Original article:

Comparison of clinical efficacy of hyperbaric solution of ropivacaine with hyperbaric bupivacaine in spinal anesthesia in transurethral resection of prostate

Dr.Rahul Maria[1], Dr. Chinar Patel [2]

[1]DM Resident, Department of Cardiac Anesthesia, U. N. Mehta Institute of Cardiology and Research Center, Affiliated to B. J. Medical College, New Civil Hospital Campus, Asarwa, Ahmedabad

[2]Professor, Department of Anesthesia , Smt.B.K.Shah Medical Institute & Research Centre &Dhiraj Hospital

Corresponding author: Dr. Rahul Maria

Funding source:

This work was supported by U.N.Mehta Institute of Cardiology and Research Center itself and received no specific grant from any funding agency, commercial or not-for-profit sectors.

Abstract

Objective: The stress response to surgery, anaesthesia and other injuries has been considered as the homeostatic defense mechanism, important for the body for adaptation and developing resistance to the noxious insults. General anaesthesia does not abolish the stress response completely. The current study was designed to compare the clinical efficacy of hyperbaric solution of Ropivacaine with that of commercially available preparation of Hyperbaric Bupivacaine in spinal anaesthesia in Transurethral Resection of Prostate (TURP).

Method: on 60 patients of ASA-I and II (American Society of Anaesthesiologist's) classification between the ages of 40-80 years, posted for TURP. The patients were randomly divided into two equal groups according to the type of local anesthetic used. The study was prospective, double blind and interventional in nature.30 patients in Group R received 3ml of 0.5% ropivacaine (in glucose 8%).30 patients in Group B received 3ml of 0.5% hyperbaric bupivacaine. All the patients were observed for the sensory block and duration analgesia and intraoperative parameters.

Result: There no such siginificant result found between the group for the demographic data, intraoperative finding. But the duration for sensory block,motoblock and analgesia were found comparable between the group.

Conclusion:In our study, we have evaluated the efficacy of Hyberbaric Ropivacaine 0.5% compared to Hyperbaric Bupivacaine 0.5% in spinal anaesthesia for Transuretheral resection of prostate, with respect to onset, maximum level of sensory and motor, degree of motor block and duration of time of sensory and motor blocks, duration of analgesia, hemodynamic stability and side effects.

Key words: Transurethral Resection of Prostate,Ropivacaine,Hyperbaric Bupivacaine

Introduction

The stress response to surgery, anaesthesia and otherinjuries has been considered as the homeostatic defensemechanism, Important for the body for adaptation anddeveloping resistance to the noxious insults. But suchexaggerated physiological changes in patients especially ifassociated with coexisting diseases may belife threatening**.**General anaesthesia does not abolish the stress responsecompletely. The local anesthetics when used intrathecally orepidurally, abolishes the response to a great extent, particularlyin lower abdominal operations[1].Regionalanaesthesia also influences the early indicators of recovery such as time to consciousness, the incidence of postoperative nausea and vomiting (PONV), return of full\ cognitive function, these benefits may occur purely as a resultof avoidingopioids[2].Spinal anaesthesia is a very old and popular anaesthetic technique, with a high success rate and a good safety profile. In order to further improve and

understand safety issues as well as the clinical use of spinal anaesthesia, new local anesthetics and analgesic additives are being investigated for different applications. Bupivacaine has been in clinical use for more than 30years. It is widely used for spinal anaesthesia but it is associated with a side effects, including persistent postoperative motor weakness, cardiovascular and central nervous system toxicity. This has resulted in the continuing search for new and safer localanesthetic agents[3].Ropivacaine (1-propyl 2`6`-pipecoloxylidide hydrochloride monohydrate) is the s-enantiomer of a new amide local anesthetic which has been extensively evaluated in adults and older children[4].Recently, it has been used in adults and several studies have reported its clinical efficacy and safety when administered for spinal anaesthesia[5]Ropivacaine has several properties which may be useful in practice, namely the potential to produce ifferential neural blockade with less motor block and reduced cardiovascular and neurological toxicity postoperatively.[4]The potency of Ropivacaine in terms of sensory blockhas now been determined in clinical use, whether for infiltrationanesthesia, peripheral nerve block,and brachial plexus block,spinal block and lumber extradural block showed thatropivacaine was a long acting local anesthetic which gavesurgical anaesthesia of good quality[6]The current study was designed to compare the clinicalefficacy of hyperbaric solution of Ropivacaine with that of commercially available preparation of Hyperbaric Bupivacaine in spinal anaesthesia in Transurethral Resection of Prostate (TURP).

