ORIGINAL ARTICLE

The effect of intravenous dexamethasone on postoperative pain, nausea and vomiting after intrathecal pethidine and bupivacaine in lower limb orthopedic surgery

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ABSTRACT

Background: Intrathecal pethidine provides excellent post-operative analgesia but is associated with significant nausea, vomiting and other side effects. Present study was done to evaluate the efficacy of intravenous dexamethasone to enhance post-operative analgesia and to reduce the side effects.

Methodology: In this prospective, randomized, double blind, placebo controlled study a total of 80 patients of American Society of Anesthesiologists (ASA) grade I and II, undergoing elective lower limb orthopedic surgery under sub-arachnoid block were randomized into two groups. Group C (n=40) received 2 ml saline (as placebo) and Group D (n=40) received 0.1 mg/kg dexamethasone intravenously as a bolus before intrathecal anesthesia. In all patients spinal anesthesia was administered with 15 mg bupivacaine and 15 mg pethidine. After surgery, patients were asked to score their pain at 2, 4, 6, 12, 18 and 24 hr by VAS score. The presence of post-operative nausea vomiting (PONV), pruritus and respiratory depression were recorded and compared between the two groups.

Results: The pain score on Visual Analogue Scale (VAS) at 6, 12, 18, 24 hours after surgery, mean number of rescue analgesic doses in 24 hours and the incidence of PONV were significantly lower ($p<0.05$) in dexamethasone group (Group D).

Conclusion: Administration of intravenous dexamethasone (0.1 mg/kg) just before subarachnoid block is an effective mode of enhancing post-operative analgesia with intrathecal pethidine and it reduces incidence of PONV.

Key words: Meperidine (Pethidine); Dexamethasone; PONV; Visual Analogue Pain Scale; Adjuvants, Anesthesia; Assessment, Pain

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INTRODUCTION

Acute pain after orthopedic surgery is the result of tissue injury.[1] Multimodal analgesia is a multidisciplinary approach to pain management. The main aim of multimodal analgesia is to obtain synergistic or additive analgesia, which can be achieved by administering a lower dose of each drug resulting in improved safety and less side effects. This can be achieved by combining analgesics acting at different sites on the pain pathways.[2]

Adjuvants like opioids are sometimes combined with local anesthetics in subarachnoid block to lower the dose of anesthetic agent and to maintain or enhance the analgesic efficacy but it may be associated with side effects. Intrathecal pethidine has good analgesic and local anesthetic effects. Side effects associated with intrathecal pethidine are bradycardia, hypotension, nausea, vomiting, pruritus, sedation

and respiratory depression.[3] Various comparative studies have shown that the incidence of these side-effects are greater with pethidine compared to conventional local anesthetics although this may be dose-dependent.[4,5]

Many drugs like antihistaminics,[6] 5-HT_3-receptor antagonists (e.g. ondansetron, granisetron),[7] opiate-antagonists (e.g. naloxone),[8] pentazocine,[9] dexamethasone,[10] low dose propofol,[11] nonsteroid anti-inflammatory drugs[12] and droperidol[13] have been used to diminish these side effects.

In this study, we evaluated the effect of intravenous dexamethasone on post-operative analgesia, incidence of nausea and vomiting, pruritus and other side effects in patients receiving intrathecal pethidine as an adjuvant.

METHODOLOGY

This prospective, randomized, double-blind, study was conducted in anesthesiology department of a tertiary care hospital. The study included 80 patients of ASA Grade I and II, age 20-50 years, body weight 50-80 kg, who underwent elective orthopedic surgery on lower limbs. Prior ethical permission was taken from the institutional ethical committee and review board.

Patients who had any deformity or local pathology in lumbar spine region, history of convulsions, allergy to the drugs used, bleeding disorders, motion sickness, PONV or addiction, were uncooperative and with severe neurological deficit, were excluded from the study. Patients with severe hypovolemia, anemia, receiving steroid medication and patients, in whom spinal anesthesia failed and general anesthesia was required, were also excluded from the study.

