Comparison of Efficacy of Epidural Ropivacaine versus Bupivacaine for Postoperative Pain Relief in Total Knee Replacement Surgeries

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Abstract

Background: Epidural analgesia has become the standard of care for knee replacement surgeries worldwide. Bupivacaine has been used successfully for many years. Epidural ropivacaine is now being used increasingly and seems to have benefits other than just pain relief, in terms of a better safety profile. Aim: To compare the efficacy of bupivacaine 0.125% (Group B) versus two concentrations of ropivacaine 0.1% (Group R1) and 0.2% (Group R2), in terms of pain scores, requirement of rescue analgesia, related adverse effects, and duration of postoperative (PO) hospital stay. Materials and Methods: A retrospective study was conducted from the acute pain service data of patients who underwent joint replacement surgeries in one or both limbs, over a span of 6 months. Patients were allocated to and analyzed under one of the three groups based on the drug concentration used postoperatively by epidural infusion. Data retrieved were demographic data, daily average visual analog scale (VAS) pain scores, rescue analgesia given, adverse effects, and PO hospital stay days for all three groups. Results: Demographic data were comparable between the three groups. Daily average VAS pain scores on days 1 and 2 were significantly higher in Group R1. Groups B and R2 were comparable. There was significantly more requirement of rescue analgesia in Group R1 on day 1. Day 2 showed no significant difference in rescue analgesic requirement in all three groups. Days of PO hospital stay were significantly higher in Group R1. Adverse effects such as hypotension and delayed motor block were higher in Group B. Conclusion: Ropivacaine 0.2% and bupivacaine 0.125% were equally efficacious in terms of VAS pain scores, rescue analgesic requirement, and duration of PO hospital stay, but ropivacaine had a better safety profile in terms of less hypotension and lesser motor block.

Keywords: Bupivacaine, epidural analgesia, knee replacement, ropivacaine, visual analog scale

INTRODUCTION

Knee replacement surgeries have been increasing in recent times and have improved the quality of life in the geriatric population. The role of an anesthesiologist has also become more important, in terms of providing good postoperative (PO) analgesia, which in turn contributes to faster mobilization, minimizes PO complications, and eventually leads to faster discharge from hospital. With enhanced skills of surgeons and better equipment, the number of simultaneous bilateral total knee replacement surgeries have also increased which poses a further challenge to the anesthesiologist. Epidural analgesia has become a standard of care for such surgeries and is utilized by multiple modes of delivery including bolus injection, continuous injection, or patient-controlled infusion. Bupivacaine has been used successfully for many years for this purpose, in concentrations ranging from 0.0625% to 0.25%. Cardiac system and central nervous system (CNS) adverse effects related to bupivacaine have led to development of relatively safer drugs such as ropivacaine and levobupivacaine.

Although bupivacaine is still a popular drug in various centers, use of epidural ropivacaine has now increased significantly as it seems to have benefits other than just good pain relief, in terms of a better safety profile. There is very little information on ropivacaine and bupivacaine use for knee replacement surgery.
Materials and Methods
A retrospective analytical study was conducted from the acute pain service (APS) data of patients who underwent joint replacement surgeries in one or both limbs, in our tertiary care hospital. The study was conducted on patients operated over the past 6 months.

A total of 135 patients were initially included in the study. The study was considered in those patients who underwent unilateral or bilateral knee replacement surgery, in whom epidural analgesia was provided as the mode of PO pain relief.

The study sample was divided into three groups, based on the concentration of epidural local anesthesia (LA) received. The three groups were 0.125% bupivacaine (B), 0.1% ropivacaine (R1), and 0.2% ropivacaine (R2).

As per the departmental and APS protocol, after a thorough preoperative evaluation and ruling out any contraindications for neuraxial anesthesia, epidural catheters were inserted preoperatively just before giving subarachnoid block for surgery, either through combined technique (L2-3) or separately (L2-3). Epidural catheters were also used to supplement anesthesia in a few prolonged surgeries. Standard 16G catheters were used in all patients. Postoperatively, patients received an epidural infusion of LA through an elastomeric pump at a fixed rate of 5 ml/h, after giving test dose of 3 ml of 2% lignocaine with 1:200,000 epinephrine.