Material and methodology

This study was conducted atDhiraj General Hospital in Department of Anaesthesiology. After obtaining consent from the ethical committee we conducted a study on 60 patients of ASA-I and II (American Society of Anaesthesiologist's) classification between the ages of 40-80 years, posted for TURP. The patients were randomly divided into two equal groups according to the type of local anesthetic used.The study was prospective, double blind and interventional in nature.30 patients in **Group R** received 3ml of 0.5% ropivacaine (in glucose 8%).30 patients in **Group B** received 3ml of 0.5% hyperbaric bupivacaine.

Inclusion Criteria: Patients in the age range 40-80 years, ASA risk category I and II, No known history of allergy, sensitivity or other form of reaction to local anesthetics of the amide type, Patient willing to sign informed consent.

Exclusion criteria: Patient refusal, Patients with coagulopathy, Patients on potent antiplatelet, or on anticoagulants, Patients with back problems, Patients with local skin infections at site of injection, Known allergy to the trial drugs, Patients with poor myocardial contractility, Patients with thoracic spine deformity, ASA III or more, Patient who needed supplementation of general anaesthesia.

Investigations included: Complete blood count, Coagulation profile, Liver and kidney function tests, ECG, random blood sugar, Chest x ray PA view, All patients were kept nil by mouth for 8 hrs.

Anesthetic technique: Informed written consent was taken from the patient. On the day of surgery, the patient was brought to the pre anesthetic room and base line vital parameters(pulse, blood pressure, respiratory rate, SpO_2 and temperature) were recorded.An 18 gauge intravenous cannula was secured and Ringer lactate solution was started as pre-load at 10ml/kg. All the patients were premedicated with Inj.Ondansetron 4mg and Inj. Ranitidine 50 mg I.V. Then patient were shifted to the operating table.On arrival of patient in the operating room standard monitoring were applied; ECG, NIBP, and oxygen saturation were monitoredvia multipara monitor and vital parameters (pulse, blood pressure,respiratory rate, SpO_2 and temperature) were recorded at regular intervals .Patients were given subarachnoid block with local anesthetics according to the respective groups.30 patients in **Group R**received 3ml of 0.5% ropivacaine (in glucose 8%). The ropivacaine solutions was prepared aseptically immediately before injection (by

www.ijbamr.com P ISSN: 2250-284X , E ISSN : 2250-2858

adding 2ml of ropivacaine 0.75% plus 1ml of glucose 25%).30 patients in **Group B** received 3ml of 0.5% hyperbaric bupivacaine which was commercially available.

The spinal technique used:

Under strict aseptic and antiseptic precaution, standard subarachnoid block was performed in the lateral decubitusposition.Identification of the level was done using line perpendicular to the iliac crest which pass throughL3-L4 intervertebral space. Skin & subcutaneous infiltration was done with 2 ml of 0.5 % Lidocaine. Spinal needle was inserted in the midline with the level facing upwards at L3-4 or L4-5 interspace. After penetration of ligamentumflavum, dura and arachanoid matter, correct needle placement was identified by free flow of cerebrospinal fluid. The appropriate local anesthetic solution was injected over 5-10 seconds. The patient was placed supine immediately after injection to achieve atleast T10 level of sensory block

Intra-operative monitoring: All patients of both groups were monitored for Pulse rate. Blood pressure (SBP&DBP), Oxygen Saturation (SpO_2) and Respiratory Rate (R.R.) at 2, 5, 10,15,20,30 minutes and then half hourly till the surgery was completed and then every hour till the block regressed fully.If the systolic blood pressure (SBP) decreased more than 30% below the pre-anestheticvalue, it was consideredto be significant hypotension and Ephedrine 6 mg was given intravenously.Significant bradycardia i.e. H.R. Lessthan 20% of baseline value was treated with atropine sulphate 0.6 mg intravenously.