Preanesthetic check-up was done on the day before surgery, and included a complete history and any known drug allergy, general and systemic examination and local examination of lumbar spine region. Pulse rate, blood pressure, respiratory rate, and weight and height of the patient were noted. Relevant investigations were done in all the patients.

Informed consent was obtained for performance of sub-arachnoid block after complete explanation about the study protocol and the procedure. Visual Analogue Scale (VAS) 0-10 was also explained to the patient.

The patients were randomized on the day of surgery into two groups of 40 each. Eighty pieces of paper, 40 with 'saline' written on them and 40 with 'dexamethasone' written were put in a box and the patients were asked to pick one piece of paper. This piece of paper was handed to an anesthesiologist unconnected to the study who prepared the medications. Group D patients received 0.1 mg/kg (maximum 8 mg) dexamethasone intravenously diluted to 2 ml in distilled water and the Group C patients received 2 ml normal saline intravenously (as placebo) just before intrathecal anesthesia.

On arrival in the operating room, fasting status (at least for 6 hours), and written consent was checked. Intravenous access with 18G cannula was secured and patients were preloaded with Ringer's Lactate 10 ml/kg. All routine monitors were attached and preoperative baseline readings of NIBP, HR and oxygen saturation were noted. Spinal anesthesia was performed at L3-L4 interspace with 0.5% 15 mg hyperbaric bupivacaine and 15 mg of preservative free pethidine using the midline approach. Total volume of intrathecal drugs in both groups was 3.3 ml which was injected over 30 seconds with the patient in sitting position using a 25G Quincke spinal needle. Patient was placed in supine position immediately after spinal injection to achieve level of block of T_8-T_{10}. Intraoperative fluid management was done according to the blood loss and hemodynamic parameters.

After surgery patients were shifted to the recovery room. The severity of post-operative pain was measured and recorded using a 10 point VAS. Patients were asked to score the pain both at rest or during movement at 2, 4, 6, 12, 18, and 24 hours after surgery.

Intravenous 75 mg diclofenac sodium was given as rescue analgesic on patient demand. Total duration of analgesia was defined as the time from intrathecal drug administration to the patient's first request for rescue analgesia either in the recovery room or on the ward, and was recorded in minutes.

Nausea was defined as a subjectively unpleasant sensation associated with awareness of the urge to vomit. The incidence and severity of nausea was evaluated by a four point scale where 0 was no nausea, 1 mild 2 moderate and 3 was severe nausea.

Vomiting was defined as rhythmic contractions of the abdominal muscles with or without expulsion of gastric contents from the mouth (i.e. including retching). The number of vomiting episodes were recorded. Patients experiencing persistent nausea score of more than 1 or those who had one or more

vomiting episodes received injection Ondansetran 0.1 mg/kg intravenously as rescue antiemetic medication.

Pruritus was defined as the subjective unpleasant skin sensation that frequently provoked scratching. It was measured on a four point categorical scale. Injection diphenhydramine 25 mg intramuscularly was prescribed for itching.

Sedation was evaluated by Ramsay sedation scale.

Urinary retention was defined as the inability to voluntarily void urine.

Patients were asked to report any adverse event (e.g. nausea, vomiting, urinary retention etc.) to the nursing staff during the following time periods 0–3, 3–6, 6–12, and 12–24 h,

Statistical analysis: Sample size was calculated at 95% confidence level, 80% study power and α- error of 0.05 assuming S.D. of 2.132 as per the results of previous study. For the minimum detectable difference of one in VAS score at 6 hours after surgery appropriate sample size required for the study was 35 patients in each group. This was enhanced to 39 patients assuming 10% dropout rate and rounded about to 40 patients in each group.

Statistical analysis was performed with SPSS, version 21.0, for Windows Statistical Software Package (SPSS inc., Chicago, IL, USA). Descriptive values were expressed as mean ± SD or number. The Student t-test was used for comparison between means of continuous variables and normally distributed data, proportions were compared using Chi-squared or Fisher's exact test as appropriate otherwise Mann-Whitney U test was used. P value < 0.05 was considered significant.

