Original Research Article

Hemodynamic variables and side effects of 0.75% preservative free Ropivacaine for lower abdominal surgeries

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Abstract

Bupivacaine has been shown to have selective cardiac effects related to the slow rate at which it dissociates from the sodium channel.4, 13 An important aspects of this toxicity is that it involves a significant degree of stereo specificity, with the 'S'–isomer showing significantly less cardiotoxic effect. After institutional ethical committee approval and after informed consent of the patients, this study was undertaken on 60 patients of either sex, aged between 20 to 60 years belonging to ASA physical status grade I and II , scheduled for elective lower abdominal surgery. There was 10% decrease in Heart rate from the base line value and the maximum drop in Heart rate occurred at mean time of 26.08 ± 4.22 minutes from the time of injecting study drug in to the epidural space. No patients had bradycardia throughout the procedure. Side effects were very minimal in the present study.

Key Word: Hemodynamic variables, Ropivacaine, lower abdominal surgeries

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INTRODUCTION

In 1850, about three centuries after the conquest of Peru by Pizzaro, the Austrian von Scherzer brought a sufficient quantum of coca leaves to Europe to permit the isolation of cocaine For many centuries the inhabitants of Peru and Bolivia chewed the leaves of the shrub Erythroxylum Coca along with lime ash to diminish fatigue. The active ingredient in Coca leaves was cocaine, which was isolated and named by Albert Niemann in 1860. As suggested by Pizzaro descriptions of the properties of the coca prompted the Austrian Karl Koller to perform in 1884 the first clinical operation under local anaesthesia, by administration of cocaine on the eye.[1] The use of cocaine for local and regional anaesthesia rapidly spread throughout Europe and America. The toxic effects of cocaine were soon identified resulting in many deaths among both patients and addicted medical staff. Local anaesthesia was in a profound crisis until the development of modern organic chemistry which led to the synthesis of pure cocaine 1891.The great advantage of local anaesthesia with Cocaine was, it anaesthetized only the part of the body on which the operation was to be performed. However a price was paid in toxicity and short duration of action. Which lead to continued investigation in search for a safe, long acting local anaesthetic agent.[2] New amino ester local anaesthetics were synthesised between 1891 and 1930 such as tropicaine, eucaine, holocaine, orthoform, benzocaine and many more including Bupivacaine, till 1972. All these drugs were ostensibly less toxic than

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cocaine, but they had differing amounts of Central nervous system and Cardiovascular toxicity. The local anaesthetic used should possess ideal characteristics like high potency and low toxicity. Bupivacaine was of special interest because of its longer duration of action and history of clinical application. Synthesized by Ekenstam in 1957 and introduced into clinical practice in 1965 by Widman became a very popular local Anaesthetic agent.[3] In an editorial published in 1979 by George. A.N. Albright stated that Bupivacaine might result in almost simultaneous seizures and cardiovascular collapse without antecedent hypoxia from typical clinical doses following inadvertent intravascular administration.[4] One of the specific features of Bupivacaine is that clinical evidence of accumulation of the drug in plasma may not be appreciated until a fairly late stage because of its high affinity for plasma protein binding sites. The free concentration of the drug in plasma remains low until all the protein – binding sites are fully occupied, after which it increase rapidly and toxicity can occur without patients exhibiting signs of CNS toxicity before cardiovascular collapse.[5] More than that Bupivacaine has been shown to have selective cardiac effects related to the slow rate at which it dissociates from the sodium channel. An important aspects of this toxicity is that it involves a significant degree of stereo specificity, with the 'S' – isomer showing significantly less cardiotoxic effect.[6] These findings generated the search for alternative to Bupivacaine. This search was concentrated on amide linked agents, which in current practice have largely suppressed the ester type drugs. With the advantage in stereoselective synthesis it was found that agents composed of single enantiomers have clinical advantages over racemic compounds.[7] The identification of optically active isomers of the mepivacaine family led to the selection of ropivacaine a pure S-(-) enantiomer. Ropivacaine is a new amide local anaesthetic agents that has been produced as a pure S – isomer which is the propyl analogue of bupivacaine having a butyl group in same position.[8] The parent compound of ropivacaine was first synthesized in the 1950's[16] but it was only when concerns about the cardiotoxicity of bupivacaine became apparent that ropivacaine was fully evaluated. Ropivacaine administered by intravenous infusion was found to be less toxic than bupivacaine in human Volunteers. Mild CNS symptoms and minor cardiovascular toxicity as measured by changes in contractility and conductivity occurred at lesser dosage and lower plasma concentration with bupivacaine compared to Ropivacaine.[9] When used for epidural anaesthesia ,ropivacaine provided satisfactory surgical anaesthesia with a long duration of action. It was found to be an efficacious and potent local Anaesthetic agent when used for epidural anaesthesia[10] When compared with same concentration of bupivacaine, ropivacaine produces identical sensory block. The motor block produced by ropivacaine was found to be slower in onset. Lessintense and shorter in duration. But some studies have shown similar motor effects with ropivacaine and bupivacaine. Both bupivacaine andropivacaine have been shown to have similar cardiovascular changes when used for epidural Anaesthesia.[11,12]

