Original Article

# Comparative study between bupivacaine heavy vs pethidine intrathecally to study early haemodynamic changes and postoperative analgesia in patients undergoing caesarean section

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#### Abstract

**Objective**: To study early hemodynamic changes and duration of postoperative analgesia between two study groups of intrathecal pethidine and bupivacaine heavy in patients undergoing caesarean section.

**Methodology:** Total number of 60 patients of ASA I and II, undergoing caesarean section were enrolled in the study. All the patients were divided into two groups: Pethidine and Bupivacaine heavy. The dose of pethidine for subarachnoid block was 1mg/kg and in Bupivacaine group 2.2ml of 0.5% bupivacaine heavy was given intrathecally. Heart rate and blood pressure of all the patients were recorded before subarachnoid block. After giving spinal anesthesia, the heart rate and blood pressure were monitored and recorded in different time intervals. The duration of postoperative analgesia in all patients was recorded in postoperative ward. The APGAR Scores of the babies were recorded in 1 and 5 minutes after delivery. The data were statistically compared using independent sample t-test.

**Conclusion:** The hemodynamic parameters (HR & BP) were compared in different time intervals. The difference in heart rate and blood pressure at different time intervals in the two study groups were statistically insignificant as (p > 0.05). The total duration of postoperative analgesia in patients receiving sole intrathecal pethidine was 8 hours and 30 minutes. Where as, in Bupivacaine group the duration was 2 hrs and 36 minutes. This has been found statistically significant (p<0.05).

Lack of information about the analgesic drugs, misconception about their potency, duration of action, side effects are the main reasons for inadequate postoperative pain management because of which patients continue to experience pain in postoperative ward.

The analgesic effect of opioid is due to binding to specific opiate receptors. With the discovery of opioid receptors in the spinal cord, postoperative pain management has taken on a new dimension. Intrathecal opioid are well established in the management of postoperative pain. In recent years, interest has been directed towards use of pethidine as a sole anesthetic agent intrathecally. Weak local anesthetic effects have been demonstrated for fentanyl and sufentanil<sup>1</sup> Pethidine differs from the other opioid in that it possesses considerable local anesthetic properties <sup>2, 3</sup>

In recent studies, pethidine compared favorably with both bupivacaine and lidocaine as the sole anesthetic agent, providing excellent conditions for lower abdominal and pelvic surgery <sup>4, 5</sup>. The side effects of pethidine in spinal anesthesia are pruritus nausea vomiting and respiratory depression <sup>6, 7, 8</sup>. A dose of 1 mg/kg intrathecal pethidine provides surgical anesthesia<sup>7,9,10</sup>.

#### Methodology

#### **Patient** selection

Sixty ASA-1 patients scheduled for LSCS were included in this randomized study after informed consent. Patients were allocated randomly into two grous: Bupivacaine group (n=30) and pethidine group (n=30). All patients in bupivacaine group received bupivacaine heavy 2.2ml and in pethidine group, pethidine 1mg/kg was given intrathecally.

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## <u>Anaesthetic Technique</u>

All patients were premedicated with inj. Ranitidine 50mg and inj. Metoclopramide 10mg intravenously before surgery. Once monitors were applied and intravenous access achieved, the lumbar area was aseptically prepared and draped with the patients in sitting position. A 25 gauze Quincke's needle was used to perform the lumbar puncture at the L3-L4 interspaces. The study solution was administered into the subarachnoid space slowly over 20sec intrathecally when patient was not complaining of pain of uterine contraction. Following injection patients were placed in supine position with the 15 degree left lateral tilt of OT table. The heart rate and the blood pressure were recorded in different time interval of 1, 2, 4, 6, 8, 10, 12, 14, 16, 18 and 20 minutes. The sensory level was checked and when it was at around T6 level surgery was allowed to proceed.