Sensory block assessment: The onset of sensory block was measured from the time of injection till T10 dermatome was achieved which was determined bilaterally using pin prick test and cold test using spirit. When the sensory block of T10was achieved surgeon was allowed to start with the surgery. To assess the maximumlevel of the block; sensory block was assessed at 2 and 5 min post-injection and at 5min intervals thereafter until two consecutive levels of sensory block were identical, after which assessment was done every 30 minutes till the completion of surgery.Duration of block was measured from time of onset till it regressed to L_1 dermatome.

Duration of Analgesia: Duration of analgesia was measured from the time of injection till the first complaint of pain which was assessed by VAS(Visual Analouge Scale) to which, the patient was familiarized pre-operatively. This was a 10cm scale with one end (zero) representing no pain and the other end (ten)representing worst imaginable pain, on which the patient has to mark the degree of pain he was suffering. The distance from the end label zero (no pain) to the mark of the patient hadmeasured in centimeter and designed as pain score. When the score was $\geq$ 3, rescue analgesic(Inj. Diclofenac 75mg I.M.) was given.

Complications or Side effects: Side effects like nausea, vomiting, bradycardia, hypotension, rigors and arrhythmia's were noted Intra and postoperatively and treated accordingly if any. Patients were also observed for delayed side effects like headache & backache for 3 days. Urinary retention could not be assessed asthe patient were catheterized at the end of surgery.

Statistical methods: Data were collected, tabulated, coded then analyzed using SPSS® computer software version 12.0.Numerical variables were presented as mean & standard deviation (SD) while categorical variables were presented as percent.For regard numerical variables; unpaired student – t test was performed, significant figures.Suggestive significance (P value: $0.05<P<0.10$) * moderately significant (P value:$0.01<P \leq 0.05$) ** highly significant (P value: $P \leq 0.01$).

www.ijbamr.com P ISSN: 2250-284X , E ISSN : 2250-2858

Result:

Table 1: Demographic Data:

	Mean±SD		P value
	Group R	Group B	
Age (years)	59.97±9.33	61.80±10.84	0.4856
Weight (kg)	57.77±9.56	58.60±9.92	0.7416
Height (cm)	161.83±7.46	163.57±7.63	0.3773

The demographic data with respect to age, weight and height distribution was of suggestivesignificance(Table 1)

Table 2: Duration of Sensory Block and Motor Block

	Mean±SD		P value
	Group R	Group B	
Duration(min) Sensory Block	136.17±20.22	202.40±17.07	0.0001
Duration (min) Motor Block	113.50±18.85	180.37±14.80	0.0022

The duration of Sensory block in Group B was much longer 202.40±17.07 min. than in Group R 136.17±20.22 min. with a P value<0.0001 which was statistically & clinically highly significant.

The duration of Motor block in Group B was 180.37±14.80 min. which was much longer than in Group R 113.50±18.85 min. with a P value = 0.0022 which was statistically & clinically highly significant

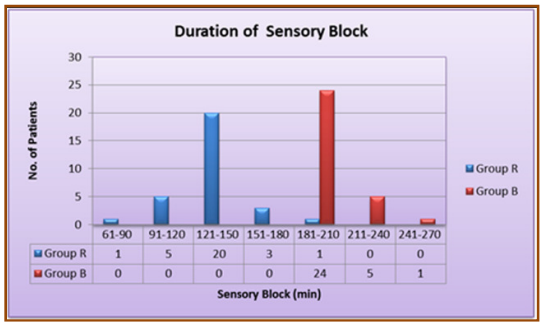
Table 3: Duration of Analgesia (min.)

