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A Comparative study for post-operative pain relief after lumbar epidural block using 0.2% Ropivacaine with two different doses of Ketamine for lower abdominal and lower limb surgeries

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Abstract

Background & Objective: By conducting this study our motive was to use a Local Anaesthetic like Ropivacaine which is very potent at lower doses and at the same time being less neurotoxic and cardiotoxic and having lower propensity of motor blockade. Simultaneously choosing an adjuvant like Ketamine which is non-opioid thus avoiding all opioid related side effects like respiratory depression,pruritis,nausea and vomiting. Our objective was to give lumbar epidural blockade with Ropivacaine (0.2%) with two different doses of Ketamine (0.3 mg/kg and 0.5 mg/kg) in all lower abdominal and lower limb surgeries and to observe onset and duration of analgesia, quality of post-operative analgesia, hemodynamic changes, side effects and complications. **Methods:** This prospective study was carried out involving randomly allocated 60 patients scheduled to undergo elective surgeries of lower abdomen and lower limb. They were randomly distributed into following groups of 30 each. The Group 1 and Group 2 patients were given 5ml (0.2%) Ropivacaine with 0.3 mg/kg and 0.5 mg/kg preservative free Ketamine via lumbar epidural catheter post operatively. The level of postoperative pain was assessed up to 48 hours(h) at intervals of 1h, 2h, 3h, 4h, 5h, 6h, 12h, 24h and 48h following surgery, using visual analogue scale (VAS). Whenever the VAS score was 4 or above epidural was charged accordingly. **Results and Conclusion:** In our present study the VAS score average was significantly lower in group 2 in which we administered 5ml (0.2%) Ropivacaine + 0.5 mg/kg Ketamine than group 1 in which we administered 5ml (0.2%) Ropivacaine + 0.3 mg/kg Ketamine at different intervals up to 48 hours. It was found that difference in mean VAS scores was significant only after 4 hours. In group 1 at 4 hours the average VAS score was 2.53±1.479. In group 2 at 4 hours the average VAS score was 1.23±2.112. We Concluded that adding Ketamine (Preservative free) to Ropivacaine(0.2%) improves the Post-operative pain outcome without any systemic side effects.

Keywords: Ropivacaine, Ketamine, Lumbar Epidural, Visual analogue Scale(VAS).

INTRODUCTION

Lower abdominal and lower limb surgeries are associated with a significant post operative pain. It has been evident from previous research that neural block is of greater benefit in these cases if it is provided in continuous method. The standard post operative analgesic protocol in our institution is to give extradural injection of Bupivacaine and fentanyl. As we already know that these drugs have well known adverse effects, Bupivacaine is associated with cardiovascular side effects and fentanyl having effects like respiratory depression, pruritus, nausea and vomiting [1].

Ropivacaine is amide type local anaesthetic similar to Bupivacaine with regard to pain relief but it causes less motor blockade at lower concentrations. It can be a better option as it has reduced neurotoxic and cardio toxic side effects and its lower tendency for motor block. Increasing the dose of Ropivacaine is associated with an increased clinical efficacy. The greater safety margin of Ropivacaine allows its use in higher doses and concentrations as compared to Bupivacaine as well as risk of its systemic toxicity is also very less.

Similarly, Ketamine offers the possibility of good postoperative analgesia thus avoiding the use of extradural opioids and lowers the total doses of local anaesthetic which is frequently used [1].

Further-more, lower limb surgeries like total knee replacement and total hip replacement surgeries are commonly performed in old age patients who usually have comorbid conditions and are more prone

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to different complications.

MATERIALS AND METHODS

This randomized controlled prospective study was carried out involving 60 patients who were scheduled for elective surgeries of lower abdomen and lower limb. The inclusion criteria were both male and female patients belonging to ASA physical status 1 and 2 weighing between 40 and 80 kgs, in the age group ranging from 20 and 70 years.

The patients exclusion criteria were,refusal,bleeding diathesis,hemodynamically unstable patients,emergency surgeries,ASA physical status 3 and 4 patients, known case of hypersensitive reactions to local anesthetics, having coagulation disorders or on any anticoagulants. Any Local site infection at the proposed site of puncture for epidural catheterisation,undergoing various elective surgical procedures of lower abdomen and lower limb.

After the approval by the institutional ethical committee, written informed consent was obtained from all the patients before they are included in the study. They were randomly distributed in the following groups of 30 each:

Group 1: Post operatively patients were given 5ml (0.2%) Ropivacaine + 0.3 mg/kg Ketamine (preservative free) via lumbar epidural catheter.

Group 2: Post operatively patients were given 5ml (0.2%) Ropivacaine + 0.5 mg/kg Ketamine (preservative free) via lumbar epidural catheter.