The administration of fluid, vasopressors, atropine in all patients was recorded in both groups. If extra analgesics or sedation were used during intraoperative period that were recorded and those patients who received extra analgesics were excluded from the study. The APGAR scores of babies were recorded at 1min and 5min. after the caesarean delivery. At the end of surgery the patients were transferred to the postoperative ward and the possible side effects (nausea, vomiting, pruritus, respiratory depression) were monitored and recorded if any. The duration of postoperative analgesia was noted when patients first demanded analgesia on request.

#### Patient monitoring and evaluation

All patients were monitored with NIBP, SPO2, ECG, pulse, heart rate and respiratory rate which was extended beyond the operating room. The attending anesthesiologist and the nurse assessing the patients after surgery were blinded to the study groups.Patient's demographic data, sensory and motor block onset were also recorded. Demographic parameters, the hemodynamic parameters and duration of analgesia in two groups were compared using t- test.

## **Objectives**

The objectives of the present study were to determine the hemodynamic effects of intrathecal pethidine and bupivacaine and to determine the postoperative analgesia in two study groups.

## Exclusion criteria

History of Coagulopathy Pre eclampsia and eclampsia Valvular heart disease (mitral stenosis or aortic stenosis) Infection at the site of needle puncture If patient denies for subarachnoid block Ineffective subarachnoid block or when extra

analgesics were given intra operatively

## Statistical method

Independent sample t-test

## Results

Thirty patients were studied in each group. The two groups were similar with respect to age and weight (table 1). The baseline hemodynamic data were also similar in two groups (table 4, 5, 6)

The baseline heart rate (mean) in bupivacaine group was 86.8 beats per minute and in pethidine group was 88.85 beats per minute.

The speed of onset of sensory block in two groups was not different statistically (p=0.723). The hemodynamic effects of subarachnoid block were studied in all patients in two study groups. The heart rate in patients receiving intrathecal pethidine was not different statistically from the baseline value (p>0.05). The difference in heart rate in two study groups at different time intervals was not significant statistically (p>0.05). The systolic and diastolic blood pressure in two study groups at different time intervals were not significant statistically (p>0.05). The mean duration of analgesia in bupivacaine group was 159 min and in pethidine group it was of 510 minutes. The difference of analgesia duration in the two study group is statistically significant (p<0.05). The APGAR scores in 1 minute and 5 minute in the twp study groups were insignificant statistically (p>0.05) (Table 2).

Table 1: Mean age (year) & body weight (kg) of patients in each group

Groups	Age (mean)	Weight (mean)	P value
Bupivacaine	$25.70 \pm 3.47$	65.48 ± 10.21	0.65
Pethidine	$26.25\pm5.51$	65.55 ± 11.09	0.98

**Table 2:** Pre load, total fluid infused intra operatively, onset of sensory effect, Apgar score at 1min and 5min and the total vasopressors used intra operatively in the two study groups

	Pre load	Total fluid	Sensory effect	APGAR 1min	APGAR 5min	Vasopressors used
Bupivacaine	307.40	1683.33	$3.44 \pm 1.67$	$7.59 \pm 1.08$	$9.22 \pm 1.0$	5.59 ±7.49
	±141.21	±284.53				
Pethidine	266.66	1685.18	3.59 ±1.36	7.49 ±0.9	8.25 ±0.69	5.62 ±7.47
	$\pm 128.60$	±314.64				
p- value	0.27	0.98	0.723	0.1	0.75	0.98

 Table 3: Postoperative and intra operative complications in each study group

Variables	Nausea	Vomiting	Pruritus	Respiratory depression	Hypotension	Urinary retention	Bradycardia
Bupivacaine	1	2	_	—	6	Catheter in situ	1
Pethidine	3	3	6	—	4	Catheter in situ	1

Table 4: Changes in heart rate at different time intervals following sub arachnoid block in the two study groups.