Fentanyl (2 µg/ml) was added to the LA in all patients. On the first PO day, all patients received intravenous (i.v.) paracetamol 8 hourly. Intramuscular diclofenac and i.v. tramadol were given for rescue analgesia. On the second PO day, patients received oral paracetamol 6 hourly and oral tramadol was given for rescue analgesia. Electrocardiogram, noninvasive blood pressure, and pulse oximetry were monitored during the epidural infusion. While mobilizing the patient in joint replacement ward, the infusion was stopped for that duration. The epidural catheter was removed after 48 h PO under aseptic precautions. Visual analog scale (VAS) pain scores were assessed and recorded every 4–5 h. Other related adverse effects such as hypotension and delayed motor recovery/paresthesia were also recorded. Hypotension was managed by fluid bolus and injection mephentermine 3 mg boluses if required.

Data was collected from the APS records. Demographic data included patient’s age and gender. Other data retrieved were daily average VAS pain scores, rescue analgesia given, complications/adverse effects, and PO hospital stay days (opioid-related side effects such as pruritus, nausea, and sedation were noted but not analyzed as fentanyl was added in all the patient groups).

Exclusion criteria included patients with significant heart, renal, and liver disease and/or patients in which catheter was removed before 2 days (any catheter-related events), where neuraxial technique failed and had to be converted to general anesthesia or where catheter insertion failed and only spinal anesthesia was given. A total of 128 patients were finally included in the study.

Statistical analysis was carried out using SPSS (Statistical Package for Social Sciences, Version 16.0. Chicago, SPSS Inc). A pilot study was conducted taking initial 10 patients from each group (B, R1, and R2). Taking 10 as a sample size in each group, and based on the mean VAS pain score at day 1, effect size was calculated as 0.657. Taking alpha error of probability as 0.05 and power required 95%, sample size was estimated to 39 in each group. Hence, a sample size of 45 in each group was selected to be appropriate for the study, considering further 10% as error correction and rounding up to next integer.

Data were presented as number percentages or mean ± standard deviation as appropriate. Level of significance was ascertained using Chi-square test, Kruskal–Wallis test, and Mann–Whitney test. \( P < 0.05 \) was considered significant, and \( P < 0.001 \) was considered highly significant.

Results
Demographic data
The mean age and sex distribution were comparable in all the three groups [Table 1].

Indication for surgery was osteoarthritis in majority of patients (77.3%), and distribution of indication for surgery was comparable in all three groups [Table 2].

Daily average visual analog scale pain scores
On day 1, significantly higher VAS score was observed in Group R1 compared to Groups R2 and B while Groups R2 and B had comparable average VAS scores \( (P = 0.114) \).

Table 1: Demographic data of sample group

| Parameters          | Drug group          | \( \chi^2 \) | \( P \) |
|---------------------|---------------------|-------------|--------|
|                     | B, \( n \) (%)      | R1, \( n \) (%) | R2, \( n \) (%) |       |
| Mean age (years):SD | 64.34±9.38          | 61.07±11.15  | 64.02±9.44 | 5.940  | 0.654 |
| Sex                 | 41                  | 44           | 43      |       |
| Male                | 15 (36.6)           | 14 (31.8)    | 15 (34.9) | 0.221 | 0.895 |
| Female              | 26 (63.4)           | 30 (68.2)    | 28 (65.1) |       |

Chi-square test: \( P<0.05 \) - significant. B=Bupivacaine 0.125%, R1=Ropivacaine 0.1%, R2=Ropivacaine 0.2%, SD=Standard deviation

Literature on comparisons between these two drugs, although a recent study has compared these two drugs for epidural anesthesia and PO analgesia in lower limb surgeries.\(^{12}\) Similar studies analyzing PO pain relief profile of the two drugs have shown results in favor of use of ropivacaine.\(^{9,10}\) The aim of the present study was to compare the efficacy of a standard, commonly used analgesic concentration of epidural bupivacaine (0.125%) versus two concentrations of ropivacaine (0.1% and 0.2%), in terms of patient pain scores, requirement of rescue analgesia, related complications, and duration of PO hospital stay.
On day 2, Group R1 again had significantly higher VAS score while Groups R2 and B showed no statistically significant difference [Figure 1].