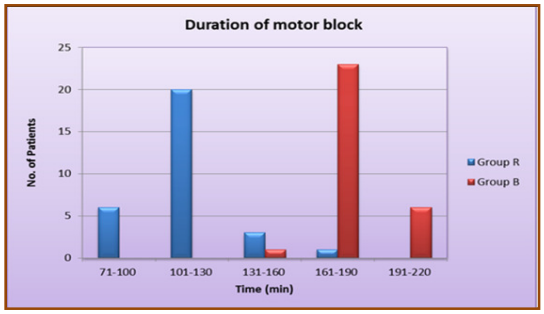
Duration of Analgesia (min.)	Mean±SD		P value
	Group R	Group B	
	98.30± 12.56	148.37± 13.91	0.0001

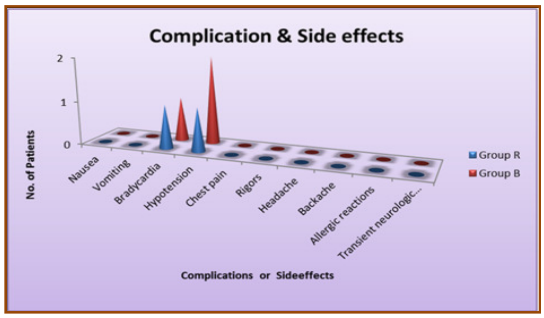
The mean duration of analgesia in Group B was 148.37± 13.91 min. which was much longer than Group R, 98.30± 12.56 min. which was statistically& clinically highly significant(P value <0.0001).(Table -3)

We found no incidence of nausea, vomiting, chest pain, rigors, head ache, backache, allergic reactions and transient neurologic symptoms in both ropivacaine and bupivacaine group.

One patient in each group had bradycardia which was treated with Inj. Atropine0.6mg i.v. One patient in Group R and 2 patients in Group developed hypotension which was treated with i.v. fluids and Inj. Ephedrine 6mg in titrated doses.







Discussion

The purpose of this study was to evaluate the efficacy and safety of spinal anaesthesia with 0.5% hyperbaric ropivacaine compared with 0.5% hyperbaric bupivacaine for Transuretheral resection of prostate.

Ropivacaine was introduced into clinical practice in 1996 [7]. A hyperbaric solution of ropivacaine in spinal anaesthesiais considered superior to isobaric solution as it is suggested that the analgesic spread with isobaric spinal ropivacaine is variable, extending from lumbosacral segments to upper thoracic segments. Actually, glucose-free ropivacaine and bupivacaine solutions are not isobaric at body temperature. Like glucose-free bupivacaine 0.5% solutions (baricity at 37°C: 0.9990), glucose-free ropivacaine solutions (baricity at 37°C: 0.9988) will behave as slightly hypobaric at body temperature. Consequently, the injection of glucose-free ropivacaine solutions may result in a higher spread when the patient is kept in the sitting position for at least 2 min after the injection [8, 9].

In spinal anaesthesia, hyperbaric solutions of local anaesthetics are known to produce a more predictable extension of the sensory block, shorter duration of block, and faster recovery than plain solutions[41]. A study showed that the hyperbaric ropivacaine solution was superior to the plain solution with respect to analgesia and maximal extent of sensory block, faster onset and offset of sensory as well as motor block [10].

www.ijbamr.com P ISSN: 2250-284X , E ISSN : 2250-2858

It is now well established that,compared with plainsolutions, the use of hyperbaric local anaesthetic solutionsresults not only in a more predictable cephalad spread, butalso increases the duration of the clinically useful block(given by duration at the T10 dermatome), and leads to a more rapid regression of sensory block and recovery from motor block.[11] In our study, the concentration of glucose used (80 mg/ ml) was theeasiest single concentration to achieve using readily availablesolutions, and provides a solution that was sufficientlyhyperbaric for its purpose and its baricitywas similar in comparison with commercially available hyperbaric bupivacaine.

The rationale for selection of the dose was that in an earlier study, 15 mg of plainropivacaine was suitable for 1-h surgery of the lower-extremities and hence it was assumed to be suitable for TURP. We selecteda fixed dose for both the drugs as one study had shown that most of the variation in height between adult patients relates to differences in the length of the lower limb long bones, not the length of the vertebral column[11].

The mean duration for onset of sensory block at T 10 in our study was 10.03±3.61 minutes in Group R whereas 8.07±3.23 minutesin Group B which was of suggestive significance (P value >0.05). The mean onset of motor block for Group R was 3.37±1.99 minutes and 2.60±1.22 minutes for Group B which wasof suggestive significance (P value >0.05).