	Base	HR1	HR2	HR4	HR6	HR8	HR10	HR12	HR14	HR16	HR18	HR20
	line HR											
Bup grp	86.88 ±13.67	98.00 ±25.03	93.88 ±16.71	88.66 ±18.12	87.22 ±14.44	83.96 ±13.01	84.62 ±14.62	81.85 ±16.52	85.29 ±17.65	90.37 ±15.1	87.74 ±13.59	89.77 ±12.16
Peth grp	88.85 ±13.08	89.59 ±18.00	82.81 ±19.09	81.55 ±15.58	76.66 ±15.79	80.70 ±16.00	82.16 ±13.43	83.59 ±17.43	87.74 ±19.51	92.40 ±19.36	90.29 ±17.81	91.25 ±16.94
p- value	0.59	0.163	0.02	0.12	0.01	0.41	0.33	0.70	.63	0.66	0.55	0.71

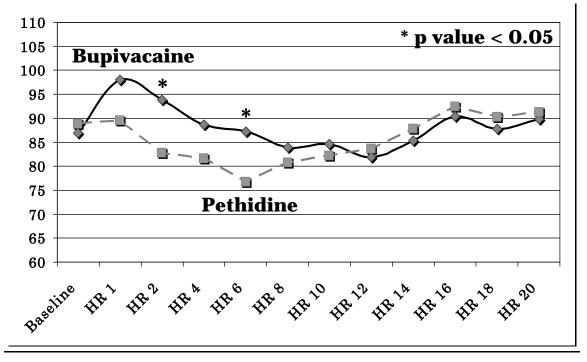
	Baseline	SBP										
	SBP	1min	2min	4min	6min	8min	10min	12min	14min	16min	18min	20min
Bup	127.74	117.66	106.88	104.77	106.25	107.33	109.72	110.48	109.92	112.55	112.18	109.62
Grp	±17.56	±21.80	±20.63	±15.70	±10.94	±10.07	±9.22	±13.80	±11.73	±14.20	±14.84	±12.00
Peth	128.18	114.96	106.81	103.97	108.66	111.37	113.77	112.40	110.77	108.88	111.37	110.07
Grp	±16.78	±19.74	±20.18	±17.50	±16.70	±14.85	±15.10	±14.27	±14.48	±13.28	±13.09	±13.40
p- value	0.92	0.63	0.98	0.85	0.53	0.24	0.24	0.61	0.81	0.33	0.83	0.89

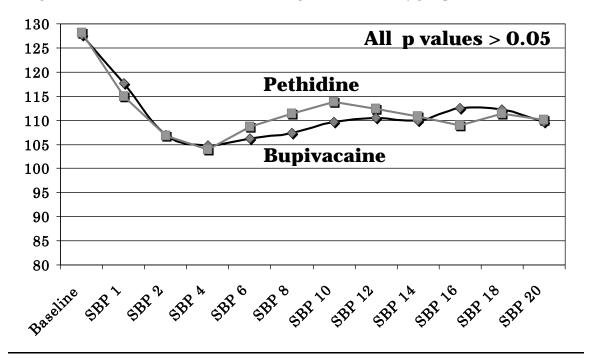
**Table 5:** Changes in systolic blood pressure at different time intervals following sub arachnoid block in the 2 study groups.

**Table 6:** Changes in diastolic blood pressure at different time intervals following subarachnoid block in the two study groups.

	Baseline	DBP										
	DBP	1min	2min	4min	6min	8min	10min	12min	14min	16min	18min	20min
Bup	77.74	60.74	68.29	63.77	60.14	61.55	60.55	62.07	62.00	61.96	62.14	62.11
Grp	±12.22	±12.19	±15.97	±19.15	±14.65	±14.04	±13.64	±12.73	±14.62	±13.14	±13.65	±14.95
Peth	77.62	56.44	68.00	64.81	61.62	63.55	67.22	66.77	63.88	62.85	56.96	59.66
Grp	±12.02	±15.10	±15.47	±13.87	±12.90	±18.56	±17.69	±14.86	±15.32	±13.20	±11.42	±13.62
p- value	0.97	0.94	0.82	0.69	0.65	0.12	0.21	0.64	0.80	0.13	0.54	0.25