**Requirement of rescue analgesia**

On day 1, 32% of all patients did not require rescue analgesia (only epidural infusion plus i.v. paracetamol QID). There was significant difference in the requirement of rescue analgesia ($P < 0.001$) between the three groups, with maximum requirement being in Group R1. Groups R2 and B were comparable in terms of requirement of rescue drugs [Figure 2].

On day 2, 85.9% of all patients did not require rescue analgesia (only epidural infusion plus oral paracetamol QID). No significant difference was found in the requirement of rescue analgesia between all three groups, $P = 0.539$ [Figure 3].

**Postoperative hospital stay**

Patients in the Group R1 had significantly higher number of days of PO hospital stay compared to Groups B and R2 ($P < 0.001$). Groups R2 and B had comparable days of PO stay, $P = 0.103$ [Figure 4].

**Adverse effects**

Incidence of hypotension was significantly higher in Group B (9.8%) compared to Group R2 2.3% ($P = 0.027$). Delayed motor block was observed in 7.3% patients in Group B compared to 2.3% in Group R2 ($P = 0.077$). In Group R1, none of these complications were observed [Table 3].

**DISCUSSION**

Literature has shown that epidural analgesia is more efficacious than systemic analgesia for PO pain relief in the lower limb orthopedic surgeries.$^{[1,13]}$ Choi et al. in their systemic review reported that patients receiving epidural analgesia in elective knee and hip surgeries had less pain at rest, especially in the first 4–6 h PO.$^{[1]}$ A continuous epidural infusion of LA with rescue doses is the most common mode of delivery although patient-controlled epidural analgesia appears to be the most cost-effective in this regard.$^{[9]}$ In the present study, only patients receiving a fixed epidural infusion of LA were included for the sake of standardization. Addition of an opioid drug to the LA infusion has proven to decrease pain scores and improve patient satisfaction.$^{[11,13,14]}$ In the present study, as per our APS protocol, fentanyl was added in the epidural infusion for all patient groups.

Bupivacaine has been a standard LA drug used for providing epidural analgesia and anesthesia in numerous scenarios including abdominal surgeries, lower limb surgeries, and even labor epidurals.$^{[1,6,10]}$ Although a very effective and satisfactory drug, apprehension and deviation away from its use have been seen due to rare but severe toxicity effects related to the cardiac system and CNS.$^{[7,15,16]}$ Ropivacaine is an amide group LA and is a pure left isomer.$^{[7,8]}$ It is less lipophilic compared to bupivacaine. This accounts for its reduced propensity to block larger myelinated motor nerve fibers and thus theoretically has better motor sensory differentiation.$^{[9]}$ This is also the

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**Table 2: Indications for knee replacement surgery**

| Diagnosis                      | Drug used | Total |
|--------------------------------|-----------|-------|
|                                | B, n (%)  | R1, n (%) | R2, n (%) |
| B/L knee OA                    | 32 (78.0) | 35 (79.5) | 32 (74.4) | 99 |
| Left knee OA                   | 2 (4.9)   | 3 (6.8)   | 5 (11.6)  | 10 |
| Right knee OA                  | 5 (12.2)  | 4 (9.1)   | 3 (7.0)   | 12 |
| Aseptic loosening right TKR    | -         | -         | 1 (2.3)   | 1  |
| B/L operated TKR, revision     | 1 (2.4)   | -         | -         | -  |
| Left infected knee prosthesis  | -         | -         | 1 (2.3)   | 1  |
| Right infected knee prosthesis | -         | 1 (2.3)   | -         | -  |
| Left knee JRA                  | -         | 1 (2.3)   | -         | -  |
| RA, B/L knee                   | 1 (2.4)   | -         | -         | -  |
| RA plus OA knee B/L            | -         | -         | 1 (2.3)   | 1  |
| **Total**                      | 41 (100.0)| 44 (100)  | 43 (100.0)| 128|

$\chi^2=15.994$, df=18, $P=0.593$. B=Bupivacaine 0.125%, R1=Ropivacaine 0.1%, R2=Ropivacaine 0.2%, OA=Osteoarthritis, B/L=Bilateral, TKR=Total knee replacement, RA=Rheumatoid arthritis, JRA=Juvenile RA

