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Original Research Article

Pethidine and bupivacaine spinal anaesthesia: a comparative evaluation of postoperative complications and recovery profile

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ABSTRACT

Background: Bupivacaine is commonly used as a sole agent for spinal anaesthesia unlike Pethidine. This study compares the immediate postoperative complications and recovery profile following spinal anaesthesia with pethidine and bupivacaine.
Methods: Fifty-two patients who required short duration surgical procedures below the umbilicus were randomized to receive spinal anaesthesia with pethidine 1mg/Kg and 2.5 mL 0.5% bupivacaine. Time to recovery of pin prick sensation at S2, plantar flexion, proprioception of the big toe, and full motor recovery were compared for the two agents. Complications of pain, sedation, nausea and vomiting, pruritus and urinary retention in the immediate postoperative period were also compared.
Results: Comparing Pethidine and Bupivacaine, time to return of pinprick sensation at S2 was 94.62±20.25 and 205.96±31.05 minutes respectively; return of plantar flexion was 92.88±12.01 and 193.85±39.56 minutes respectively; recovery of proprioception of the big toe was 31.15±9.41 and 172.50±42.70 minutes respectively; complete motor recovery was 47.89±14.08 and 221.73±44.72 minutes respectively. All the differences in recovery times were statistically significant ($p<0.0001$). There was no statistically significant difference in the incidence of pain and sedation. Only 4 (15.38%) patients in the Bupivacaine group experienced mild pain. There was no incident of nausea and vomiting. However, pethidine group experienced pruritus (19.22%) and bupivacaine group none. Bupivacaine group also had urinary retention (11.54%), while pethidine group had none. These differences were statistically significant ($p=0.01$).
Conclusions: Pethidine exhibited a shorter recovery profile than Bupivacaine and also caused no significant complication in the immediate postoperative period.

Keywords: Bupivacaine, Pethidine, Postoperative complications, Recovery, Spinal anaesthesia

INTRODUCTION

Pethidine is a lipophilic opioid analgesic with local anaesthetic effects when administered intrathecally.[1,2] It can be used as a sole agent for spinal anaesthesia. However, it is not as widely used as bupivacaine for this purpose and consequently its effects and recovery parameters are not widely available in recent anaesthetic literature. Marshall and Chung described recovery as an ongoing process that begins from the end of intraoperative care until the patient returns to his or her preoperative physiological state.[3] In a resource-poor environment, where there is scarcity of medical gases and specialist anaesthetists, spinal anaesthesia is a cheaper alternative to general anaesthesia for surgical procedures of the lower trunk, perineum and lower limbs. An added

advantage is that the patient's airway is not compromised. Communication is maintained with the patient, enabling the physician to monitor the patient and any co-morbidity effectively. As in other regional techniques, complications are detected at an early stage and can be treated before any major sequel occurs.[4]

Bupivacaine hydrochloride a long-acting amide is a local anaesthetic agent now commonly used for spinal anaesthesia. Lignocaine (heavy) was withdrawn because of radiculopathy caused by its injection intrathecally.[5]

The objective of this study is to compare the immediate postoperative complications and recovery profile following spinal anaesthesia with pethidine and bupivacaine in our study setting at the University of Calabar Teaching Hospital (UCTH) Calabar Nigeria. The specific objectives include the comparative evaluation of the return of the ability to plantar- flex the foot in patients after pethidine and bupivacaine spinal anaesthesia , the time of recovery of proprioception of the big toe in patients after pethidine and bupivacaine spinal anaesthesia, the full motor recovery of the lower limb in patients after pethidine and bupivacaine spinal anaesthesia, the recovery of sensation to pin-prick of S2 dermatome in patients after pethidine and bupivacaine spinal anaesthesia and the prevalence of immediate postoperative complications such as pain, nausea, and vomiting, sedation and pruritus, in patients after pethidine and bupivacaine spinal anaesthesia .

Background and concepts: spinal anesthesia

Regional anaesthesia was first introduced by Harvey Cushing in 1901 to describe techniques of abolishing pain using local anaesthetic agents as opposed to general anaesthesia.[6] August Bier is credited with administering the first spinal anaesthetic in 1898; he used 3 ml of 0.5% cocaine intrathecally.[7]

Wagner and Eaton et al studied rat skeletal muscles and observed that pethidine blocked voltage-dependent Na^+ channels supporting its classification as a local anaesthetic.[4] In a similar study, Wolff et al observed that pethidine inhibits the complex mechanism of generating action potentials in spinal dorsal horn neurons by blockade of voltage-gated Na^+ and K^+ channels.[2]

