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Haemodynamics of 2-chloroprocaine and bupivacaine for lower limb surgeries under spinal anaesthesia

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Abstract

The lipophilic portion is essential for anaesthetic activity and therapeutically useful local anaesthetics require a delicate balance between lipid solubility and water solubility. Addition of a butyl group to the Piperidine nitrogen of Mepivacaine results in bupivacaine, which is 35 times more lipid soluble and has a potency and duration of action three to four times that of Mepivacaine. Inclusion criteria were American Society of Anaesthesiologists (ASA) physical status I or II, either sex, age 18-60 years, presenting for lower limb surgeries. Exclusion criteria were patient allergic to drug, heart block/dysrhythmia. Hundred slips were made in such a manner that fifty slips had Group 1 written on it and the other fifty had Group 2. In the present study it was observed that there was no statistically significant difference in distribution of patients based on ASA grade in between the two groups $p > 0.05$. In the present study it was observed that there was there no statistically significant difference in adverse events in between group.

Keywords: haemodynamics, 2-chloroprocaine, bupivacaine

Introduction

Local anaesthetic drugs have similar configuration. They have one aromatic lipophilic part (benzene ring) and one hydrophilic part (quaternary ring) connected by an intermediate ring either an ester (-COO-) or an amide (-NHCO-). The lipophilic portion is essential for anaesthetic activity and therapeutically useful local anaesthetics require a delicate balance between lipid solubility and water solubility. Addition of a butyl group to the Piperidine nitrogen of Mepivacaine results in bupivacaine, which is 35 times more lipid soluble and has a potency and duration of action three to four times that of Mepivacaine [1].

After accidental IV injection of bupivacaine the protein binding sites (alpha1 acid glycoprotein and albumin) are quickly saturated, leaving a significant mass of unbound drug available for diffusion into the conducting tissue of the heart. This may result in precipitous hypotension, cardiac dysrhythmias and atrioventricular heart block [2].

Cardiotoxic plasma concentration of bupivacaine is 8 to 10 µg/ml. The threshold for cardiac toxicity produced by bupivacaine may be decreased in patients being treated with drugs that inhibit myocardial impulse propagation (beta adrenergic blockers, digitalis preparations, calcium channel blockers) [3].

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It depresses the maximal depolarization rate of cardiac action potential (Vmax) by virtue of their ability to inhibit sodium ion influx via sodium channels. Bupivacaine depresses Vmax considerably more than lidocaine. The resulting slowed conduction of the cardiac action potential manifest on the electrocardiogram as prolongation of the P-R and QRS intervals and re-entry ventricular cardiac dysrhythmias. The R enantiomer of bupivacaine is more toxic than the S enantiomer [4].

Chloroprocaine, like other local anaesthetics, blocks the generation and the conduction of nerve impulses, presumably by increasing the threshold for electrical excitation in the nerve, by slowing the propagation of the nerve impulse and by reducing the rate of rise of the action potential. In general, the progression of anaesthesia is related to the diameter, myelination and conduction velocity of affected nerve fibres. Clinically, the order of loss of nerve function is as follows:

1. Pain.
2. Temperature.
3. Touch.
4. Proprioception.
5. Skeletal muscle tone [5].

Systemic absorption of local anaesthetics produces effects on the cardiovascular and central nervous systems. At blood concentrations achieved with normal therapeutic doses, changes in cardiac conduction, excitability, refractoriness, contractility and peripheral vascular resistance are minimal. However, toxic blood concentrations depress cardiac conduction and excitability, which may lead to atrioventricular block and ultimately to cardiac arrest. In addition, with toxic blood concentrations myocardial contractility may be depressed and peripheral vasodilation may occur, leading to decreased cardiac output and arterial blood pressure [6].

Methodology

After obtaining the approval of scientific, ethics committee and written informed consent, a total of 100 patients undergoing elective lower limb surgeries under spinal anaesthesia were selected. Patients were explained before operative procedure. Pre-anaesthetic check- up was carried out preoperatively with a detailed history, general physical examination and systemic examination. Airway assessment and spinal column examination was done.