The patients were instructed regarding the use of 100-mm visual analogue scale (VAS) for assessing the pain scores (where 0 mm means no pain and 100 mm means worst pain imaginable) at their preoperative visit.

Procedure

All the routine investigations like blood grouping and Rh typing, complete hemogram, electrocardiogram (for patients having age more than 40 years), X-ray chest, blood sugar(random) was done for all cases involved in the study. Pre-anaesthestic evaluation was done one day before the surgery. All patients were given tab. Alprazolam 0.25mg orally, tab. Ranitidine 150mg orally and tab. Metoclopramide 10mg orally on the night before surgery and 2 hours prior to surgery as premedication. An 18 gauge peripheral intravenous cannula was secured in one of the upper limb and adequate preloading was done.

Lower back of patients was painted with betadine povidone iodine, and chlorhexidine. Sterile drapes were placed. Planned needle insertion point was infiltrated with local anaesthetic. An extradural 18-gauge multi-eye catheter was placed at the L3–4 or L2–3 intervertebral space using a 16-gauge tuohy needle. The space was further checked by loss of resistance technique and simultaneously confirmed by the meniscus sign. After 5-7 cm of catheter was inserted in the epidural space, a test dose was given with 3 ml of 2% lignocaine and adrenaline (1:200000). The non appearance of tingling and numbness in the lower limbs and absence of an increase in heart rate was confirmed. After fixation of epidural catheter, patients was made supine and an injection of normal saline was given through the catheter was checked for its patency. Baseline blood pressure, pulse rate, and SpO2 were recorded.

Postoperatively, patients were shifted to recovery area. Patient's vitals were monitored and hemodynamic stability was confirmed, and visual analog scale (VAS) score was assessed before giving the respective drug mentioned in aim of our study.

5ml of 0.2% Ropivacaine with two different doses i.e. in group 1 (0.3 mg /kg) and group 2 (0.5mg/kg) of Ketamine (preservative free) along with normal saline was injected in patients via epidural catheter. The total volume of the injection in each group was made up to 10 ml with 0.9% saline making concentration of Ropivacaine as 1 mg/ml. Patients were observed in the recovery room for one hour for any hemodynamic changes and then shifted to the postoperative ward.

The level of postoperative pain was assessed upto 48 hours(h) at intervals of 1h, 2h, 3h, 4h, 5h, 6h, 12h, 24h and 48h following surgery, using visual analogue scale (VAS). Whenever the vas score was 4 or above epidural was charged accordingly.

Statistical Analysis

The Statistical Analysis was done with SPSS software (Statistical Package for the Social Sciences for windows Version 23.0). For categorical variables Chi-Square test was used. For paired samples Paired t test was used. Pearson's correlation coefficient was used to correlate to continuous data. P-value <0.05 is considered as statistically significant**.**

RESULTS

Age group of the study population was ranging from 20 to 70 years. The mean age of the population in group 1 and group 2 was 54.70±8.27 years and 53.60±9.53 years respectively. The p value was found to be 0.635 by applying independent samples'*t*' test, the which was statistically insignificant. The mean height of the patients in group 1 and group 2 was 157.10±9.083 cm and 157.10±9.083 cm respectively. The p value was found to be 0.803 by applying independent samples'*t*' test which was statistically insignificant. The mean weight of the patients in group 1 and group 2 was 58.17±9.010 kgs and 60.17±8.383 kgs respectively. The p value was found to be 0.432 which was statistically insignificant on applying independent samples'*t*' test. Therefore both the groups were comparable. Comparison of parameters like heart rate(HR),systolic and diastolic blood pressure(SBP/DBP), mean arterial pressure(MAP) and room air saturation via pulse oximetry (SpO2) of both groups as base line and after giving first epidural dose were statistically not significant.

The analysis of pain scores was done using students '*t*" test.

Table no. 1 showing statistical comparison of mean VAS scores at different intervals of time in group 1 and group 2.

Table 1: Table showing comparison of mean VAS scores between two Groups.

Time interval	Mean±SD		T-value	P-value
	(group 1) N=30	(group 2) N=30		
VAS 1hr	0.00±0.000a	0.00±0.000a	-	-
VAS 2hr	0.40±0.498	0.30±0.596	0.705	0.484
VAS 3hr	0.53±0.681	0.60±0.932	-0.316	0.753
VAS 4hr	2.53±1.479	1.23±2.112	2.761	0.008
VAS 5hr	1.90±1.807	0.87±1.502	2.408	0.019
VAS 6hr	1.70±1.643	0.67±0.758	3.128	0.003
VAS 12hr	4.10±1.494	3.03±1.790	2.506	0.015
VAS 24hr	4.00±0.983	3.03±1.377	3.130	0.003
VAS 48hr	2.40±1.522	1.00±1.339	3.782	<0.001

