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SPINAL ANAESTHESIA;
EFFECTS OF ADDING PETHIDINE WITH BUPIVACAINE

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ABSTRACT... drshaukatrz@yahoo.com. **Objectives:** To investigate the effects of adding pethidine with intrathecal bupivacaine, in patients having elective Caesarian section under spinal anaesthesia. **Design:** A prospective randomized double blind study. **Setting:** Department of Anaesthesiology in Combined Military Hospital, Rawalpindi **Period :** 15th June 2002 to 15th October 2002. **Material and Methods:** One hundred patients received intrathecal injection of 0.5 % bupivacaine 2.0 ml plus either normal saline 0.2 ml (control group) or 0.2 ml 5% pethidine equivalent to 10mg of the drug (pethidine group). Duration of effective analgesia (defined as the time duration from the intrathecal injection to first patient demand of analgesia) was recorded. Other variables recorded were Hypotension (defined as when systolic blood pressure drops to less than 90 mm of Hg or a decrease of 25% from base line blood pressure), pruritis and occurrence of nausea and vomiting. **Results:** The duration of effective analgesia was greater in the pethidine group (mean 238.70 minutes) compared with control group (mean 120.88 minutes), this difference was statistically significant with $p<0.05$. Hypotension was more common in the pethidine group 70% compared to 52% in the control group ($P=0.06$), while pruritis occurred in 20 % patients of Pethidine group compared to only 6% of control group ($p=0.038$). Nausea and vomiting were also common in pethidine group (52% vs. 10%) with a p value of 0.001. **Conclusion:** Addition of 10 mg of pethidine to 2 ml of 0.5% bupivacaine results in significant rise in early postoperative analgesia but at a cost of higher rate of side effects.

Key words: Anaesthesia, Obstetrics, Analgesics, Opioid, Pethidine, Subarachnoid.

INTRODUCTION

Pain is extraordinary complex sensation which is difficult to define and equally difficult to measure in an accurate objective manner. The international association for study of pain defines pain as “An unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage1” Due to high rates of complications of general anaesthesia in caesarean section, regional anaesthesia has gained popularity for maternal safety and better foetal outcome. Regional techniques provide the best analgesia with minimum complications and side effects[2].

For caesarean section a more intense motor and sensory block from T4 to S5 is needed.

Subarachnoid anaesthesia is still popular for caesarean section because the technique is easy and brief for the parturient and spinal local anaesthetics produce adequate relaxation of abdominal muscles with few effects on the neonate. Although a local anaesthetic solution may be used alone for spinal anaesthesia, opioid are commonly added. Other adjuvant including epinephrine, neostigmine, clonidine[3] and ketamine are also used. When the lipophilic opioids fentanyl and sufentanyl were added to local anaesthetics, early post-operative analgesia was prolonged compared with local anaesthetics alone[4-6]. In these studies, the reported times to first post-operative analgesic requirement ranged from 4-13 hours[7]

Pethidine is an opioid of intermediate lipid solubility and is unique in having significant local anaesthetic properties[8]. It has been used as a sole agent for spinal anaesthesia for caesarean section[9]. However, few data are available on the effects of adding pethidine to local anaesthetic. Secondly non-availability of lipophilic opioids i.e., fentanyl and sufentanyl in Pakistan has reduced the choice available to the anaesthetists practicing obstetric anaesthesia.

Therefore the purpose of this study was to investigate the effects of adding preservative free pethidine to bupivacaine in patients having elective caesarean section under spinal anaesthesia. The primary variable was the duration of early postoperative analgesia whereas secondary variables included intraoperative side effects, hypotension, pruritis and nausea or vomiting.

MATERIAL AND METHODS

This randomized double-blind study comparing bupivacaine alone and bupivacaine with pethidine for spinal anaesthesia was carried out at the Department of Anaesthesiology in Combined Military Hospital, Rawalpindi. After approval from the Armed Forces Advisor in Anaesthesiology and the Commanding Officer of the hospital, a total of one hundred patients undergoing elective caesarean section were selected for this study. The patients were briefed about the study and their informed consent was also taken. The patients were between 20 to 35 years of age, falling in ASA physical status I and II, having single gestation of more than 36 weeks. Patients with pre-existing or pregnancy-induced hypertension, known foetal abnormality, allergic to bupivacaine or pethidine, or having any other known contraindication to spinal anaesthesia and those patients who refused for being included in the study were excluded from the study.

Randomly the patients were divided into two groups i.e., 'A' and 'B'. The randomisation was achieved by selection of the uppermost envelope from a set of pre-shuffled envelopes containing a code. Two millilitres of 0.5% bupivacaine was drawn into a 5 ml syringe, to which was added either 0.2 ml saline (control group or group A) or 0.2 ml preservative free pethidine 5% (pethidine group or group B). To facilitate blinding, two identical 1 ml syringes containing either saline or pethidine were prepared. The anaesthetist was kept blind while the code was revealed to the scrub nurse, who selected the appropriate syringe and discarded the other. The content of the selected syringe were then added to the bupivacaine.