Subarachnoid pethidine has been used successfully for procedures of the inguinal area, lower limb and perineum.[7-10] The analgesic effect of intrathecal opioids of which pethidine is one, is derived from binding of the agent to opioid receptors in the substantia gelatinosa of the spinal cord.[11] Agonist effect at the opioid receptors cause inhibition of transmission of nociceptive stimuli by inhibiting the presynaptic release and post synaptic response to excitatory neurotransmitters from nociceptive neurons.[6] Bupivacaine is a long-acting local anaesthetic of the amide type. It is 95% protein bound with pKa of 8.1, and has a long elimination half-life (2.7h). It is metabolized in the liver with 16% excreted unchanged in urine. When administered, it diffuses in its unchanged base form through neural sheaths and axonal membranes to the internal surface where it combines with hydrogen ions to form cationic species that block sodium ion channels. This blockade decreases ion conductance and prevents depolarization of the cell membrane.[12] Conduction of nerve impulse is thus prevented.

There is a dearth of information in local studies in our sub-region including low and medium income countries like Nigeria on the recovery profile of patients following the use of either pethidine or bupivacaine as sole agents for lumbar spinal anaesthesia. Famewo and Naguib published their work on Spinal anaesthesia with pethidine as sole agent over 3 decades ago.[13] They recorded the most common adverse effect as hypotension, bradycardia and hypoxaemia occurring 20-30 minutes after injection. They also found that reversal was easily obtained by the administration of pressor drugs and artificial ventilation.

Hansen and Hansen investigated the effects of different doses of pethidine for spinal anaesthesia on duration and level of sensory block as well as the incidence of side effects on forty five African men randomly allocated to receive one of three doses of intrathecal pethidine; 1.2mg/kg, 1.5mg/kg and 1.8mg/kg.[14] They observed that 1.5mg/kg and 1.8mg/kg provided longer duration of anaesthesia compared with 1.2mg/kg. However, nausea, pruritus and respiratory depression were common to all the dose groups. Intrathecal pethidine dose of 1mg/kg is said to provide only 40 to 90 minutes of surgical anaesthesia.[14]

METHODS

The study was carried out in the UCTH, Calabar following approval by the Health Research and Ethics Committee (HREC) of the hospital. The hospital is a tertiary healthcare facility with 500 beds. It serves as a training institution for medical students, postgraduate doctors and allied medical personnel.

The patients included both males and female in-patients between the ages of 18 and 60 years old who were scheduled for lower abdominal or lower limb surgery. All the patients were classified as having physical status I and II according to the American Society of Anesthesiologists (ASA) physical status classification. The exclusion criteria included; patient's refusal, severe spinal deformity, previous back surgery, spinal cord lesions, infection at the site of injection, active neurological disease, history of psychiatric illness, history of coagulopathies, morbid obesity (BMI>35), history of allergy to bupivacaine or pethidine, procedures exceeding 60 minutes, procedures involving blood loss >500mL, and obstetric cases. Patients who met the inclusion criteria were randomly placed in two groups: Group A (pethidine) and Group B (bupivacaine) to receive lumbar spinal anaesthesia with either preservative-free pethidine

or bupivacaine. Informed consent was obtained from each patient. Randomization to each group was by balloting. The anaesthetist giving the block and the nurse assessing the patient's recovery were blinded to the study groups (randomized double-blinded study).

During the preoperative visit, Numerical Rating Scale for pain was introduced to the patients. Also, proprioception which is the ability to sense the position, orientation and movement of the big toe, was introduced to the patient. With the eye shielded, the patient was asked to tell in which direction the big toe was being moved. There was no premedication. In the operating room, baseline blood pressure and pulse rate were recorded. Perioperatively non-invasive blood pressure monitor and a pulse oximeter probe were applied. Every patient was preloaded with 500 mL of Ringer's lactate using an 18G intravenous cannula.

With the patient in the sitting position the skin was cleansed successively with chlorhexidine and methylated spirit. The L2-3 or L3-4 interspace was identified using as landmark the intercristine or Tuffier's line (the line joining the iliac crests) which is at the body of L4. The chosen interspace was infiltrated at the midline with 2mL of 1% lidocaine using a 23G hypodermic needle. Dural puncture was performed with a 26G Quincke needle inserted via a 21G hypodermic needle. The bevel of the Quincke needle was placed parallel to the dural fibers.

The end point was a free flow of cerebrospinal fluid. Thereafter, 1mg/kg of 5% preservative-free pethidine made up to 2.5mL with normal saline or 2.5mL of isobaric 0.5% bupivacaine was injected. The patient was made to lie supine and flat for at least 5 minutes to achieve sensory blockade up to T10 before being positioned for surgery.