The two main factors, the baricity of the injected solution and the patient's position immediately after intrathecal injection, are amenable to alteration by the clinician [12]. Given that there was little difference between the density of 5 mg/ ml[12] solutions of the two local anaesthetic agents (with glucose 80 mg)[13], and that a standardized protocol for positioning was used immediately after injection to standardize the effect of gravity on spread, it was observed that the pattern of onset of the sensory and motor block was similar in both thegroups. However, patients in the ropivacaine group experienced a less intense motor block with 66.67% of patients achievingBromage scores of 3, in contrast to the 96.67% in bupivacaine group. Hyperbaric ropivacaine produces a spinal block which has sensory block onset characteristics similar to equivalent doses of hyperbaric bupivacaine, but with a less intense motor block[14, 15].Both the sensory and motor blocks were clinically indistinguishable but also subject to a more rapid recovery with ropivacaine compared with bupivacaine[14, 15].This suggests that ropivacaine may be suitable for short procedures where a rapid return of ambulatory functionis desirable, such as in the day-case setting, where its recovery profile could confer a distinct clinical advantage [14,15].

The studies carried out byGautier and his colleagues in 1999[14], observed when equal doses of bupivacaine and ropivacaine were compared, the onset and extent was similar(14 min. in bupivacaine group and 15 min. in ropivacainegroup) similar toour present study.The duration of sensory block and the degree of motor block were both less with ropivacaine.

McDonald and his colleagues, 1999 [16]who compared hyperbaric bupivacaine and ropivacaine (0.25% in glucose 5%) in volunteers, equal doses of ropivacaine and bupivacaine produced sensory blocks of similar onset(9min.) and extent, but there was less motor block, which regressed faster, withropivacaineand foundthat equal doses have similar actions.Whiteside and his colleagues,2001[17] used 15mg of ropivacaine with 10mg / ml glucose found that the onset of sensory loss of Pin-Prick at T10 was 10minutes(2±2.5min.) which was comparableto our group.

Mahmoud Ahmed Abd El HakeemGalaland colleaguesin 2007[18]gave 3ml of hyperbaric ropivacaine0.5% in glucose 10% intrathecally, while comparing with commercially available hyperbaric bupivacaine.His studies showed that ropivacainegroup had producedinsignificant slower onset of action as compared with bupivacaine group which is in accordance with our study.

www.ijbamr.com P ISSN: 2250-284X , E ISSN : 2250-2858

In ourstudy theMaximum Level of sensory block was T6 in both Group R and Group B but majority of the patientsattained T8 level in both groups.Our results also coincides with Whiteside and his colleagues, 2001[17] who compared intrathecal hyperbaric ropivacaine0.5 % in glucose 10 mg/ml and showed no significant differences between both groups as regarding the height which was (T6).Mahmoud Ahmed Abd El HakeemGalaland colleagues in 2007[18] had similar results when compared to our study in which the mean height of sensory block was T6 in bupivacaine group while it was T7 in ropivacaine group and this difference was insignificant (P value >0.05).Our study also coincides with Whiteside and his colleagues, (2003) [17]found that ropivacaine produced a somewhat less maximum cephalad spread as compared to bupivacaine (T7 versus T5).

The results of our study hasshown that degree ofmotorblock for ropivacainegroup was lower (66.67% at grade 3 and 33.33% at grade 2 MBS) compared with bupivacaine group (96.67% at grade 3and 3.33% at grade 2 MBS) which was statistically & clinically significant.

Fettes and his colleagues,(2005)[19] developedgrade 3 MBS in 72.5% of patients, in hyperbaric ropivacaine group which was in accordance with our study. Our results were also comparable with Kallioand his colleagues, (2004)[20]as regards degree of motor block(75% developed grade 3 MBS), after spinal anaesthesia with 15 mghyperbaric ropivacaine. The study done by Whiteside and his colleagues, (2003)[17]confirmed our results that ropivacaine withglucose 10 mg /ml had a less potent effect on motornerves with degree of motor block in comparison tohyperbaric bupivacaine, with grade III block i.e. 70% in ropivacaine group whereas 100% in bupivacaine block.