Pre-operative assessment of every patient was done preceding evening of surgery. They were reassured and an informed consent was taken. They were thoroughly examined and investigated. As all the patients for the study were undergoing elective caesarean section, they were kept nil by mouth for 8 hours preoperatively. A wedge was placed under the right hip of the patients to avoid aortocaval compression. After passing a wide bore cannula, the patients were infused 1500ml of lactated Ringer's solution. Under strict aseptic conditions, the lumbar puncture was performed at the L_{3-4} inter-space with a 25-G Quincke Babcock spinal needle with the patient in the sitting position. After confirmation of free flow of CSF , the patients of group 'A' received 2ml 0.5% bupivacaine mixed with 0.2 ml of normal saline and the patients of group 'B' received 2ml 0.5% bupivacaine

mixed with 0.2 ml of 5% pethidine, the anaesthetist being blind of the code as mentioned above. The patients were then immediately placed supine.

ASA standard monitoring was applied. Oxygen saturation and heart rate were continuously recorded. A baseline blood pressure was measured and then every 5 min after induction of spinal anaesthesia. Hypotension, defined as systolic blood pressure $\leq$ 90mmHg or decrease of 25% from baseline was treated with volume expansion. The rostral dermatome level of sensory anaesthesia to pinprick was determined and motor block was assessed using the Bromage scale (0, no impairment of the legs or feet; 1, barely able to flex the knees, no impairment of the feet; 2, unable to move knees or feet). Intra-operative pain and pruritus were assessed according to a three point scale (0=no symptom, 1=symptom present but not requiring treatment, 2= symptom present and treatment given on patient request) pruritus was treated with iv. chlorpheneramine 10 mg as required. Nausea and vomiting were treated with metoclopramide 10 mg intravenously.

Patients were shifted to recovery room after operation. During the postoperative period, blood pressure was measured at 15-min intervals for 1 h and then every hour up to the 12 h after the patient's arrival at the postoperative ward. The level of sensory and motor block during the postoperative period were assessed every 30 min until they reached the L_5 dermatome and the Bromage scale was 0, respectively. When the patients fulfilled the discharge criteria from recovery room they were shifted to postoperative ward.

Nurse on duty was given a detailed description of the study being performed. She was handed over the study Performa and asked to observe the patient. We defined the duration of effective analgesia as the time from administration of spinal anaesthetic agent to the first demand for analgesia by the patient. The severity of postoperative pain was measured using a 10-cm visual analogue scale (0, 'no pain'; 10, 'excruciating pain') and a verbal pain rating scale (0, no pain; 1, mild pain; 2, moderate pain; 3, strong pain) every hour for 12 h or whenever the patient requested analgesia.

Postoperative analgesia was provided by Intramuscular diclofenac 75 mg if the visual analogue scale was $\geq$4 or the verbal rating scale was $\geq$2. This was followed by an Intravenous injection of pethidine 50 mg if the patient was still in pain (visual analogue scale $\geq$4 or the verbal rating scale $\geq$2) 1 h after diclofenac. If necessary, diclofenac was repeated 12 h after the previous injection and pethidine 2 h after the previous injection. The patient stayed in the post-operative ward for 24 h. The time for first analgesic request and pethidine injection was arbitrarily recorded as 24 h for those patients who did not request any supplemental analgesic for up to 24 h after intrathecal administration.

The primary variable was the duration of post-operative analgesia. The secondary variables were the incidence of side effects i.e., intra-operative hypotension, pruritis, and nausea / vomiting.

The results were analyzed using Statistical Package for Social Sciences (SPSS vs 8.0). Student 't' test was used to analyze the continuous data i.e., post-operative analgesic duration while chi-square test was used for the dichotomous data i.e., the side effects. A p value of <0.05 was taken as significant.

RESULTS

Maternal characteristics except parity were comparable in the two groups. All patients had adequate sensory block for the surgery. Block height for group 'A' ranged from T_1 to T_6 levels, while it was C_7 to T_4 for the second group (Table I). The times from spinal injection to delivery and uterine incision to delivery and the duration of surgery were similar between groups. Neonatal outcome was also similar between groups.

Mean duration of effective analgesia was longer in the pethidine group (238.70 min 95% confidence interval) compared with control group (120.88 min 95% CI) p=0.001 (Table II).

The incidence of adverse intra-operative events were slightly more in the pethidine group (Table-III).

Table-I. Level of sensory block		
Dermatome	**Group 'A' (n=50)**	**Group 'B' (n=50)**
C6	0	0
C7	0	1
C8	0	2
T1	1	2
T2	3	6
T3	18	21
T4	23	18
T5	3	0
T6	2	0

Table-II. Duration of analgesia					
Group	**n**	**Mean**	**Std. Deviation**	**Std. Error Mean**	**P value**
Group 'A'	50	120.88	16.05	2.27	0.001
Group 'B'	50	238.70	32.90	4.65	

Table-III. Incidence of adverse intra-operative events			
Adverse events	**Group 'B' n=50**	**Group 'A' n=50**	**P value**
Hypotension	35 (70%)	26 (52%)	0.066
Pruritis	10 (20%)	3 (6%)	0.038
Nausea / vomiting	26 (26%)	5 (10%)	0.001

35 patients of group 'B' had hypotension compared with 26 in the other group (p= 0.06) . Similarly the incidence of pruritis was more in pethidine group 20% as compared with only 6% in saline group (p=0.038), whereas Nausea and vomiting were also common in pethidine group (52% vs. 10%) with a p value of 0.001.

