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Comparison of Intrathecal Bupivacaine with or without Buprenorphine for Postoperative Pain Relief in Caesarean Section

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Abstract
Background: *Intrathecal route of administration has the advantage of greater technical ease, lower dose requirement and more selective analgesia. Intrathecal Bupivacaine with Buprenorphine seems to be an ideal combination of this purpose. This study was conducted to compare the effects of intrathecal Bupivacaine alone and its combination with Buprenorphine to assess the extent of postoperative pain relief in caesarean section patients.*
Materials and Methods: *Fifty patients were divided into two groups of twenty-five each. Group I received 10 mg of 0.5% heavy Bupivavacine with 1μg/kg of preservative free Buprenorphine upto a maximum of 60 μg intrathecally and Group II received 10 mg of 0.5% heavy Bupivacaine alone intrathecally.*
Statistical Analysis used: *To compare the statistical difference in various parameters, the arithmetic mean and standard deviation were calculated. The comparison between the two groups were accomplished using the student's two sample "t" test.*
Results: *The onset of analgesia was considerably shorter in Group I than Group II. The duration of postoperative analgesia was significantly longer in Group I than in Group II. No major side effects or respiratory depression were observed in the study. However the mild side effects observed such as drowsiness, nausea and vomiting raise an element of caution.*
Conclusion: *From the present study it is evident that intrathecal Buprenorphine in a dose of 1 μg/kg in combination with Bupivacaine offers a simple, inexpensive, effective and safe means of good quality postoperative analgesia.*
Keywords: *Bupivacaine , Buprenorphine, Postoperative analgesia, Intrathecal, Caesarean.*

Introduction

Pain relief is a basic human right and failure to relieve pain is morally and ethically unacceptable. Inadequate post operative analgesia has an adverse physiological impact leading to increased postoperative morbidity. Postoperative pain can be a major cause of fear and anxiety in hospitalized patients and when prolonged it can lead to anger and insomnia[1].

Post operative pain is unique by its transitory nature, which makes it amenable to therapy. The identification of spinal cord receptors and neuraxial administration of opioids has revolutionized the concept of intraoperative and postoperative pain relief. Opioid receptors are present in great concentration in the dorsal horn of spinal cord lamina I and II; Lamina II being the substantia gelatinosa. Direct application of opioids

to these receptors produces intense analgesia[2]. Intrathecally administered opioids act through the inhibition of release of Substance P, a neuro transmitter substance responsible for relaying nociceptive impulses[3].

Intrathecal opioids have the special advantage of producing excellent analgesia with minimal systemic adverse effects. The main advantage of selective blockades by spinal opioids- both intrathecal and epidural, is the absence of sympathetic blockade and postural hypotension in the background of excellent analgesia[4]. Buprenorphine with its high lipid solubility, high affinity for opioid reception and prolonged duration of action makes it a suitable choice for intrathecal administration.

In this study, the effects of intrathecal Bupivacaine with or without Buprenorphine were compared for postoperative pain relief in caesarean section patients.

Aims

To compare the adequacy of postoperative pain relief in caesarean section patients after intrathecal administration of Bupivacaine with or without addition of preservative free Buprenorphine.

Primary objectives

To compare the postoperative pain relief parameters after intrathecal administration of Bupivacaine with or without addition of preservative free Buprenorphine with regard to the onset of analgesia and the duration of analgesia.

Secondary objectives

To compare intrathecal administration of Bupivacaine with or without addition of preservative free Buprenorphine with regard to possible incidence of side-effects.

Materials and Methods

The study has taken place at Government Medical college Hospital, Alappuzha. Pregnant patients aged 40 years or less, ASA grade I/II, with weight upto 60kg, undergoing elective Caesarean section surgery under spinal anesthesia were eligible. Exclusion criteria included patient refusal, history of drug allergy, surgeries lasting more than 2 and half hours and patients with serious co-morbidities like hypertension, diabetes, bronchial asthma, epilepsy.

Design of study

A double blinded randomised control trial with a sample size of 50 allocated into two groups of 25 each is performed. Group I receives 10mg (2ml) of 0.5% heavy Bupivacaine with 1 µg/kg of preservative free Buprenorphine up to a maximum of 60 µg intrathecally. Group II receives 10mg (2ml) of 0.5% heavy Bupivacaine alone intrathecally. Two anaesthesiologists assisted by an experienced anaesthesia assistant are present throughout the procedure. This study involves the blinding of the drug administrator and anaesthesiologist performing the procedure.