METHODOLOGY

This study was a prospective study conducted in Medical college and Hospital.A written and informed consent was taken from allthe patients included in the study. Ethical clearance was taken from the hospital ethical committee as per protocol. After institutional ethical committee approval and after informed consent of the patients, this study was undertaken on 60 patients of either sex, aged between 20 to 60 years belonging to ASA physical status grade I and II , scheduled for elective lower abdominal surgery.

Inclusion Criteria

- Patients aged between 20-60 years.
- Patients of either sex.
- Patients with ASA Grade I and II.

Exclusion Criteria

- Pregnant women.
- Patients with H/o Cardio-Respiratory disorders
- Patients with Hepatic and Renal disesase.
- Patients with h/o convulsions and neurological deficits.
- Patients with Spinal deformities and Psychiatric diseases.
- Patients with Aspirin ingestion / anticoagulants in the preceding week.

Haemodynamic and vital parameters like ECG, blood pressure (Systolic, Diastolicand Mean arterial bllod pressure), heart rate, SpO_2 monitoring was done continuously every 5 minutes for 1st hour, every 15 mins for next 2 hours and every 30 minutes later on until complete recovery from sensory block. Continuous monitoring of ECG and changes in Heart rate and rhythm noted till the patient was shifted out from post anaesthesia recovery room. In the event of fall of heart rate lessthan 60 beats/minute, it was treated with Inj: Atropine IV and Mean arterial blood pressure fall less than 60 mm of Hg, it was treated with vasopressors and intravenous fluids. Crystalloid IV fluids given intra operatively and quantity given were recorded. Side effects like Hypotension, Bradycardia, Nausea, Vomittingand Shivering in Intra-operative period were noted. Patients were educated about the verbal numerical scale to quantify pain in the

post operative period. All patients were observed in the post *anaehesia* recover room and in the ward until complete recovery from sensory blockade and duration of post operative analgesia and any side effects if present were recorded . Rescue analgesia was given when VAS score was between 2.5 to 5 and time noted. Patients were also observed for next 24 hours after the procedure.

