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Isobaric levobupivacaine and fentanyl with isobaric ropivacaine and fentanyl in patients undergoing TURP: Hemodynamic changes

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Abstract
When hypotension occurs after SAB, patients often do not develop reflex tachycardia, this phenomenon may result from blockade of cardio-accelerator sympathetic fibers at T1 to T4 and possibly the "reverse" of the Bainbridge reflex. Rapid infusion of blood or saline sometimes produces an increase in heart rate if the initial HR is slow. This effect was described by Bainbridge in 1915.After SAB, HR decreases as a result of decrease in right atrial filling (secondary to systemic vasodilatation), which in turn leads to a decrease in outflow from intrinsic chronotropic stretch receptors in the right atrium and great veins. In fact, severe bradycardia and even cardiac arrest have been reported after spinal anaesthesia. In this study, 30 males in each group (group R and group L) satisfying the inclusion criteria. Group R: 2.6 cc of 0.75% isobaric ropivacaine (19.5mg) with 0.4cc of fentanyl (20 microgram).Group L: 2.6 cc of 0.5% isobaric levobupivacaine (13 mg) with 0.4cc of fentanyl (20 microgram). There is no statistically significant difference in systolic blood pressure between both the two groups at various intervals. There is no statistically significant difference in mean arterial pressure between the two groups. Ten patients in ropivacaine 0.75% group and seven patients in levobupivacaine 0.5% group developed hypotension which was managed by inj. Mephentermine 6 mg IV.

Keywords: Isobaric Ropivacaine, fentanyl, hemodynamic changes

Introduction
The prostate gland is located between the bladder and the rectum and wraps around the urethra. It is traversed by prostatic part of urethra and ejaculatory ducts. Its base is towards the bladder neck and apex merges with the membranous urethra to rest on the urogenital diaphragm. It is the largest accessory gland of the male reproductive system.

The credit for introducing neuraxial block into clinical practice for the first time goes to August Bier in 1898. Local anaesthetics injected into the spinal subarachnoid space, block the nerve conduction to an extent determined by the concentration and volume injected. The sensitivity of different fibres varies by the drug employed. All types of nerve fibres are affected by the local anaesthetics, but within any one fibre type there is tendency for smaller slower conduction fibers to be more readily blocked than larger faster conducting fibres. Between fibre types however, these rules do not hold good. It is well established that myelinated preganglionic B fibres which have a faster conduction time are about three times more sensitive to local anaesthetics than the slower unmyelinated postganglionic C fibres.

Hypotension during central neural block may occur by three main mechanisms: decrease in venous return, vasodilatation and decreased cardiac output. Bladder distension during central nerve block has been shown to produce hypotension inappropriate to the level of block and vagal overactivity may contribute in the unsedated patient [1].

When hypotension occurs after SAB, patients often do not develop reflex tachycardia. This phenomenon may result from blockade of cardio-accelerator sympathetic fibers at T1 to T4 and possibly the "reverse" of the Bainbridge reflex. Rapid infusion of blood or saline sometimes produces an increase in heart rate if the initial HR is slow. This effect was described by Bainbridge in 1915. After SAB, HR decreases as a result of decrease in right atrial filling (secondary to systemic vasodilatation), which in turn leads to a decrease in outflow from intrinsic chronotropic stretch receptors in the right atrium and great veins . In fact, severe bradycardia and even cardiac arrest have been reported after spinal anaesthesia [2, 3].

Most local anaesthetics block the unmyelinated C and myelinated Aδ fibres that transmit pain

impulses at the same rate. However the rate of blockade of Aα and Aβ (that carry motor impulses) depends on the physicochemical properties, pKa and lipid solubility of the individual local anaesthetic drugs. As ropivacaine is less lipid soluble when compared to bupivacaine, the blockade of Aα and Aβ is slow and hence produce less motor blockade than bupivacaine.

Levobupivacaine exerts its pharmacological action through reversible blockade of neuronal sodium channels. Myelinated nerves are blocked through exposure at the nodes of Ranvier more readily than unmyelinated nerves; and small nerves are blocked more easily than larger ones. In general, the progression of anaesthesia is related to the diameter, myelination and conduction velocity of the affected nerve fibers.

Levobupivacaine is an interesting alternative to bupivacaine for spinal anaesthesia with similar sensory and motor characteristics and recovery like bupivacaine. The regression of motor block occurs earlier with isobaric levobupivacaine as compared with isobaric bupivacaine. Intrathecal administration of 15mg of isobaric levobupivacaine provides an adequate sensory and motor block lasting for approximately 6.5 hrs. Smaller doses (i.e., 5-10 mg) are used in day-care surgeries. At low concentrations, levobupivacaine produces a differential neuraxial block with preservation of motor function, which may be favourable for ambulatory surgery. Minimum effective local anaesthetic dose of levobupivacaine as recommended by an up and down sequential design study is 11.7mg [4].