Monitoring of blood pressure, pulse rate and arterial oxygen saturation was carried out every 5 minutes. Adequacy of block was tested by loss of sensation to pin-prick. Any patient that required supplementary analgesia before the end of surgery was excluded from the study.

After instituting the spinal anaesthesia, regression of sensory block was assessed by loss of sensation to pin-prick every 15 minutes until it reached S2 dermatome. The test was performed in a cephalad-to-caudad direction with a disposable test pin. The right C5, C6 dermatomes were used as the unblocked reference point. Bromage score, return of proprioception of the big toe, ability to plantar-flex, were assessed every 15 minutes after injection of pethidine or bupivacaine until Bromage score was zero, and the return of proprioception of the big toe and ability to plantar-flex were positive. Postoperative motor recovery was assessed using the modified Bromage scale.

Pain, nausea and vomiting, sedation and pruritus were recorded in the immediate postoperative period. If a patient failed to void 3 hours after surgery and had signs of urinary retention, a catheter was inserted, bladder drained and catheter removed.

A spreadsheet of data obtained from the patients was prepared. Relevant tables were drawn and simple statistical analysis such as arithmetic mean, percentages and standard deviation, levels of significance, carried out using EPI info software. Level of statistical significance was set at 95% ($p \leq 0.05$). t-test and Chi-Square tests were used to test for associations among continuous and categorical variables respectively.

RESULTS

A total of 52 subjects, American Society of Anesthesiologists (ASA) I and II physical status, were recruited for the study. They were randomized into two groups to receive lumbar spinal anaesthesia with either preservative free pethidine, group A (n=26) or bupivacaine, group B (n=26).

The mean age of all the subjects was 33.48±12.74 years; the mean age of those who received pethidine was 33.69±13.59 years and the mean age of those who received bupivacaine was 33.27±12.11 years but this difference was not statistically significant (p=0.906) as shown in Table 1.

Table 1: Socio-demographic variables.

Variable	Drug		Total (n=52)	Test statistic (p-value)
	Pethidine (n=26)	Bupivacaine (n=26)		
Mean age (years)	33.69±13.59	33.27±12.11	33.48±12.74	t-test value-0.119 (0.906)
Sex n (%)				
Male	20 (76.92)	19 (73.08)	39 (75.00)	$X^{2=}$0.1026 (0.749)
Female	7 (23.08)	7 (26.92)	13 (25.00)	
Mean height (cm)	167.89±4.43	163.77±6.80	165.83±6.05	t-test value-2.587 (0.013)
Mean weight (Kg)	67.48±6.80	63.65±5.55	65.53±5.56	t-test value-2.593 (0.013)
BMI (kg/m^2)	23.90±1.38	23.75±1.63	23.82±1.50	t-test value-0.367 (0.715)

Overall, there were more males (75.0%) than females (25.0%) but there was no statistically significant difference (p=0.749) between males who received pethidine (76.9%) and bupivacaine (73.1%) and females who received pethidine (23.1%) and bupivacaine (26.9%)

The overall mean height of the subjects was 165.83±6.05 centimeters; the mean height of those who received pethidine was 167.89±4.43 centimeters and those who received bupivacaine was 163.77±6.80 centimeters and this difference was statistically significant (p=0.013).

The overall mean weight of the subjects was 65.53±5.56Kg; the mean weight of those who received pethidine was 67.48±6.80Kg and those who received bupivacaine was 63.65±5.55Kg and this difference was statistically significant (p=0.013).

The overall mean BMI of the subjects was 23.82±1.50Kg/m^2; the mean BMI of those who received pethidine was 23.90±1.38Kg/m^2 and those who received bupivacaine was 23.75±1.63Kg/m^2 but this difference was not statistically significant (p=0.715).

Table 2: Recovery characteristics of spinal anaesthesia.

Variable	Drug		t-test (p-value)
	Pethidine (n=26)	Bupivacaine (n=26)	
Mean time to return of pinprick sensation to S_2 (min.)	94.62±20.25	205.96±31.05	15.318 (<0.0001)
Mean time to plantar-flexion (min.)	92.88±12.01	193.85±39.56	12.453 (<0.0001)
Mean time to recovery of proprioception in big toe (min.)	31.15±9.41	172.50±42.70	16.487 (<0.0001)
Mean time to complete motor recovery (Bromage 0) (min.)	47.89±14.08	221.73±44.72	18.907 (<0.0001)

In Table 2, the mean time of return of pinprick sensation to S2 among subjects who received pethidine and bupivacaine was 94.62±20.25 minutes and 205.96±31.05 minutes respectively and this difference was statistically significant (p<0.0001).

