart Rate (HR)	80.20 ± 7.02	80.10 ± 5.71	0.961
Systolic Blood Pressure (SBP)	120.10 ± 10.37	121.30 ± 7.90	0.683
Diastolic Blood Pressure (DBP)	77.20 ± 6.47	76.10 ± 6.17	0.585
Respiratory Rate (RR)	20.60 ± 1.60	20.90 ± 2.55	0.66
Oxygen Saturation (SpO_2)	98.30 ± 0.86	98.20 ± 1.06	0.745

TABLE VI: SIDE EFFECTS

	Group A (0.2 mg Intrathecal Morphine)	Group B (0.3 mg Intrathecal Morphine)	P value
Nausea	6	13	1.000
Vomiting	6	13	1.000
Pruritus	3	3	1.000
Oxygen Saturation < 93%	Nil	Nil	
Respiratory Rate < 8/min	Nil	Nil	
Sedation Score of 6	Nil	Nil	
Bradycardia (HR < 50/min)	Nil	Nil	

DISCUSSION

Pain is one of the main postoperative adverse outcomes, which determines post-surgical morbidity, ambulation and discharge from hospital. Most patients complain of severe pain at rest during the first 12 hrs after lumbar spine decompression and instrumentation surgery. This pain increases considerably with mobilization because of the reflex spasm of paraspinal muscles that is triggered by the primary wound pain. On movement, pain remains severe for 48 hrs and produces discomfort that can interfere with patient mobilization and with discharge time.[1,4]

Analgesics given before the onset of pain, or "preventive analgesia", prevent plasticity of the central nervous system and provide more effective pain relief [5]. It has been seen that low doses of morphine used for preventive analgesia prevent central sensitization and prevent chronic pain.[6]

In a meta-analysis of ITM, the seriousness of the induced respiratory depression was related to the dose of ITM.[7] The incidence of late respiratory depression is reported to be 4% to 7% for patients receiving ITM (0.8 mg to 2 mg). Lower doses of ITM (0.3 mg to 0.4 mg) are linked to minimal risks of respiratory depression.[7]

Recently, practice guidelines for the administration of neuraxial opioids have been published by ASA Task Force.[8] According to the guidelines, the lowest efficacious dose of neuraxial opioid should be used to minimize the risk of respiratory depression. The present study has used the same approach of low dose to prevent respiratory depression.

Single-shot intrathecal technique using ITO with long-lasting analgesia, offers many advantages compared with epidural catheter or IV PCA. Technically, the intrathecal injection is easier to perform than epidural catheter placement and does not need additional equipment as required in epidural catheter or IV PCA. The single-shot approach precludes the risk of catheter dislodgement or catheter related infection.[9]

Meylan N. et al had done a metanalysis of 27 studies (15 concerning cardiothoracic, 9 abdominal, and 3 spinal surgeries) with a total of 645 patients who received doses between 100 and 4000 µg of intrathecal morphine without local anaesthetic in patients undergoing major surgeries. They had seen that pain intensity was

significantly decreased at 2, 4, 12, and 24 h.[10] Up to 4 hours after surgery, pain intensity at rest was decreased by about 2 cm on the 10 cm visual analogue scale. At 12 and 24 hr, pain intensity was decreased by about 1 cm. This degree of analgesic efficacy appears to be greater than with intraoperative low-dose ketamine (reduction in pain intensity at 24 hr, about 0.4 cm), and post- operative non-steroidal anti-inflammatory drugs or epidural analgesia with local anaesthetic (with both, reduction in pain intensity at 24 hr, about 1 cm). These findings were similar to the present study in which pain intensity was significantly low in 0.3 mg intrathecal morphine at 4, 8, 12 and 24 hours.

In this review study authors did not detect a linear relationship between the dose administered and degree of analgesia reached. They concluded that they do not know the optimal dose of intrathecal morphine when used alone. In contrast to this review, in the present study, a superior analgesic effect was recorded with 0.3 mg ITM as compared to 0.2 mg at all recorded times.

Masaaki Machino et al and Darshan Ashvin Trivedi et al had observed that the patients who received intrathecal morphine had significantly lower VAS score.[11,12] They had used lower dose of intrathecal morphine in combintion with local anaesthetics. In contrast, present study had used low dose ITM alone but had found the same results.

Annette Rebel et al had combined high dose ITM with IV naloxone.[9] They had seen that the IV naloxone infusion combined with high dose ITM control opioid side effects without affecting analgesia.

Khaled Mohamed Fares et al compared 0.2 mg, 0.5 mg and 1 mg ITM.[13] They had seen that 1 mg morphine provided superior analgesia for 48 hours postoperative. Both these studies had used higher doses of ITM in contrast to the present study where we had used lower doses.

Ross DA et al concluded from their study that consumption of parenteral narcotics decreases in correlation with increasing doses of intrathecally administered morphine without increase in parenteral narcotic side effects because of less consumption postoperatively.[14] This was similar to our study. In our study as we increased the dose of ITM from 0.2 mg to 0.3 mg, there was a decrease in morphine consumption over 24 hours. The difference was found to be statistically significant (p value 0.001).

Beaussier et al had compared 0.3 mg ITM with intravenous PCA morphine. They had seen the patients who received ITM had less daily intravenous morphine requirement for two days.[15] Similarly, Ziegeler et al compared 0.4 mg ITM with placebo and had seen decreased PCA requirement in 0.4 mg morphine group throughout the observed 20 hours after surgery.[16] Both these studies had shown decreased opioid requirement in postoperative period in patients who received ITM as seen in our study.

Dalia Essam Eissa et al had seen a significant difference among the four groups regarding cumulative morphine consumption over 48 hours.[1] The placebo group and group receiving 5 mcg/kg diamorphine had the higher morphine consumption for 48 hours (102±13 mg and 42 ± 9 mg respectively) compared with patients in other two groups i.e. 10 mcg/kg and 15 mcg/kg diamorphine where morphine consumption was 20 ±6 mg and 17±4 mg respectively. These results were similar to our study that high dose ITM 0.3 mg resulted in low morphine PCA consumption in 24 hours postoperative.

The patient satisfaction in group B was much higher than in group A. In all the above quoted studies, we had seen that use of ITM results in lower pain scores with higher patient satisfaction.

Hemodynamic parameters (HR, SBP, DBP, RR and SpO_2) were within the normal limit during the entire 24 hour postoperative period. There was no occasion when the RR was < 10/min or oxygen saturation was < 93% in either group.

The incidence of nausea, vomiting and pruritus was comparable in both the groups. The sedation score was higher in group B as compared to group A. However, we have not seen a clinically significant sedation score of 6 in any of the patient.

CONCLUSION

Intrathecal morphine is a simple, safe, reliable technique that provides very good postoperative analgesia in patients after posterior lumbar spine surgery. Side effects like sedation and respiratory depression could be minimized by using appropriate dose of ITM and minor side effects like nausea. vomiting and pruritus could be managed by inj. ondansetron. The present study found that single shot of 0.3 mg ITM provided superior analgesia with higher patient satisfaction without increase in the side effects as compared to 0.2 mg morphine. A larger study would be required to confirm the suggestion of 0.3 mg ITM as highly efficient analgesic with minimal side effects after posterior lumbar spine decompression and instrumentation surgery.

Limitations

- Small sample size
- Inter patient pain threshold variability
- No exact record of pre-operative analgesia was kept. However, no patient was on any long acting analgesic preparation.
- Exact time of first use of rescue analgesia could not be determined as PCA pump was used.

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