Methodology

Study Subjects: Patients hospitalized for TURP.

Study Design: Randomized clinical trial

Sample Size: 30 males in each group (group R and group L) satisfying the inclusion criteria.

Group R: 2.6 cc of 0.75% isobaric ropivacaine (19.5mg) with 0.4cc of fentanyl (20 microgram).

Group L: 2.6 cc of 0.5% isobaric levobupivacaine (13 mg) with 0.4cc of fentanyl (20 microgram).

Sample Size: A pilot study was done before starting the actual study. From the pilot study, effect size of 0.868 was obtained. Considering alpha to be 0.05 and beta to be 0.20, the sample size was calculated. Thus the number of subjects in each group was found to be 30.

Sampling Method: Simple random sampling.

Inclusion Criteria

- Male patients aged 40 to 80 years with ASA grade I-III, scheduled for elective TURP.

Exclusion Criteria

- Patient's refusal, known case of hypersensitivity to amide group of local anaesthetics.
- Patients with medical complications like: (a) Hypertension, IHD, Valvular diseases (b) Anemia (c) Hypovolemia (d) Septicaemia (e) Coagulation disorders or on anticoagulant therapy.
- Local infection at the site of proposed puncture for spinal anaesthesia.
- Psychiatric disorders.
- Height <145 centimeters, morbid obesity (BMI≥ 40 kg/ m^2).
- Patients who were unable to understand pain scales.
- History of chronic analgesic therapy, arthrosis or severe deformity of spine, peripheral neuropathy, mental disturbance or epilepsy.

Results

Table 1: Heart Rate (In Bpm) In Both the Groups over a Period of Time

Time	Ropivacaine And Fentanyl Group			Levobupivacaine And Fentanyl Group		
	Mean	SD	N	Mean	SD	N
AT O Minutes	80.07	12.61	30	80.07	9.40	30
AT 2 Minutes	81.07	11.61	30	82	8.84	30
AT 4 Minutes	79.87	11.62	30	80.33	9.06	30
AT 10 Minutes	74.83	11.30	30	71.7	9.67	30
AT 16 Minutes	75.76	7.88	30	73.06	11.53	30
AT 20 Minutes	76.36	7.57	30	74.36	9.11	30
AT 25 Minutes	77.50	8.60	30	75.4	10.38	30
AT 40 Minutes	77.77	8.77	30	76.33	6.60	30
AT 60 Minutes	78	0	1	77	2.82	2

There is no statistically significant difference in the mean heart rate between the two groups at various intervals. Two patients in each group developed bradycardia which was managed by inj. atropine 0.6 mg IV.

Table 2: Systolic Blood Pressure (In Mm Hg) In Both the Groups over a Period of Time

Time	Ropivacaine And Fentanyl Group			Levobupivacaine And Fentanyl Group		
	Mean	SD	N	Mean	SD	N
AT O Minutes	138.96	8.15	30	141.93	8.76	30
AT 2 Minutes	136.17	7.03	30	139.63	8.67	30
AT 4 Minutes	136.80	7.79	30	140.13	10.95	30
AT 10 Minutes	135.40	9.02	30	139.15	8.67	30
AT 16 Minutes	135.86	10.94	30	138.06	8.85	30
AT 20 Minutes	136.53	15.66	30	138.66	10.29	30
AT 25 Minutes	138.73	30.07	30	139.23	15.57	30
AT 40 Minutes	139.22	13.07	30	139.05	13.29	30
AT 60 Minutes	136	0	1	137	1.41	2

There is no statistically significant difference in systolic blood pressure between both the two groups at various intervals.

Table 3: Diastolic Blood Pressure (In Mm Hg) In Both the Groups over a Period of Time

Time	Ropivacaine And Fentanyl Group			Levobupivacaine And Fentanyl Group		
	Mean	SD	N	Mean	SD	N
At O Minutes	80.06	8.25	30	82.76	4.92	30
At 2 Minutes	77.93	6.68	30	80.8	4.83	30
At 4 Minutes	77.76	5.87	30	80.7	5.92	30
At 10 Minutes	76.16	5.16	30	78.23	4.21	30
At 16 Minutes	76.86	8.77	30	78.96	7.59	30
At 20 Minutes	77.93	9.54	30	78.8	9.07	30
At 25 Minutes	76.86	15.72	30	77.3	7.95	30
At 40 Minutes	76.11	9.31	30	77.27	7.20	30
At 60 Minutes	78	0	1	77	1.41	2

There is no statistically significant difference in diastolic blood pressure at various intervals between both the groups.