The mean time to plantar-flexion (Table 2) among subjects who received pethidine and bupivacaine was 92.88±12.01 minutes and 193.85±39.56 minutes respectively and this difference was statistically significant (p<0.0001).

Table 3: Pain score as an immediate postoperative complication.

Drug	Pain score (%)			Fisher's test (p-value)
	0	1	2	
Pethidine	26 (54.20)	0 (0.00)	0 (0.00)	3.315 (0.110)
Bupivacaine	22 (45.80)	2 (7.69)	2 (7.69)	
Total	48	2	2	

The mean time to recovery of propioception in big toe (Table 2) among subjects who received pethidine and bupivacaine was 31.15±9.41 minutes and 172.50±42.70 minutes respectively and this difference was statistically significant (p<0.0001). Table 2 also shows that the mean time to complete motor recovery (Bromage score 0) among subjects who received pethidine and bupivacaine was 47.89±14.08 minutes and 221.73±44.72 minutes respectively and this difference was statistically significant (p<0.0001).

In Table 3, there was no statistically significant difference (p=0.110) in the incidence of pain (pain score ranging from 0 to 10) as an immediate postoperative complication between respondents who received pethidine and those who received bupivacaine.

Nausea and vomiting was not an immediate postoperative complication in this study (not shown in tabular form).

Table 4: Incidence of sedation as an immediate postoperative complication.

Drug	Sedation		Fisher's-test (p-value)
	Present	Absent	
Pethidine (n=26)	1 (3.90)	25 (96.10)	1.00
Bupivacaine (n = 26)	0 (0.00)	26 (100.00)	

In Table 4, there was no statistically significant difference (p=1.00) in the incidence of sedation as an immediate postoperative complication between respondents who received pethidine (3.9%) and those who received bupivacaine (0.0%).

Table 5: Incidence of pruritus as an immediate postoperative complication.

Drug	Pruritus		Fisher's-test (p-value)
	Present	Absent	
Pethidine (n=26)	5 (19.22)	21 (80.78)	<0.0001
Bupivacaine (n=26)	0(0.00)	26 (100.00)	

In Table 5, there was statistically significant difference (p<0.0001) in the incidence of pruritus as an immediate postoperative complication between subjects who received pethidine (19.22%) and those who received bupivacaine (0.0%).

Table 6: Incidence of urinary retention as an immediate postoperative complication.

Drug	Urinary retention		Fisher's-test (p value)
	Present	Absent	
Pethidine (n=26)	0 (0.00)	26 (100.00)	0.01
Bupivacaine (n=26)	3 (11.54)	23 (88.46)	

In Table 6, there was statistically significant difference (p=0.01) in the incidence of urinary retention as an immediate postoperative complication between subjects who received pethidine (0.0%) and those who received bupivacaine (11.54%).

DISCUSSION

The use of pethidine or bupivacaine as single agent for spinal anaesthesia in a resource poor environment will save needed funds provided they give adequate surgical anaesthesia with rapid recovery and minimal side effects in the immediate postoperative period.

The criteria used in this study for comparing the recovery profiles following spinal anaesthesia with pethidine or bupivacaine as sole agent included: (1) return of pinprick sensation to Sacral dermatome; (2) plantar flexion of the foot (while supine); (3) return of proprioception in the big toe and full motor recovery of the lower limb (Bromage score 0).

The mean time to complete motor recovery (Bromage score 0) among subjects who received pethidine was significantly shorter (p<0.0001) than for bupivacaine as shown in the results. This disparity is broadly in keeping with the findings of Grace and Fee who compared intrathecal pethidine with intrathecal bupivacaine and observed that while there was incomplete motor block in both groups, it was significantly greater with the pethidine group.[8] In their study of low dose pethidine for spinal anaesthesia, Patel et al, observed that though surgical anaesthesia was adequate, motor block was absent in 10% of subjects.[10]

The mean time of return of pin prick sensation to S_2 among respondents who received pethidine was also significantly shorter than for bupivacaine. The finding also correlates well with that of previous workers.[8] Patients who received pethidine spinal block were able to plantar-flex after 92.88±12.01 minutes whereas those in bupivacaine group recovered plantar-flexion after 193.85±39.56 minutes. Similarly, pethidine group also recovered proprioception of the big toe faster than those in the bupivacaine group. Above findings have revealed that patients who received pethidine spinal anaesthesia recovered faster than those who received bupivacaine.