A thorough history and clinical examination of the patient is conducted. All solid and liquid foods are restricted for upto 6 hours before surgery. Oral premedication of Tab Ranitidine 50mg and Tab metoclopramide 10mg are given 1 hour prior to surgery. The anaesthesia machine is checked. The intubation cart with all emergency intubation equipment is kept ready. The drug cart is kept ready. The patient vitals are checked.

All patients are brought to the theatre in left lateral position. An intravenous access is obtained with Normal Saline using 18 gauge IV canula. ECG, pulse oximeter, and non invasive blood pressure monitors are attached. Additionally, foetal heart sounds monitoring was also done. Under strict aseptic precautions, lumbar subarachnoid block was performed by a median approach at the L_{3-4} interspace using a 25 gauge spinal needle. After the subarachnoid injection, patients were turned to supine position and a 10cm height wedge was placed under the right buttock. Vitals are checked and noted at five minute intervals.

The onset of analgesia was noted as loss of pain to pinprick. The duration of surgery was noted and time of completion of surgery was taken as the postoperative zero hour. Postoperatively the pulse rate, blood pressure and respiratory rate were monitored every 15 minutes for a period of 2

hours in the recovery room and thereafter every 2 hours in the postoperative ward for 24 hours. The duration of postoperative analgesia was calculated as the time interval between the completion of surgery to the appearance of discomfort due to pain (score-2). Systemic analgesics (Inj Diclofenac sodium 50mg/ Inj Tramadaol 50mg) were administered when the patients complained of pain.

Assessment

The efficacy of postoperative analgesia was evaluated using the McGill's Scoring system. According to this Subjective rating scale;

Score	Quality of analgesia
0	No pain
1	Slight pain
2	Discomfort due to pain
3	Unbearable due to pain
4	Excruciating pain

Postoperative incidences of side effects were closely watched for. Patients who had severe nausea and/or vomiting were treated with Inj metoclopramide 10 mg IV. Urinary retention could not be assessed as bladder catheterization was performed in all patients. Patients were closely monitored for the appearance of postoperative drowsiness, pruritis and for respiratory depression.

Statistical analysis used

The arithmetic mean and standard deviation of the various parameters were calculated. The comparison between the two groups were accomplished using the student's two sample "t" test. Whenever applicable, a p value <0.05 was considered to be significant.

Results

Two groups of 25 each were labeled as Group I (10mg of 0.5% heavy Bupivacaine with 1 µg/kg of preservative free Buprenorphine) and Group II (10mg of 0.5% heavy Bupivacaine alone). The mean and standard deviation of the patients age and weight were calculated between the two groups and were charted as shown below. It was concluded that the age and weight among the two groups were comparable and these factors did not have any influence on outcome.

Table 1: Age distribution of patients

Age group (in years)	Group I (study)		Group II (control)	
	Number	Percentage (%)	Number	Percentage (%)
20-25	8	32	7	28
26-30	15	60	17	68
31-35	2	8	1	4
36-40	0	0	0	0
Mean	26.52		26.88	
Standard Deviation	2.58		2.74	

t=0.478 p=0.635

Table 2: Weight distribution of patients

Weight (kg)	Group I (study)		Group II (control)	
	Number	Percentage (%)	Number	Percentage (%)
40-44	0	0	2	8
45-50	4	16	3	12
51-55	8	32	9	36
56-60	13	52	11	44
Mean	55.60		54.28	
Standard Deviation	4.03		5.17	

t=1.007 p=0.319

The mean time of onset of analgesia between the two groups is compared and charted as shown below. The mean score of Group I was 2.84 minutes and Group II was 4.80 minutes. Applying the student's t test, a p value of <0.001 was

obtained indicating that the difference was statistically significant.