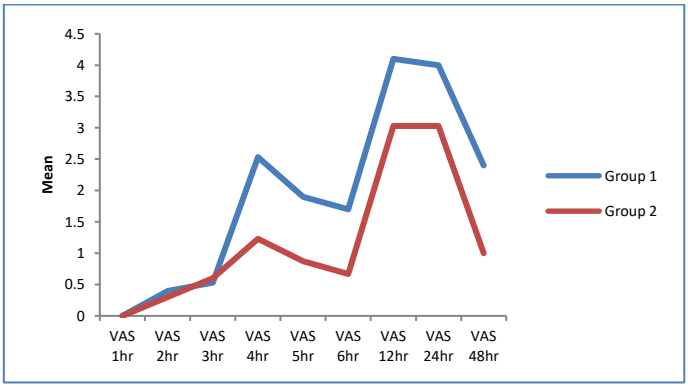

Figure 1: Line Graph showing Comparison of mean VAS scores between two groups.

VAS scores were insignificant at 1 hour,2 hours,3 hours. It was found significant only after 4 hour.

In group 1 at 4 hours the average VAS score was 2.53±1.479.

In group 2 at 4 hours the average VAS score was 1.23±2.112.

By statistical analysis, the p value and was found to be 0.008 which was statistically significant.

DISCUSSION

The primary aim of our study was comparing the post operative analgesia after lumbar epidural block using 0.2% Ropivacaine with two different doses of Ketamine(0.3mg/kg and 0.5mg/kg) for lower abdominal and lower limb surgeries, thus avoiding the frequently used combination of Bupivacaine and opioids like fentanyl,butrophenol etc. which are comparatively toxic and having more side effects and also to observe the onset and duration of analgesia achieved by increasing the dose of Ketamine added to Ropivacaine.

Both the Pt. groups were comparable as far as age, sex, height and weight are considered.

The distribution of patients among ASA physical status 1 and 2 was also comparable in both groups.

In our present study the VAS score average was significantly lower in group 2 in which we administered 5ml (0.2%) Ropivacaine + 0.5 mg/kg Ketamine(preservative free) via lumbar epidural catheter for post operative analgesia as compared to group 1 in which we administered 5ml (0.2%) Ropivacaine + 0.3 mg/kg Ketamine(preservative free) at different intervals up to 48 hours.

It was found that difference in mean VAS scores was significant only after 4 hour.

In group 1 at 4 hours the average VAS score was 2.53±1.479.

In group 2 at 4 hours the average VAS score was 1.23±2.112.

By statistical analysis, the p value was found to be 0.008 which was found significant statistically.

This was similar to study done by M sethi, N sethi, P. jain and J. sood in which Ketamine was added to mixture of Bupivacaine and morphine for postoperative epidural analgesia after upper abdominal surgery [17].

Patients in the groups 1 and 2 had no incidence of pruritus, nausea and vomiting. There was no significant difference between the two groups regarding hemodynamic variables like blood pressure and heart rate which were comparable to the study done by J shah and R parikh comparing the continuous epidural infusion of 0.1% Ropivacaine versus 0.125% Bupivacaine for the post-operative pain relief after total knee replacement surgery [18].

Psychomimetic effects which the most troublesome side-effects of Ketamine, were not seen in any of our patients which was similar to study done by P.S. weir and J. P. H. Fee comparing extradural block with three Bupivacaine-Ketamine mixtures in knee arthroplasty [1].

Using epidural analgesia for management of post operative pain has been evolving as popular and safe component of multimodal analgesia with an improved outcome.

Epidural analgesia also provides superior postoperative pain relief compared to the systemic opioids. In addition to the improved pain control, epidural analgesia also improve patient's outcome by attenuating the deleterious preoperative physiology [2, 3].

Combining Ropivacaine and Ketamine provides more effective analgesia than using Ropivacaine alone which is similar to bupivacaine regarding pain relief but it causes less motor blockade at low concentrations. It is also preferred option because of its reduced neurotoxic and cardio toxic potential and its lower propensity for motor block.

For more than 30 years Ketamine has been used as an analgesic and its mechanism of action was under dispute but it is now generally understood that one mechanism is specific that is binding to the phencyclidine site on the n-methyl-d-aspartate (NMDA) receptor ion channel and also its ability to produce a lamina specific suppression of dorsal-horn unit activity [4].

Some investigations also suggest that Ketamine acts as an opiate agonist [5, 6]. Despite the fact that opposing views exist [7]. Perhaps intrathecal administration, rather than epidural, would provide more effective results [8].

In other experimental studies, the NMDA receptor was found to play an important role in injury-induced spinal hypersensitivity [9]. This sensitization of the central nervous system may be responsible for significant postoperative pain. Different clinical and experimental studies have demonstrated that blocking of the NMDA receptor before or during injury may prevent and reduce the central sensitization.