Inclusion criteria were American Society of Anaesthesiologists (ASA) physical status I or II, either sex, age 18-60 years, presenting for lower limb surgeries. Exclusion criteria were patient allergic to drug, heart block/dysrhythmia. Hundred slips were made in such a manner that fifty slips had Group 1 written on it and the other fifty had Group 2. The slips were numbered from 1 –100, mixed and kept in a box. One slip was taken and the drug was drawn accordingly and labelled with the number in accordance with the randomization. The slips were coded and the solution was prepared by an anaesthesiologist who was not involved in the study. At the end of the study, decoding was done.

Study design

A Prospective randomized study.

Place of the study

Department of Anaesthesiology

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Study population

Total 100 patients of 18-60 years of age belonging to ASA grade I and ASA grade II scheduled to undergo lower limb surgeries will be studied.

The inclusion criteria

- Patients of both sex aged between 18 to 60 years.
- Patients undergoing lower limb surgery under spinal anesthesia.
- ASA grade I and II.

The exclusion criteria

- Patient's refusal to participate.
- Patients suffering from cardiac (Arrhythmias, heart blocks) and pulmonary diseases.
- Patients with known allergy to test drug.
- Patients with gross spinal abnormality, localized skin sepsis, hemorrhagic diathesis, neurological involvement/diseases.
- Patients with head injury, raised intra cranial pressure, raised intra ocular pressure.
- Patients with psychiatric disorders.
- Patients with asthma.
- Patients with epilepsy.
- Pregnant patients undergoing non-obstetric surgeries.

Group 1: 50 patients will receive intrathecal 50 mg of 1% 2-CHLOROPROCAINE.
Group 2: 50 patients will receive intrathecal 10mg of 0.5% HYPERBARIC BUPIVACAINE.

Results

Table 1: Age distribution of patients in both groups

	Group I		Group II		t value	p value
	Mean	SD	Mean	SD		
Age	39.72	11.49	36.44	10.99	1.458	0.148

In the present study it was observed that there was no statistically significant difference in the mean Age (in years) between the study groups p >0.05.

Table 2: Distribution of patients based on Gender

	Group I		Group II	
	No.	%	No.	%
Male	40	80	40	80
Female	10	20	10	20
Total	50	100	50	100
chi square	0		p value	1

In the present study it was observed that there was no statistically significant difference in distribution of patients based on gender in between the two groups p >0.05.

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Table 3: Baseline clinical characteristics

	Group I		Group II		t value	p value
	Mean	SD	Mean	SD		
PR	77.6	7.97	77.7	7.39	0.091	0.928
MAP	77.5	6.3	75.8	8.8	1.09	0.278
SPO2	99.74	0.56	99.58	0.78	1.14	0.245

In the present study no statistically significant difference was observed in the mean PR, MAP and SPo2 in between the two groups p >0.05.

Table 4: Distribution of patients based on ASA grade

	Group I		Group II	
	No.	%	No.	%
ASA grade I	39	78	38	76
ASA grade II	11	22	12	24
Total	50	100	50	100
chi square	0.056		p value	0.812

In the present study it was observed that there was no statistically significant difference in distribution of patients based on ASA grade in between the two groups p >0.05.

Table 5: Incidence of Adverse Events in both groups

	Group I		Group II	
	No.	%	No.	%
Hypotension	1	50	1	33.3
Shivering	1	50	0	0
Nausea & vomiting	0	0	1	33.3
Hypotension &bradycardia	0	0	1	33.3
Total	2	100	3	100
chi square	2.91		p value	0.405

In the present study it was observed that there was there no statistically significant difference in adverse events in between group.