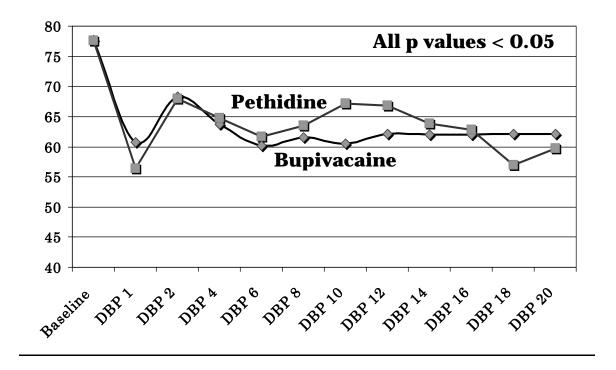
Fig 1: Changes in HR at different time intervals following SAB in the 2 study groups







Changes in DBP at different time intervals following SAB in the 2 study groups



#### Discussion

This studv showed that pethidine 1mg/kg intrathecally provides a longer duration of postoperative analgesia of 8hrs and 30mins .In the study conducted by Cozian et al <sup>11</sup> reported a duration of analgesia of 112 min sensory block with the same dose of intrathecal pethidine. The difference may be due to the variation in methodology, patient population and different surgery. In the study conducted by Murto and Kimmo<sup>12</sup> with the addition of 0.3mg/kg pethidine to spinal lignocaine produced analgesia for 4-10 hours. Single intrathecal pethidine of 60mg in the study by <sup>13</sup> provided analgesia for  $447.6 \pm 184.0$  minutes. The most commonly studied dose of intrathecal pethidine is 1mg/kg 4,5,8,10,11. Thus we chose the same dose in our present study. Nguyen Thi et al <sup>9</sup> have suggested that the safety margin of intrathecal pethidine is narrow and side effects like respiratory depression, sedation, nausea and vomiting, pruritus can occur with doses as low as 0.5mg/kg. Nausea and vomiting is frequently encountered with pethidine intrathecally <sup>4,8,10</sup> and this incidence is higher than with local anesthetic block <sup>8</sup>In our study the incidence of nausea was 1 in bupivacaine group 3 in pethidine group, incidence of vomiting was 2 in bupivacaine group 3 in pethidine group, incidence of pruritus was 6 in pethidine and none in bupivacaine group. The nausea and vomiting seems to be related with central opioid receptor effect. The incidence of itching can be 10% to  $35\%^{-6}$ , 7, 8, 11.

The incidence of respiratory depression is controversial. Some authors reported none <sup>6, 7, 9, 10, 14</sup>, where as, others reported hypoxia in up to 10% of patients <sup>8.</sup> The respiratory depression may occur as late as 40 minutes after intrathecal injection, possibly due to systemic reabsorption of pethidine from the cerebrospinal fluid<sup>5</sup>. Pethidine is metabolized to nor pethidine which has central nervous system excitatory effects. Nor pethidine toxicity results when the daily dose of intravenous pethidine exceeds 25mg /kg especially in the presence of renal failure<sup>15</sup>. There is little probability that pethidine toxicity would occur after intrathecal administration in a dose not exceeding 1mg/kg<sup>15</sup>.

In our study patients were monitored with SpO2 and respiratory rate intraoperatively and beyond the operating room in postoperative ward. We did not encounter respiratory depression in this study. The baseline hemodynamic parameters heart rate, blood pressure in two study groups were statistically insignificant in this study (p>0.05) (Table 4, 5, and 6). Following spinal anesthesia with bupivacaine or

pethidine the heart rate and blood pressure did not change significantly from their baseline values. There was one episode of bradycardia in bupivacaine and in pethidine group which was successfully treated with intravenous atropine. In bupivacaine group, there was hypotension (systolic blood pressure < 30% of base line pressure) in 6 cases and in pethidine group hypotension was encountered in 4 cases. The hypotension was corrected with intravenous fluids and vasopressors. The total fluid and vasopressors administered in two groups were not statistically different (p<0.05).