It has been observed in the findings of other studies done before that NMDA receptor antagonists enhance the efficacy of other analgesics, such as morphine,NSAIDS and local anaesthetics.The mechanism of this potentiation can be the reduced tachyphylaxis to local anaesthetics and reduced development of tolerance to opioids. As an NMDA receptor antagonist, Ketamine may produce synergistic effects being a part of balanced treatment for allaying the postoperative pain.

Some authors also found that when Ketamine is given alone via epidural route it is a safe and effective for postoperative analgesia [10]. But some researchers have not found it to be adequate [11]. Concern has been raised regarding the potential psychomimetic side effects of ketamine if used in higher doses.

J islas, J astorga and M laredo reported that administering 4 mg Ketamine via epidural route is effective in controlling the postoperative pain following lower extremity or minor lower abdominal procedures but their sample size was small. If epidural Ketamine is effective following a major surgery, it would be more useful as there will be no respiratory depression and also there are chances of early mobilization of the patient [12].

M. aguib, Y. adu-gyamfi, G.H. absood, H farag and H.K. gyasi used epidural injection of ketamine with dose of 30 mg after cholecystectomy and considered it to be an effective and safe method [13].

On the other contarary, Ivankovich and McCarthy commented that its usefulness is doubtful following major surgical procedures like thoracotomy [14].

E. mankowitz, J.G. brock-utne, J.E. consnett Aand R. green-thompson also mentioned that giving epidural Ketamine in doses up to 50 mg, failed to provide satisfactory analgesia after surgery, despite their initial report regarding its effectiveness in relieving symptoms of chronic pain [15, 16].

The use of local anaesthetics is restricted by the duration of its action and the dosage dependant adverse effects on the cardiovascular and central nervous systems in discussing emerging trends according to A. swain, D. S. nag, S. sahu and D.P. samaddar.

Adjuvants or additives are utilised for their synergistic impact in local anaesthetics, increasing the length of the sensory- motor block and lowering the local anaesthetic cumulative-dose requirements. With the passage of time, the armaments of local anaesthetic adjuvants have changed from traditional opioids to a broad range of pharmaceutical drugs comprising several groups and different mechanisms of action.

A wide range of opioids have been utilised with diverse effectiveness ranging from morphine, fentanyl, sufentanyl, and hydromorphone, buprenorphine and tramadol. Their usage has however been restricted by their adverse effects, especially neuraxial use, such as respiratory depression, nausea, vomiting and itching.

The antinociceptive characteristics of Epinephrine, mediated by the alpha-2 adrenoreceptor activation and the vasoconstrictive properties which restrict the systemic absorption of local anaesthetics, potentiate local anaesthetics.

Alpha 2 adrenoreceptor antagonists are one of the most often utilised classes of local anaesthesia additives such as clonidine and dexmedetomidine. Different drugs have also been used such as steroids (dexamethasone), anti-inflammatory drugs (parecoxib and lornoxicam),ketamine,magnesium sullfate,midazolam and neostigmine.

Current investigation is aimed at finding drugs and procedures that would extend the local anaesthetic action without their negative repercussions. These include innovative forms like using charged compounds to produce local anaesthesic action (tonicaine and n-butyl tetracaine), new age delivery mechanisms for extended bioavailability (liposomal systems, microsphères and cyclodextrin), and more research of other drugs(neuromuscular blockers, dextrans and adenosine) [19].

CONCLUSION

This randomized prospective study were carried out on 60 patients of ASA physical status 1 and 2 scheduled for elective surgeries under lumbar epidural block. All 60 patients have been divided into two groups of 1 and 2; each group included 30 individuals.Post operatively patients in group 1 were given 5ml (0.2%) Ropivacaine + 0.3 mg/kg Ketamine(preservative free) and group 2 were given 5ml (0.2%) Ropivacaine + 0.5 mg/kg Ketamine(preservative free) via lumbar epidural catheter respectively.The demographic data like age, sex,weight and height was compared between the two groups.In statistical analysis student t test was used to compare and find out if any significant difference among the two groups is present. Regarding the age, sex, height, weight and baseline hemodynamic parameters like HR, SBP, DBP and MAP there was no significant difference and hence both the groups were comparable.Regarding the post operative VAS score, there is significant difference between both the groups only after 4 hours thus we can conclude that adding Ketamine for lumbar epidural analgesia increases the duration of post operative analgesia.There were no major changes in hemodynamic parameters like HR, SBP, DBP and MAP after giving the first dose for epidural analgesia in both the groups.None of the patients in both the groups in our study had any side effects and complications.

Conflict of Interest

We declare that we have no conflict of interest.

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None declared.

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