RESULTS

The mean age of the patients was 39.18±8.49 years. The gender distribution was equal ie. there were 30 Male and 30 Female patients parameters like Heart rate, Systolic blood pressure, Diastolic blood pressure and mean arterial blood pressure were recorded and monitored every 5 minutes for first hour, then every fifteen minutes for next 2 hours and later every 30 minutes till complete recovery from the sensory block. There was 10% decrease in Heart rate from the base line value and the maximum drop in Heart rate occurred at mean time of 26.08 ± 4.22 minutes from the time of injecting study drug in to the epidural space. No patients had bradycardia throughout the procedure. (Table 2) In our study, it was observed a fall of 10% in the mean systolic pressure from the base line value and the maximum decrease occurred at a mean time period of 30.41 ± 4.04 minutes.(Table 3) Even the mean Diastolic blood pressure showed a fall of 12% from the base line value and the maximum fall occurred at a mean time of 26.08 ± 4.22 minutes.(Table 4) The mean arterial blood pressure showed a similar trend like diastolic blood pressure and maximum decrease occurred at a mean time of 26.08 ± 4.22 minutes. ECG was monitored continuously for all patients and none of the patients had any significant change from pre operative period ECG. All the patients were given 100% Oxygen through plain face mask @4L/min. The mean SpO2 was 99%-100% in all the patients. All the patients were spontaneously breathing and no significant change noted. (Table 5) In the present study, all the patients were pre-loaded with Rnger's Lactate fluid @ 10 ml/Kg over 30-60 minutes before the epidural procedure was started. The mean intra operative crystalloid requirement was1000 ± 225 ml. The Mean arterial pressure fell less than 60 mmHg in 3 patients and were treated with Inj. Mephenteramine 6 mg-one dose. All of them responded and no further dose of vasopressor agent was required. No patients developed bradycardia and none of the patient received Inj Atropine.

Table 1: Age and sex distribution

Age	Male		Female		TOTAL	
	No	%	No	%	No	%
20-30	8	26.7	0	0.0	8	13.3
31-40	9	30.0	20	66.7	29	48.3
41-50	10	33.3	10	33.3	20	33.3
51-60	3	10.0	0	0.0	3	5.0
TOTAL	30	100.0	30	100.0	60	100.0

Table 2: Heart rate distribution

Heart rate	Mean ± SD (n=60)
At 0 minutes	81.93 ± 10.61
At 10 minutes	73.57 ± 12.04
At 20 minutes	71.61 ± 13.72
At 30 minutes	71.5 ± 14.46
At 40 minutes	76.54 ± 17.24
At 50 minutes	76.25 ± 13.89
At 60 minutes	76.43 ± 12.89
At 70 minutes	81.79 ± 11.74
At 80 minutes	81.36 ± 10.4
At 90 minutes	83.04 ± 9.43
At 120 minutes	78.39 ± 4.21
At 150 minutes	84.54 ± 11.77
At 180 minutes	80.61± 9.11

Table 3: Systolic blood pressure distribution

SBP	Mean ±SD (n=60)
At 0 minutes	120.57 ± 10.79
At 10 minutes	103.89 ± 14.19
At 20 minutes	94.68 ± 7.9
At 30 minutes	92.61 ± 8.86
At 40 minutes	97.5 ± 6.93
At 50 minutes	100 ± 6.41
At 60 minutes	103.57 ± 5.37
At 70 minutes	117.29 ± 6.04
At 80 minutes	112.68 ± 9.98
At 90 minutes	117.54 ± 4.82
At 120 minutes	114.61 ± 8.23
At 150 minutes	117 ± 4.69
At 180 minutes	114.29 ± 6.08

Table 4: Diastolic blood pressure distribution

DBP	Mean ±SD (n=60)
At 0 minutes	77.29 ± 6.02
At 10 minutes	66.82 ± 8.94
At 20 minutes	60.32 ± 8.06
At 30 minutes	62.11 ± 7.08
At 40 minutes	63.75 ± 5.2
At 50 minutes	65.29 ± 5.33
At 60 minutes	68.86 ± 4.7
At 70 minutes	73.21 ± 6.96
At 80 minutes	76.07 ± 3.58
At 90 minutes	77± 4.25
At 120 minutes	76.57 ± 4.38
At 150 minutes	78.11 ± 4.73
At 180 minutes	78 ± 9.01

Table 5: Respiratory rate distribution

Respiratory rate	Mean ±SD (n=60)
At 0 minutes	19.86 ± 1.88
At 10 minutes	20.07 ± 1.92
At 20 minutes	20.21 ± 1.83
At 30 minutes	19.43 ± 1.32
At 40 minutes	19.86 ± 1.8
At 50 minutes	19.79 ± 1.57
At 60 minutes	20 ± 1.72
At 70 minutes	20 ± 1.88
At 80 minutes	19.64 ± 1.64
At 90 minutes	19.36 ± 1.64