Table 3: Onset of analgesia

Onset of analgesia (min)	Group I (study)		Group II (control)	
	Number	Percentage (%)	Number	Percentage (%)
0-2	9	36	0	0
3-5	16	64	16	64
6-8	0	0	9	36
Mean	2.84		4.80	
Standard Deviation	0.75		1.61	

t=5.530 p< 0.001

The mean duration of analgesia between the two groups is compared and charted as shown below. The mean score of Group I was 14 hours and Group II was 4.12 hours. Applying the student's t test, a p value of <0.001 was obtained indicating that the difference was statistically significant.

Table 4: Duration of Postoperative analgesia

Duration of postoperative analgesia (hours)	Group I (study)		Group II (control)	
	Number	Percentage (%)	Number	Percentage (%)
0-3	0	0	8	32
4-6	1	4	17	68
7-12	8	32	0	0
13-18	14	56	0	0
19-24	2	8	0	0
Mean	14		4.12	
Standard Deviation	3.55		1.27	

t=13.112 p< 0.001

The mean efficacy of analgesia during the 24 hour postoperative period between the two groups is compared and charted as shown below. Applying the student's t test, a p value of <0.001 was obtained indicating that the difference was statistically significant.

Table 5: Efficacy of Analgesia (during 24 hour postoperative period)

Maximum Pain Score attained over 24 hours	Group I (study)		Group II (control)	
	Number	Percentage (%)	Number	Percentage (%)
0	0	0	0	0
1	20	80	5	20
2	4	16	5	20
3	1	4	13	52
4	0	0	2	8

p< 0.001

Ten patients in the study group had drowsiness in the postoperative period. None developed pruritis. None developed respiratory depression. In the control group no side effects were seen.

Table 6: Side effects

Side effects	Group I (study)		Group II (control)	
	Number	Percentage (%)	Number	Percentage (%)
Nausea	2	8	0	0
Vomiting	2	8	0	0
Pruritis	0	0	0	0
Drowsiness	10	44	0	0
Respiratory depression	0	0	0	0

Discussion

Clinical observations have clearly indicated that opioids and local anesthetics administered

intrathecally have synergistic effect[5]. The intrathecal route of administration has the advantage of greater technical ease and single injection produces pain relief of longer duration. Buprenorphine, because of its high lipid solubility, high affinity for opioid receptors and prolonged duration of action is a suitable choice for intrathecal administration.

Studies on tissue compatibility have proved that Buprenorphine may be safely administered intrathecally with Bupivacaine[6]. Dr Kaur and colleagues conducted a similar study where the mean onset of analgesia was 2.37 minutes in the study group and 6.73 minutes in the control group[7]. Capnoga et al used two doses of intrathecal Buprenorphine; patients who received 30 µg Buprenorphine had duration of postoperative analgesia of 5-8hours; while patients who received 45 µg Buprenorphine had 7-12 hours[8]. The addition of intrathecal Buprenorphine might potentiate the analgesic effect of intrathecal Bupivacaine both by its spinal and supraspinal analgesic effects[9].

Early respiratory depression occurring in the first 2hours following spinal administration is the result of vascular uptake and distribution. Delayed respiratory depression occurring 6-12 hours later is due to rostral spread of opioids in the CSF. It is gradual in onset and reversible with small doses of naloxone[10]. A global assessment is necessary which includes the assessment of the level of consciousness, since increasing sedation has been noted with advanced respiratory depression[11]. The etiology of prutitis is unclear, but its occurrence appears unrelated to direct opioid induced histamine release, as the peak onset occurs 3-6 hours after administration[12]. Nausea and vomiting following spinal opioids could be due to the modulation of the afferent input at the area postrema or at the nucleus of the tractus solitarius[13].

Being a lipophilic opioid the onset of action of Buprenorphine is faster and the duration of action is dose dependant[14]. Besides the clinical benefits of reduced systemic morbidity, sufficient post operative analgesia will reduce hospital stay and decrease the need for intensive care management after surgery, both having implications on cost reduction[15].

Conclusion

The present study proves that the addition of Buprenorphine to intrathecal Bupivacaine hastens the onset of analgesia. The duration of analgesia is prolonged as well with this combination. No major side effects or respiratory depression were observed in this study. However mild side effects like drowsiness, nausea and vomiting did raise an element of caution. From the present study it is evident that intrathecal Buprenorphine in a dose of 1 µg/kg in combination with Bupivacaine offers a simple, inexpensive, effective and safe means of a good quality post operative analgesia.

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