**Table 3: Incidence of adverse effects**

| Adverse effect                              | Drug used | $P$     |
|---------------------------------------------|-----------|---------|
| Hypotension                                 | B, n (%)  | R1, n (%) | R2, n (%) | $P$  |
|                                             | 4 (9.8)   | 0       | 1 (2.3)   | 0.027*|
| Delayed motor block                         | 3 (7.3)   | 0       | 1 (2.3)   | 0.077*|

Fisher’s exact test: *$P<0.05$ - not significant, *$P<0.05$ - significant.

B=Bupivacaine 0.125%, R1=Ropivacaine 0.1%, R2=Ropivacaine 0.2%

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**Figure 1: Daily average visual analog scale mean pain scores**

**Figure 2: Rescue analgesia requirement on day 1**
mechanism for its minimal potential to cause CNS and cardiac toxicity. Ropivacaine for epidural analgesia has generally been used in concentrations ranging from 0.1% to 0.3%. In our institution, it was used mainly in the concentration of 0.1% or 0.2% for knee replacement surgeries. Thus, we compared these two concentrations with the standard 0.125% bupivacaine.

In the present study, significantly higher average VAS scores were observed in Group R1 compared to Groups R2 and B on both days 1 and 2. Groups R2 and B had similar VAS scores. Bertini et al. in their study comparing 0.2% ropivacaine and 0.2% bupivacaine in hip replacement surgeries had similar findings, in terms of equal analgesic effect. Sitzen et al. also reported similar pain scores in all three groups, although, in our study, the 0.1% ropivacaine group had higher mean VAS scores, which is in keeping with the findings of Sawhney et al. Kanai et al. also reported significantly less maximal VAS scores in 0.2% ropivacaine with fentanyl, compared with 0.125% bupivacaine (without fentanyl).

In the present study, requirement of rescue analgesia on day 1 was significantly higher in Group R1. Requirements in Groups R2 and B were lower but comparable. Sawhney et al. brought out that 0.2% ropivacaine had the least rescue analgesia requirement compared to other groups. The difference from the present study was that fentanyl was not added in all the groups. Perhaps that is why in the present study, ropivacaine 0.2% and bupivacaine 0.125% were comparable. Khanna et al. in their study reported significantly higher rescue drug requirements in 0.1% ropivacaine-only group, although they compared it with 0.0625% bupivacaine with fentanyl. No significant difference was found in the requirement of rescue analgesia between all three groups on day 2, which suggests that epidural analgesia is perhaps most effective in the first 24 h PO.

Patients in the Group R1 had significantly higher number of days of PO hospital stay compared to Groups B and R2, which were comparable. There is not much literature regarding analysis of number of days of PO stay, but general consensus is that use of ropivacaine leads to faster recovery and shorter PO period in the hospital. Indirect evidence of this fact is also elicited by the low incidence of adverse effects such as delayed or prolonged motor block (which might delay ambulation) with bupivacaine as compared to ropivacaine. In the present study, delayed/prolonged motor block and hypotension were both observed to significantly higher in Group B compared to other groups. Unlike Group R1, none of these complications were observed. Most of the similar studies all report similar findings, except Sawhney et al. and Sitzen et al., where motor block was minimal and comparable in all groups.

**Limitations**

This was a retrospective study as data were retrieved from previous APS documents. A randomized experimental study would be ideal. Impact of opioids in terms of efficacy and adverse effects was not assessed as all groups received fentanyl. Analysis of total epidural LA consumption and cost-effectiveness was also not within the scope of this study.

**Conclusion**

Ropivacaine 0.2% and bupivacaine 0.125% were equally efficacious in terms of VAS pain scores, rescue analgesic requirement, and duration of PO hospital stay, but ropivacaine had a better safety profile in terms of less hypotension and lesser motor block. Hence, it is recommended as the current best possible choice for use in epidural analgesia preferably in combination with an opioid, for use in lower limb surgeries such as total knee replacement surgeries.

**Financial support and sponsorship**

Nil.

**Conflicts of interest**

There are no conflicts of interest.

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