At 120 minutes	19.36 ± 1.45
At 150 minutes	19.57 ± 1.99
At 180 minutes	19.86 ± 1.8

Side Effects

Side effects were very minimal in the present study. None of the patients had any incidence of bradycardia. Only 3 patients had MAP fall of less than 60 mm of Hg and were treated accordingly with Inj: Mephenteramine 6 mg. 6 patients had shivering which was reduced after applying warm blankets. 2 patients had vomiting and treated with Inj: ndansetron 4mg IV. No other complications were noted until complete recovery from sensory block.

DISCUSSION

Pain relief is necessary for both humanitarian and therapeutic reasons. Surgery produces tissue injury with consequent release of histamine and inflammatory mediators which activates peripheral nociceptors, which initiate transmission of nociceptive information to the central nervous system (CNS). Transmission of nociceptive stimuli from the periphery to the CNS results in the neuroendocrine stress response which may potentiate detrimental physiologic effects in other areas of the body[1].Therefore it is utmost important to block this transmission by adopting good anaesthesia procedures of highestquality and safety.[13] Epidural anaesthesia is superior to Spinal as the desired block levels can be achieved without significant haemodynamic disturbances and top-up doses of anaesthetics and analgesics can be given. In modern anaesthesia practice Epidural anaesthesia is widely being used especially in patients undergoing surgical procedures involving lower parts of the body. To fulfill this demand, there is a need for local anaesthetic with desirable properties like longer duration of sensory blockade and shorter duration of motor blockade.[14] Bupivacaine is widely used drug in epidural anaesthesia but many studies have documented the serious adverse effects of it and concern about therapy-resistant cardiovascular toxicity with bupivacaine led to introduction of the newer agent ropivacaine (1996). Bupivacaine binds to sodium channel in a time and voltage dependant manner. It's slow dissociation time from the channel.ie. fast in and slow out produces slow conduction of action potential (manifested as prolongation of PR and QRS intervals on the ECG) pre disposing to development of re-entrant arrhythmias. This can be detected indirectly by measuring Vmax(upstroke velocity of action potential) .Pitkenen and *et al* confirmed this effect on sodium channels using rabbit ventricular myocytes and illustrated similar channels with racemic bupivacaine showing greater affinity. Ropivacaine is a long acting enantiomerically pure(S-enantiomer) amide local anaesthetic with a high pKa and low lipid solubility which blocks nerve fibres involved in pain transmission to a greater degree than those controlling motor function. The very slow reversal of Na^+ channel blockade after a cardiac action potential, which is a hallmark of bupivacaine, is considerably faster with ropivacaine.[15] Ropivacaine is used in 0.5% to 1.0% concentrations for surgical anesthesia. In clinical studies comparing potencies of ropivacaine and bupivacaine administered for brachial plexus or lumbar epidural block, the anesthetic profiles of the drugs were almost identical. Both 0.75% ropivacaine and 0.75% bupivacaine provide adequate surgical anaesthesia for lower abdominal surgery when administered epidurally. Ropivacaine is a well tolerated anaesthetic with an efficacy similar to that of bupivacaine and much higher than that of etidocaine. Indeed, studies have shown ropivacaine to have less cardiovascular and CNS toxicity than bupivacaine. Studies in human volunteers have shown that ropivacaine is associated with atleast 25% less CNS and cardiovascular adverse effects than bupivacaine. Ropivacaine seems to have the greatest margin of safety of all long-acting local anaesthetics at present. Thus ropivacaine with its efficacy, lower propensity for motor block and reduced potential for CNS toxicity and cardiotoxicity, is an important option for regional anaesthesia.

CONCLUSION

There were not many changes in the haemodynamics and incidence of side effects and requirement of vasoactive drugs were minimal.

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