Discussion

Spinal anaesthesia is the most preferred regional anaesthesia technique as it is easy to perform, produces rapid onset of anaesthesia and complete muscle relaxation and is also economical. These advantages are sometimes offset by a relatively short duration of action.
The first spinal analgesia was administered in 1885 by James Leonard Corning (1855-1923), a neurologist in New York. He was experimenting with cocaine on the spinal nerves of a dog when he accidentally pierced the Dura matter.
The first planned spinal anaesthesia for surgery in man was administered by August Bier (1861-1949) on 16 August 1898.
The availability of reliable and safe short-acting local anaesthetics has recently developed interest in spinal technique for ambulatory surgery, offering an alternative to general anaesthesia.
Taniguchi *et al.* [7] study debated the concept that 2-Chloroprocaine-related neurologic toxicity reported in the 1980s after unintentional spinal injection during attempted epidural anaesthesia was caused by the combination of low pH and the antioxidant sodium bisulphite. The mechanism of sulphite toxicity to the nervous cells is related to the alteration of the

energetic metabolism in the cell mitochondria and rats have a 10-fold larger expression of the sulphite oxidase enzyme than other species, including humans. The small sample size of the present investigation prevented them from drawing any conclusion about the safety profile of this drug for spinal injection and additional data are needed to clarify this aspect.
However, studies in volunteers and reports on off-label use of spinal 2-Chloroprocaine in clinical practice support the safety profile of the preservative-free formulation of this drug for intrathecal injection.
Yoos *et al.* [8] compared 2-CP (2-chloroprocaine) 40 mg with Bupivacaine 7.5 mg. They concluded that spinal 2-CP provides adequate duration and density of block for ambulatory surgical procedures, and it has a significantly faster resolution of block and return to ambulation compared with Bupivacaine. This study was designed to compare 2-CP with Bupivacaine for spinal anaesthesia in elective ambulatory surgeries. They hypothesized that 2-CP can provide spinal anaesthesia with a shorter recovery profile than Bupivacaine, permitting earlier discharge from hospital after ambulatory surgery. However, Bupivacaine often produces inadequate surgical anaesthesia and has an unpredictable duration. Preservative-free 2-chloroprocaine (2-CP) has re-emerged as an alternative for outpatient spinal anaesthesia.
They designed this double-blind, randomized, crossover, volunteer study to compare 40 mg of 2-CP with small-dose (7.5 mg) Bupivacaine with measures of pinprick anaesthesia, motor strength, tolerance to tourniquet and electrical stimulation, and simulated discharge criteria. Peak block height (2-CP average T7 [range T3–10]; Bupivacaine average T9 [range T4–L1]), regression to L1 (2-CP 64 ± 10 versus Bupivacaine 87 ± 41 min), and tourniquet tolerance (2-CP 52 ± 11 versus
Bupivacaine 60 ± 27 min) did not differ between drugs (P = 0.15, 0.12 and 0.40, respectively). However, time to simulated discharge (including time to complete block regression, ambulation, and spontaneous voiding) was significantly longer with Bupivacaine (2-CP 113 ± 14, Bupivacaine 191 ± 30 min, P = 0.0009). No subjects reported transient neurologic symptoms or other side effects. They concluded that spinal 2-CP provides adequate duration and density of ambulatory surgical procedures, and has significantly faster resolution of block and return to ambulation when compared with 7.5 mg of Bupivacaine.
Gonter AF, Kopacz DJ [9] Recent studies using preservative-free 2- Chloroprocaine (2-CP) for spinal anaesthesia have shown it to be a reliable short- acting drug that provides similar anaesthesia to lidocaine. In this randomized, double- blind, crossover study, they compared the characteristics of spinal 2-CP (30 mg) with those of procaine (80 mg) in eight volunteers to determine whether either drug produces spinal anaesthetic characteristics ideal for outpatient surgery. By using sensation to pinprick, transcutaneous electrical stimulation, tolerance to thigh tourniquet, and motor blockade as surrogates for surgical efficacy, 2-CP compared similarly to procaine [10].

Conclusion

In the present study it was observed that there was there no statistically significant difference in adverse events in between group.

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