Table 4: Mean Arterial Pressure (In Mm Hg) In Both the Groups over a Period of Time

Time	Ropivacaine And Fentanyl Group			Levobupivacaine And Fentanyl Group			
	Mean	Sd	N	Mean	SD		N
At O Minutes	99.69	8.21	30	102.48	6.2		30
At 2 Minutes	97.34	6.79	30	100.41	6.11		30
At 4 Minutes	97.44	6.51	30	100.51	7.59		30
At 10 Minutes	95.90	6.44	30	98.53	5.69		30
At 16 Minutes	96.52	9.49	30	98.66	8.01		30
At 20 Minutes	97.46	11.58	30	98.75	9.47		30
At 25 Minutes	97.48	20.50	30	97.94	10.49		30
At 40 Minutes	97.14	10.56	30	97.86	9.23		30
At 60 Minutes	97.33	0	1	97	1.41		2

There is no statistically significant difference in mean arterial pressure between the two groups. Ten patients in ropivacaine 0.75% group and seven patients in levobupivacaine 0.5% group developed hypotension which was managed by inj. mephentermine 6 mg IV.

Discussion

Lower urinary tract symptoms suggestive of BPH are frequently encountered in ageing men. Over the age of 40, about one quarter of men suffer from BPH [1]. The mean age of patients in our study was 64.85yrs. Over the past few decades, TURP has become the ‘‘gold standard’’ of surgical treatment for patients with BPH [5].

There has been a significant transformation in the choice of local anaesthetics for use during spinal anaesthesia. A metanalysis showed that the relative risk of developing transient neurological symptoms was about seven times higher for spinal lignocaine than other local anaesthetics [4]. With abandonement of lignocaine for use in spinal anaesthesia, bupivacaine gained popularity and widespread clinical acceptance. However, as reports of dangerous CNS and cardiotoxicity surfaced with use of bupivacaine, the quest for invention and evaluation of newer local anaesthetic molecules with a better safety profile started [6]. Ropivacaine hydrochloride which is a pure S(-) enantiomer of bupivacaine is one of the fruits of that research and has shown a lot of promise as effective and safe local anaesthetic.

A number of studies have shown the use of plain ropivacaine in the dose range of 8 to 25 mg for various surgeries like arthroplasties, cesarean sections, knee arthroscopies, endoscopic procedures like TURP, etc. [2, 3, 4] But the above mentioned studies found that intrathecal injection of isobaric ropivacaine produced a sensory block of very variable extent and a proportion of patients needed general anaesthesia because of inadequate distribution of block at lower doses. The dose of 15 mg of intrathecal ropivacaine was associated with a 5 % inadequate anaesthesia in lower limb surgeries and 20 % inadequate anaesthesia in abdominal surgeries and hence in order to produce a reliable and effective sensory level for the planned surgical intervention, uniform dose of 19.5mg (2.6 ml of 0.75% isobaric ropivacaine) was selected.

Levobupivacaine is a preferred local anaesthetic due to its longer sensory block, lower cardiac and central nervous system toxicity Mantouvalou M *et al*. Used 15mg (3cc) of levobupivacaine which provided adequate sensory and motor block for abdominal surgeries. Lee YY *et al*. concluded that 2.6ml of 0.5% levobupivacaine can be used as an alternative to 0.5% racemic bupivacaine in spinal anaesthesia [7].

Opioids and local anaesthetics, when administered together intrathecally, have a potent synergistic analgesic effect. Intrathecal opioids enhance and extend the period of analgesia from sub therapeutic doses of local anaesthetics without prolonging recovery [8]. Lipophilic opioids (e.g., fentanyl and sufentanyl) are increasingly being administered intrathecally as adjuncts to local anaesthetics. They enhance spinal anaesthesia without prolonging motor recovery or discharge time [9].

The drug selected for subarachnoid block in our study was 13.5mg (2.6cc) 0.5% isobaric levobupivacaine + fentanyl 20µg (0.4cc), total 3cc versus 19.5mg (2.6cc) 0.75% isobaric ropivacaine + fentanyl 20µg (0.4cc), total 3cc.

All patients in our study groups were injected the study drugs into the subarachnoid space at the L4-5 interspace with patients in left lateral position and then turned supine immediately after the block. Patients were placed in lithotomy position on confirmation of sensory block higher than T10. If this was not achieved within 5min after SAB a head down tilt of the table was given to achieve a level of sensory block higher than T10.

Conclusion

There is no statistically significant difference in systolic blood pressure, Diastolic blood pressure and Mean arterial pressure between both the two groups at various intervals.

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