RESULTS

The mean age, body weight, height, ASA grading and duration of surgery were similar in both the groups with no statistical significant difference. (P > 0.05)(Table 1).

The median VAS pain scores at 2 hours and 4 hours were comparable(p > 0.05) between groups whereas at 6, 12, 18 and 24 hours the difference was statistically significant (Table 2).

The duration of analgesia and requirement of rescue analgesic was significantly lower in dexamethasone group than the control group (Table 3 & 4).

The incidence of nausea, vomiting, pruritus and urinary retention was significantly lower in Group D. Bradycardia and hypotension were statistically insignificant in between groups (Table 5).

Table 1: Demographic data (mean ± SD)

Variables	Group D (n=40)	Group C (n=40)	P value	Significance
Age(years)	35.08 ± 8.071	35.20 ± 7.753	0.944	NS
Weight(kg)	60.75 ± 8.714	61.00 ± 8.061	0.894	NS
Height(cm)	157.1 ± 7.88	158.3 ± 6.42	0.761	NS
ASA(I/II)	36/4	33/7	0.33	NS
Duration of surgery (min)	71.70±19.75	64.18±17.17	0.073	NS

n = number of patients, group C = control group, D = Dexamethasone group, ASA = American Society of Anesthesiologists, SD = standard deviation, S = significant, NS = Not significant

Table 2: VAS score at different time points

Group	VAS Score						ANOVA	p value
	2 Hours	4 Hours	6 Hours	12 Hours	18 Hours	24 Hours		
Group D	0.74 ± 0.59	1.96 ± 0.94	3.96 ± 1.64	4.12 ± 1.59	3.20 ± 1.38	1.613 ± 0.74	50.54	.000
Group C	0.69 ± 0.58	2.21 ± 0.70	5.90 ± 1.49	5.11 ± 1.57	4.52 ± 1.43	2.30 ± 1.81	109.32	.000
Mann Whitney U Value	758.500	672.000	276.500	466.000	414.500	518.000		
p value	0.68	0.20	<0.001	0.001	<0.001	0.006		

n = number of patients, group C = control group, D = Dexamethasone group, SD = standard deviation

Table 3: Duration of analgesia (mean ± SD)

Variables	Group D (n=40)	Group C (n=40)	P value	Significance
Duration of Analgesia(min)	499.00 ± 173.79	352.70 ± 69.97	<0.001	S
Onset of sensory block (mins)	7.75 ± 0.89	7.50 ± 0.72	0.173	NS
Onset of motor block(mins)	9.70 ± 1.42	9.25 ± 1.27	0.140	NS
Two segment regression (mins)	102.78 ± 12.361	89.88 ± 10.309	<0.001	S
Duration of motor block (mins)	110.40 ± 8.84	112.38 ± 9.43	0.337	NS

n = number of patients, group C = Control group, D = Dexamethasone group, SD = standard deviation, S = significant, NS = Not significant

Table 4: Comparison of number of rescue analgesic doses between the two groups

Group	Number of rescue analgesic doses				
	0	1	2	3	
Group D	1	26	13	0	$X^2 = 45.789$
Group C	0	0	25	15	$p \leq 0.001$

Table 5: Comparison of post- operative complications between the two groups

Complication	Group D N = 40	Group C N = 40	X^2 Value	P Value
Nausea	0	12 (30)	14.118	<0.001
Vomiting	0	10 (25)	11.429	0.001
Pruritus	0	8 (20)	8.889	0.003
Urinary Retention	0	7 (17.5)	4.622	0.032
Hypotension	2 (5)	1 (2.5)	0.346	0.556
Bradycardia	3 (7)	4 (10)	0.157	0.692

There was no incidence of respiratory depression in any patient.

Degree of sedation was statistically insignificant in between groups (Table 6).