Patient satisfaction with their perioperative experience and quality of recovery is improved when the anaesthetic technique chosen for the procedure is associated with a low incidence of postoperative side effects.[16] In this study, complications in the immediate postoperative period were considered and compared for the two agents. Only two subjects in the bupivacaine group experienced pain in the immediate postoperative period. However, the pain scores were low on the numeric analogue scale (NAS), and hence tolerable. There was no statistically significant difference (p=0.110) in the incidence of pain as an immediate postoperative complication between subjects who received pethidine and those who received bupivacaine. This finding does not agree with the work by Chaudari et al who observed that 42% of patients who had spinal anaesthesia with pethidine had pain though it was tolerable.[9] This observation of pain was probably due to the dose of pethidine used for the block. They used 0.5mg/Kg of pethidine whereas in this study 1mg/Kg was used. Shrestha and colleagues using a similar dose as ours in their study found postoperative analgesia lasting 8hours 30 minutes in the Pethidine group and 2 hours 36 minutes in the Bupivacaine group.[17] Patel and associates observed a postoperative analgesia of 968 minutes.[10] Chaudhari et al also recorded as much as 15 hours (900 minutes) of postoperative analgesia with pethidine.[9] Unrelieved pain in the postoperative period can lead to anxiety, fear, fatigue, sleep disturbance, depression, pulmonary dysfunction, stimulation of sympathetic nervous system, increased risk of deep vein thrombosis, ileus, nausea, vomiting, urinary retention, increased blood glucose and immunologic impairment among other complications. Postoperative pain management aims to minimize or eliminate patient discomfort and the above complications. This management should be cost effective with minimal side effects.

Five subjects (19.22%) in pethidine group experienced pruritus. No one from Bupivacaine group had it. This finding is in keeping with that of other workers.[7-9] Reported side effects from subarachnoid pethidine have included nausea and vomiting, pruritus, urinary retention, respiratory depression, and hypotension.[13,18] Grace and Fee observed that only subjects in the pethidine group experienced pruritus.[8]

Three subjects (11.54%) from bupivacaine group developed urinary retention while none from pethidine group experienced it. Bupivacaine is said to have prolonged paralysing effects on the detrusor muscles, increasing the risk of urinary retention and unwarranted catheterization.[19] There was no statistically significant difference in the incidence of sedation as an immediate postoperative complication between subjects who received pethidine (3.9%) and those who received bupivacaine (0.0%) in this study. The only subject who

experienced sedation probably did so as a result of cephalad spread of pethidine to the brain. However, it is supposed to be rare considering the fact that its high lipophilicity reduces rostral spread. Spinal anaesthesia even without sedative medication, may cause sedation.[20] Various theories have been put forward to explain the phenomenon. One of them attributes it to the rostral spread of the local anaesthetic agent with direct action on the brain.[21] Another theory on causes of sedative effect of neuraxial anaesthesia is the interruption of spinal afferent input with a decrease in stimulation of reticular activating system and a resultant hypnotic effect.[21] Urinary retention, another immediate postoperative complication, is associated with prolonged postoperative spinal block due to prolonged paralyzing effects on the detrusor muscles.[19]

The study did not reveal any incident of nausea or vomiting in the immediate postoperative period. This is in contrast to a prevalence of 11.45% and 13.35% for nausea and vomiting respectively observed in patients undergoing surgery under general anaesthesia in the same institution.[22] Nausea and vomiting often associated with spinal anaesthesia have multifactorial origin. These include patient factors, arterial hypotension, hypoperfusion of the central nervous system and psychological changes (anxiety). Patient specific risk factors associated with postoperative nausea and vomiting include female gender, a history of postoperative nausea and vomiting or motion sickness. These factors are associated with increased incidence of postoperative emetic symptoms.[23]Anxiety which leads to high circulating levels of catecholamines acting via the chemoreceptor trigger zone, may be a contributing factor.[23] Considering that PONV is a major cause of unplanned admission of patients following ambulatory surgery, it's prevention is a great advantage in contributing to postoperative patient satisfaction. Pethidine subarachnoid block has been shown to be comparable to 5% lignocaine with fewer side effects, additionally, there is less requirement for postoperative analgesia and prevention of postoperative shivering.[24,25] With these advantages, pethidine subarachnoid block is suitable for day care surgery where early ambulation, street fitness, adequate analgesia without postoperative nausea and vomiting are desirable to prevent unplanned admission.

The limitation of the study was: patients undergoing surgery are usually draped, therefore assessment of the various recovery parameters as shown in present study protocol, was sometimes difficult and required the full cooperation and understanding of the operating surgeons.

CONCLUSION

Under the present study conditions, pethidine exhibited a shorter recovery profile than bupivacaine and also caused no significant complications in the immediate postoperative period.

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