The mean duration of sensory block for Group B was longer (202.40±17.07 min.) than Group R (136.17±20.22min.) which was statistically&clinically highly significant (P value< 0.0001).

The duration of motor block, was significantly shorter with Group R with mean of (113.50±18.85 min.) Comparedwith Group B (180.37±14.80min.)which was statisticallyand clinically highly significant (P value = 0.0022).

Many of the earlier studies have suggested that ropivacaine is less potent than bupivacaine, however J.F. Luck et al., (2008)[21] stated that the issue of potency is complex when considering a local anesthetic block and that both sensory and motor components must be considered. They also suggested that potency of the drug relates to the effect produced and not to the duration of that effect.

In our study we found no difference in the onset and effect of sensory and motor block in boththe groups.But only in the duration of analgesia. Although some authors have suggested that the lesser intensity of motor block and a more rapid recovery of sensory and motor functions has been attributed to a specific drug effect of ropivacaine demonstrating an increased separation of the sensory and motor blocking effects by virtue of alower lipid solubility and not due to lower potency.

Luck et al(2008)[21]compared hyperbaric bupivacaine (15mg)with hyperbaric ropivacaine(15mg) and found that the duration of sensory blockade in bupivacaine group was 270 minutes which was comparable to our study however in the ropivacaine group it was 210 minutes which was much longer than our study.

Our study is in accordance with the studies done by McDonald and colleagues, (1999)[16], found that the duration of sensory and motor block was shorter with ropivacaine (S)143 min.& (M)104 min compared with bupivacaine (S)246 min. & (M)143 min. respectively at doses of 12mg.

In our study mean duration of analgesia for Group R was 98.30± 12.56 min. as compared with Group B which was (148.37± 13.91 min.) which was highly statistically & clinically highly significant(P value<0.0001).

www.ijbamr.com P ISSN: 2250-284X , E ISSN : 2250-2858

Delfino*et al* (1999) [22], compared bupivacaine with ropivacaine at the same doses of 3ml of 0.5% (5 mg/ml) and found that there was shorter duration of analgesia in ropivacaine group (106min) as compared with bupivacaine group(167min) which is comparable with our study.

Chan-Jong Chung in (2001)[23],evaluated the clinical efficacy and safety of spinal anaesthesia with 0.5% hyperbaric ropivacaine compared with 0.5% hyperbaric bupivacaine for elective cesarean delivery. The time to first request of analgesics was earlier (110min.) in the Ropivacaine group than in the Bupivacaine group (159min.) ($P< 0.05$).

LIM *et al.* in 2004[24],compared 2.5 ml of both ropivacaine and bupivacaine as part of a CSE-technique in which VAS pain scores were recorded before and after the block was placed. The primary outcome was duration of analgesia, which was the highest (162min.) in the bupivacaine group.

In our study there was no significant difference between both groups as regard to safety profile. In Group R, out of 30 patients, 1 patient, had bradycardiaand 1 patient, had hypotension. In Group B, out of 30 patients, 1 patient had bradycardia and 2 patients, had hypotension. In both groups, we found no evidence of any transient neurologic symptoms which have been attributed to the use of intrathecal ropivacaine in various studies.

Our results agree with the study done by Gautier and colleagues(1999)[6],comparing between intrathecalBupivacaine and Ropivacaine for kneearthroscopy showed that 1 patient had bradycardia and 2 patient had vomiting in both the groups. There was no record of any postoperativeneurologic symptoms in any of their patients at 24 hrs afteradministration of spinal ropivacaine. Together with otherpublished reports, this suggests that ropivacaine is asuitable alternative for spinal anaesthesia.

Also the resultcoincides with Chung and his colleagues(2001)[23].They found thatthere is no difference as regards side effects between bothgroups.3 patients in the Bupivacaine and 1 patient in the Ropivacaine group hadbradycardia.

Also the result coincides with Kim (2002) [24],Whiteside(2003) [17]and Mahmoud Ahmed Abd El HakeemGalal(2007)[18] found that there was no postoperativeneurologicalsymptoms in both the groups.