DISCUSSION

Pethidine was the first synthetic opioid which was used to provide analgesia in humans.[3] Pethidine when added to local anesthetics in spinal anesthesia, prolongs the duration of analgesia, thus allowing better post-operative patient comfort and decreasing post-operative systemic analgesic consumption.[14] However, the incidence of side-effects is greater with pethidine compared with the other commonly used intrathecal opioids. The incidence of side-effects is less when the dose is limited to 0.5 mg/kg.[3] In our study we used a dose of 15 mg in both the groups.

A multimodal approach is the current and preferred concept of acute and chronic pain management for enhancing analgesia and minimizing adverse effects. Intravenous dexamethasone attenuates the post-operative need for analgesics in different clinical settings including orofacial, general, urological, and orthopedic surgeries.[15] The mechanism of analgesia induced by dexamethasone is not well understood. It is presumed to be mediated by anti-inflammatory or immune-suppressive effects of dexamethasone. Cell membrane injury during surgical trauma releases phospholipids which are degraded by a chain reaction leading to production of different pro-inflammatory mediators. Steroids inhibits this chain reaction and reduce the levels of prostaglandin E_2 and are effective in controlling inflammation and post-operative pain.[16] Waldron *et al* performed a meta-analysis involving 45 studies to evaluate the impact of a single i.v. dose of

Table 6: Ramsay Sedation Assessment Scale

Degree of Sedation	Group D N (%)	Group C N (%)
Anxious, agitated or restless	-	-
Cooperative, oriented and tranquil	27 (67.5)	32 (80)
Responsive to commands	13 (32.5)	8(20)
Brisk response to light glabellar tap	-	-
Sluggish response to light glabellar tap		
Asleep, no response		
X^2 value	$X^2 = 1.61$	
p value	0.20	

dexamethasone on post-operative pain and adverse events associated with this treatment. They found that perioperative single-dose dexamethasone was associated with small but statistically significant reductions in post-operative pain, post-operative opioid consumption, need for rescue analgesia and less stay in post anesthesia care unit.[17]

In another meta-analysis, De Oliveira et al. concluded that preoperative administration of dexamethasone appeared to produce a more consistent analgesic effect compared with intraoperative administration. They found that Dexamethasone at a dose of more than 0.1 mg/kg is an effective adjunct in multimodal strategies to reduce post-operative pain and opioid consumption after surgery.[18] In our study we obtained significant results with 0.1 mg /kg of dexamethasone.

The mechanism of the antiemetic action of dexamethasone is still not clearly known. Glucocorticoid receptors are present in the nucleus of the solitary tract, the raphe nucleus, and the area postrema. They help in regulation of nausea and vomiting. Dexamethasone may be effective in management of PONV by modulating neurotransmission or receptor density in these nuclei. Wang *et al* evaluated the effect of timing of dexamethasone administration on its efficacy as a prophylactic antiemetic on post-operative nausea and vomiting and found that dexamethasone, when given immediately before the induction of anesthesia, was more effective than when given at the end of anesthesia.[19] In our study we administered dexamethasone intravenously just prior to administration of spinal anesthesia and found that none of the patient suffered from nausea or vomiting in dexamethasone group.

Movafegh *et al*. found that the administration of intravenous dexamethasone prior to intrathecal pethidine injection reduces post-operative pain, nausea, and vomiting.[20] Our results are similar to their study. We found that VAS pain scores and the number of rescue analgesic doses were significantly reduced in dexamethasone group.

In our study, we found significant delay in two-segment regression time in dexamethasone group. A significant number of cases suffered from post-operative urinary retention in control group.

CONCLUSION

To conclude, our study shows that the administration of intravenous dexamethasone with intrathecal pethidine significantly prolonged post-operative analgesia and reduced the incidence of post-operative nausea, vomiting, pruritus and urinary retention as compared to the control group.

Conflict of interest: None declared by the authors.

Authors' Contribution :

1. SK: Concept, conduction of study work and manuscript editing
2. FA: Concept, conduction of study work and manuscript editing
3. AP: Concept, conduction of study work
4. MK: Manuscript editing
5. TM: Manuscript editing

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