The BP changes in the study groups remained statistically insignificant (p>0.05) (Table 4, 5, 6) indicating that intrathecal pethidine causes a sympathetic block similar to that of intrathecal hyperbaric bupivacaine. The analgesic effect of opioid is due to binding to specific opioid receptors. Pethidine has strong local anesthetic effects providing surgical anesthesia after intrathecal administration 6, 7 and intrathecal pethidine provides extended postoperative analgesia <sup>7, 8, 9</sup>. This makes pethidine a good alternative to local anesthetics for intrathecal use. The sensory block occurred in 3.44 minutes and 3.59 minutes after intrathecal heavy bupivacaine and pethidine intrathecally respectively. The difference is statistically not different (p=0.72) The Apgar score of the babies in 1 minute and 5 minutes in the two study groups were statistically insignificant (Table 2). Thus according to this study intrathecal pethidine can be used safely.

#### Conclusion

The hemodynamic parameters in patients following intrathecal pethidine or bupivacaine heavy was not different in two study groups and the total duration of postoperative analgesia in patients receiving sole intrathecal pethidine was of 8 hours and 30 minutes and in patients receiving intrathecal bupivacaine heavy it was of 2 hours and 36 minutes. Hence intrathecal pethidine provides extended duration of postoperative analgesia and it has been found safe.

#### Reference

- 1. Gissen AJ, Gugino LD, Datta S et al. Effects of fentanyl and sufertanil on peripheral mammalian nerves. Anesth Analg 1987; 66:1272-76.
- 2. Way EL. Studies on the local anesthetic potency of isonipecaine. Journal of American Associations 1946; 35:44-57.
- 3. Beyazova M, Babacan A, Bilier E, Akcabay M, Kaya K, Baysal A. Perineural pethidine. Effects

of different doses on nerve conduction. Ear J Anaesthesiol 1993; 10:353-6.

- Lewis RP, Spiers SPW, Mc Laren IM, Hunt PCW, Smith HS. Pethidine as a spinal anesthetics agent – a comparison with plain bupivacaine in patients undergoing transurethral resection of the prostate. Eur J Anaesthesiol 1992; 9:105-9.
- Maurette P, Tauzin Fin P, vincon G, Brachet-Lierman A. Arterial versus ventricular CSF pharmacokinetics after intrathecal meperidine in humans. Anesthesiology 1989; 70:961-6.
- Grace D, Fee JPH. Anesthesia and adverse effects after intrathecal pethidine hydrochloride for urological surgery. Anesthesia 1995; 50:1036-40.
- Kafle SK. Intrathecal meperidine for elective CS: a comparison with lidocaine. Can J Anesth 1993; 40:718-21.
- Sangarlangkarm S, Klaewtanong V, Jonglerttrakool P, Khankaew V. Meperidine as a spinal anesthetic agent a comparison with lidocaine- glucose. Anesth Analg 1987; 66:235-40.

- 9. Acalovschil, Bodolea C, Manoiu C. Spinal anesthesia with meperidine: effects of added alpha adrenergic agonists- epinephrine versus clonidine. Anesth Analg 1997; 84:1333-9.
- Fanewo CE, Naguib M. Spinal anesthesia with meperidine as the sole agent. Can Anesth Soc J 1985; 32:533-7.
- 11. Cozian A, Pinaud M, Lepage J Y, et al. Effects of meperidine spinal anesthesia on hemodynamic, plasma catecholamine, angiotensin I, aldosterone, and histamine concentrations in elderly men. Anesthesiology 1986; 64: 815-9.
- 12. Norris MC, Honet JE, Leighton BL, Arkoosh VA. A comparison of meperidine and lidocaine for spinal anesthesia for postpartum tubal ligation. Reg Anesth 1996; 21: 4-8.
- Nguyen, Thi TV, Orliaguet G, Liu N, Delaunay L, Bonnet F. A dose- range study of intrathecal meperidine combined with bupivacaine. Acta Anesthesiol Scand 1992;36:516-8
- 14. Stone PA, Macin tyre PE, Jarvis DA. Norpethidine toxicity and patient controlled analgesia. Br J Anesth 1993; 71:738-40.