Gautier and hiscolleagues(1999)[6]and McDonald and his colleagues(1999)[16],compared hyperbaric bupivacaine and ropivacaine and found there was no significant change in blood pressure throughout the procedure which was comparable to our study .However, the study done by Casati and his colleagues, (2006)[25], who studied the frequency of hypotension during conventional or asymmetric hyperbaric spinal block, they found that hypotension occurred in 22.5% in both the groups. Our study agrees with the study done byWhiteside and colleagues, (2001)[17]who used 15mg of ropivacaine with 10mg / ml glucose and found that there was hemodynamic stabilityin both groups.However Craig and his colleagues,(2002)[26],comparing bupivacaine versusropivacaine in cesarean section, they also found that 37% ofpatients in B group had hypotension in comparison to35% of patients in R group which was much higher than in our study.

Hence we found that 3ml of 0.5% hyperbaric ropivacaineproduced spinal anaesthesia of similar and effective clinical quality with a shorter duration of sensory and motor block,with minimal haemodynamic disturbances and decreased incidents of complications or side effects compared with same concentration of hyperbaric bupivacaine for Transuretheral resection of prostate.

Conclusion

In our study, we have evaluated the efficacy of HyberbaricRopivacaine 0.5% compared to Hyperbaric Bupivacaine 0.5% in spinal anaesthesiafor Transuretheral resection of prostate, with respect to onset, maximum levelof sensory and motor, degree of motor block and duration of time of sensory and motor blocks, duration of analgesia, hemodynamic stability and side effects.Thus it is concluded from the present study that, 3 ml of 0.5% hyperbaric

www.ijbamr.com P ISSN: 2250-284X , E ISSN : 2250-2858

ropivacaine as compared to same concentration of hyperbaric bupivacaine in spinal anaesthesia for Transuretheral resection of prostate showed : Similar and effective clinical quality of onset of sensory and motor block, Similar extent of sensory block, Decreased degree of motor block, Shorter duration of sensory and motor block, Shorter duration of analgesia, Hemodynamic stability, with no significant changes respiratory rate and oxygen saturation, No significant complications or side effects.

Bibliography

1. Manorama Singh: Stress response and anaesthesia altering the peri and post-operativemanagement.Indian J. Anaesth. 2003, 47 (6):427-434.
2. Dalens BJ and Hasnaoui A: Caudal anaesthesia in pediatric surgery: success rate and adverse effects in 750consecutive patients. Anesth. Analg, 1989, 68: 83 – 89.
3. De Beer DA and Thomas ML: Caudal additives in children—solutions or problems? Br J Anaesth; 2003, 90:487-98.
4. McClure JH: Ropivacaine: An excellent historical, pharmacological and clinical review article. Br. J.Anaesth., 1996, 76: 300 – 309.
5. Habre W, Bergesio R, Johnson C, et al: Pharmacokinetics of ropivacaine following caudal analgesia in children. PediatrAnesth; 2000, 10: 143-7.
6. Gautier PE De Kock M, Van SteenbergAV,et al: intrathecal ropivacaine in ambulatory surgery: a comparison between intrathecal ropivacaine for knee arthroscopy. 1999
7. Stoelting RK: Clinical anaesthesia Philadelphia-New York, Lippincott-Raven. Sixth edition; 2009 Chapter 1: 1 – 7.
8. Cheri A. Sulek and Gary R. Strichart: Local Anesthetics. In: Miller RD (ed): Anaesthesia, 2005, 6th edition. Churchill Livingstone, section 2(C), chapter 14.
9. Miller RD: Local anesthetics (ch 13), 2005, Churchill Livingstone,6th edition
10. Khaw KS, Kee WDN, Wong M, and Ng F, Lee A: Spinal ropivacaine for cesarean delivery: a comparison of hyperbaric and plain solutions. AnesthAnalg; 2002, 94: 680–5.
11. McNamee DA, McClelland AM, Scott S, Milligan KR, Westman L, Gustafsson U. Spinal anaesthesia: comparison of plain ropivacaine 5 mg · ml^{-1} with bupivacaine 5 mg · ml^{-1} for major orthopaedic surgery. Br J Anaesth; 2002, 89:702–6.
12. Schug S A: Correction factor for comparisons between levobupivacaineand racemic bupivacaine. RegAnesth. 2001,Pain Med; 26:91
13. McLeod G A: Density of spinal anaesthetic solutions of bupivacaine, levobupivacaine, and ropivacaine with and without dextrose. Br J Anaesth; 2004, 92: 547–51
14. Hocking G, Wildsmith JAW: Intrathecal drug spread. Br J Anaesth; 2004, 93: 568–78.
15. Pitkanen MT: Body mass and spread of spinal anaesthesia with bupivacaine. AnesthAnalg; 1987, 66: 127–31.
16. McDonald SB, Liu SS, Kopacz DJ, Stephenson CA: Hyperbaric spinal ropivacaine: a comparison to bupivacaine in volunteers. Anesthesiology; 1999, 90:971–7.
17. Whiteside J., Burke D., Wildsmith J: Spinal anaesthesia with ropivacaine 5 mg/ml in glucose 10 mg/ml or50 mg/ml, BR. J. ANAESTH. 2001, 86 (2), 241-244.
18. Mahmoud Ahmed Abd El Hakeem Galal, Medhat Mohamed MohamedYounis, Azza Youssef Ibrahim, BassemBoulosGhobrial and Ahmed Mohamed Khamis: compare between intrathecal hyperbaric ropivacaine (0.5% in glucose10%) and Intrathecal hyperbaric bupivacaine in TURP. Anaesthesia & intensive care , Faculty of Medicine , Ain Shams University .2007
19. P. D. W. Fettes, G. Hocking1, M. K. Peterson2, J. F. Luck and J. A. W. Wildsmith: Comparison of plain and hyperbaric solutions of ropivacaine for spinal anaesthesia {University Department of Anaesthesia, Ninewells Hospital and Medical School, Dundee DD1 9SY, UK Present addresses: 1Department of Anaesthesia, John Radcliffe Hospital, Oxford OX3 9DU, UK .Department of naesthesia, Frimley Park Hospital, Camberley GU16 7UJ, UK Br J Anaesth; 2005, 94: 107–11.