DISCUSSION

Although the advantage of epidural anaesthesia and analgesia is evident in most of the operative settings and for postoperative pain, the standard technique for Caesarian section remains the subarachnoid block[10]. The unavailability of spinal catheters and side effects related to them once they were used has resulted in research for an ideal drug, which can be used as single shot technique and can provide postoperative analgesia with minimum of side effects[11].

Opioids alone are used for the caesarean section but their side effects were too much to make them a good choice as routine[12]. The major side effects were respiratory depression, nausea and vomiting and pruritis. Although local anaesthetics are standard in subarachnoid block their role for postoperative pain relief is limited. A rational use will be combining local anaesthetics with opioids in such a combination to avoid side effects of both drugs.

Bupivacaine is the standard local anaesthetic drug used in the spinal block for Caesarian section[13]. This drug was combined with morphine, fentanyl and sufentanil for favourable results[14,15]. The combination with morphine has resulted in prolongation of analgesia for 24 hours while with that of lipophilic opioids is 4–13 hours[16]. Pethidine is an opioid with intermediate lipid solubility having local anaesthetic like activity appears to help more.

In our study the effective analgesia time was significantly higher in the Group B i.e. the pethidine group. The mean time of postoperative analgesia was nearly double from control group (120 min Vs 238 min). Yu et al had added pethidine to hyperbaric bupivacaine and studied the post op pain relief and documented 234 min of pain free time. He used the patient controlled analgesia technique so drug was immediately administered as the patient had felt any pain but in our study patient had to request. Secondly he had used the hyperbaric 0.5% bupivacaine and we have used 0.5% bupivacaine. Despite the

difference the results were comparable[17]. Murto et al had added pethidine to lignocaine and had achieved a pain free mean time of 429 minutes. In his study the level of anaesthesia achieved was higher in pethidine group as in our study (table I); this may show the local anaesthetic property of pethidine. He had used lignocaine which has shorter duration of action but in his study the dose of Pethidine was much larger than ours i.e. 0.3 mg/kg body weight (this amount to 21 mg of pethidine for a 70 kg person) secondarily his studied population was old male undergoing transurethral prostatectomy[18].

Nausea and vomiting are troublesome side effects encountered during spinal anaesthesia for Caesarian section. Possible aetiologies include hypotension and peritoneal manipulation that stimulate vagal afferents. With intrathecal opioids, a direct opioid effect can also be a factor. We found an increased incidence of peri-operative nausea and vomiting in the pethidine group compared with the saline group. Previously intrathecal pethidine 10 mg alone was found to be associated with more nausea and vomiting than sufentanil and fentanyl when used for the continuous spinal analgesia for labour[19]. Larger doses of intrathecal pethidine used as the sole agent for spinal anaesthesia in Caesarian section has also been associated with nausea and vomiting [12,20,21] . These studies indicate that intrathecal pethidine, in low doses as 10 mg can increase nausea and vomiting. In contrast the randomized controlled trial with the opioids used in spinal anaesthesia for Caesarian section showed that nausea and vomiting is not increased with fentanyl and sufentanil but increased with the morphine.[22].

Pruritis has been associated with the intrathecal fentanyl[14,23] ,intrathecal sufentanil[15],diamorphine[23] and morphine[16]. In our study 20% of the patient complained of pruritis compared to 6% control group, the incidence of pruritis is said to be 10.2 –32% in patients who had received the 50 mg dose of intrathecal pethidine. This disparity of high rate of pruritis with 10 mg dose of pethidine in our study is not completely understood.

Hypotension secondary to intrathecal local anaesthetic is a known effect and one of the advantages of adding opioids is to avoid or minimize this side effect. In our study 70% of the patients of pethidine group had developed hypotension compared to 52% of the control group. This augmentation of the effect may partially be explained by the local anaesthetic properties of the pethidine. Murto who had studied addition of pethidine to lignocaine for transurethral resection had reported no addition of hypotension incidence with pethidine but reported a higher incidence of braycardia[18]. Bradycardia was not the feature in our study but probably the different population, higher block and changes peculiar to the pregnancy had augmented the hypotension in our patients.

CONCLUSION

The addition of 10 mg of Pethidine to the local anaesthetic solution of Bupivacaine significantly increases the postoperative analgesia but there is definite rise in the occurrence of side effects of nausea and vomiting, pruritis and hypotension, fortunately these complications are not life threatening and generally easily manageable so this addition will help the patients in the postoperative period.

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