20. H. Kallio,E. V. T. Snall , C.A. Tuomas and P . H. Rosenberg: Comparison of hyperbaric and plain ropivacaine 15mg in spinal anaesthesia for lower limb surgery, Department of Anaesthesia, Forssa Hospital, Forssa, Finland. Department of Anaesthesiology and Intensive Care Medicine, Helsinki University Central Hospital, Helsinki, Finland 2004, 685-9.

21. J. F. Luck, P. D. W. Fettes and J. A. W. Wildsmith: Spinal anaesthesia for elective surgery: a comparison of hyperbaric solutions of racemic bupivacaine, levobupivacaine, and ropivacaine University Department of Anaesthesia, Ninewells Hospital and Medical School, Dundee DD1 9SY, UK Br. J. Anaesth; 2008, 101: 705–10

22. Delfino J., Pontes S., Gondim D., Do Vale N: Isobaric 0.5% bupivacaine and 0.5% ropivacaine in spinal anaesthesia for orthopedic surgery: a comparitive study, REV.BRAS. ANESTH, 1999, 49 (3), 160-164.

23. Chan Jong Chung C., Choi S., Yeo K., Park H., Lee S., Chin Y:Hyperbaric spinal ropivacaine for cesarean delivery : a comparison to hyperbaric bupivacaine, ANESTH. ANALG. 2001, 93, 157-161.

24. Kim Khaw S, NganKee WD: High Failure Rate of Small Doses of Ropivacaine When Used Alone for Spinal Anaesthesia for Cesarean Delivery. RegAnesth Pain Med; 2002, 27:533.

25. Andrea Casati and Marco Baciarello: Enantiomeric Local Anesthetics: Can Ropivacaine and Levobupivacaine improve Our Practice? Department of Anesthesiology and Pain Medicine, University of Parma, Italy Current Drug Therapy, 2006,1, 85-89

26. Craig H. Leicht, MD MPH and Ivan A Velickovic, MD: Bupivacaine VS. Ropivacaine for spinal anaesthesia for c-section Canadian Journal of Anaesthesia. 2002, 49: a 59