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Efficacy of Epidural Ropivacaine with Fentanyl as Postoperative Analgesia in Total Knee Replacement Surgeries

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Abstract

Context: Ropivacaine is a new agent introduced recently which can provide differential blockade. It has been reported to produce greater degree of analgesia at the same time producing lesser motor blockade compared to bupivacaine. *Aims:* To compare the postoperative analgesia between 0.2% Ropivacaine with 4 mcg/ml of Fentanyl with 0.125% Bupivacaine with 4 mcg/ml of Fentanyl in knee joint replacement surgery. *Settings and design:* Present study was prospective randomized study carried out at SVS Medical College, Mahabubnagar. *Methods:* In this double blinded prospective study, 59 patients were selected and allotted into two groups, 30 in Group R and 29 in Group B by computer based randomised selection program. Combined spinal epidural technique was performed on the patient. After the completion of the surgical procedure when the patient complained of pain; basal pulse rate, mean arterial pressure, pain scores and degree of motor blockade were noted. *Statistical analysis:* Data was expressed as means and standard deviation and compared by using students t test. *Results:* The onset of action was significantly quick with ropivacaine i.e. 5.53 min compared to 6.96 min for bupivacaine; but there was no significant difference when time and duration of peak action was studied. Modified Bromage scale was used for measuring motor blockade and it was found that motor blockade was significantly less with ropivacaine group compared to the bupivacaine group. Both the agents were found to be comparable in terms of hemodynamic parameters. *Conclusion:* Ropivacaine in combination with fentanyl was found to be more effective than bupivacaine in same combination.

Keywords: Ropivacaine; Fentanyl; bupivacaine; patients; total knee replacement surgeries.

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Introduction

Management of post operative pain is important as this pain is likely to affect functioning of all organs. It can also contribute to increased morbidity and mortality. Management of post operative pain is a part of the post operative care. With recent advances in pharmacology, newer agents with potent action are becoming available [1].

But it is not easy to manage the post operative pain. It is necessary to manage the post operative pain effectively to make the patient comfortable and satisfied post operatively. This also enhances the recovery for the patient both physically and psychologically [2].

"The International Association for the Study of Pain [3] defines pain as, "the sensory and emotional experiences associated with actual or potential tissue damage."

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Pain affects the patient not only psychologically but also physically. Already there is damage to the tissues due to surgery. This leads to release of substances like histamine, substance P and prostaglandins. These irritants cause stimulation of the free nerve endings and lead to pain [4].

Many interacting factors influence the pain psychological aspects. These factors are fluctuating and dynamic. Pain is such thing which is subjective in nature hence there can not be single pain definition and hence can not be quantified. Anxiety and fear are associated with increased pain that is felt by the patient. Other factors like hospital facilities, attitude of the patient as well as doctor also influence [5].

Post operative pain can be managed by using variety of agents. Latest technique is to give the agent epidurally with intermittent bolus doses combined with continuous epidural infusion. Epidural narcotics not only reduce the post operative pain but also reduce the depression of central nervous system and also reduce irritation of the gastrointestinal tract compared to opioids given intravenously. Review of literature shows that infusion of epidural opioids is effective to manage the acute surgical pain [5].

The concept of differential blockade was coined after the bupivacaine was introduced. Bupivacaine causes sensory block only without affecting the motor activity whereas local anesthetics block both motor as well as sensory. This property of bupivacaine is especially found to be useful for those patients who undergo orthopedic surgery. This helps to mobilize early and leads to very good prognosis [6].

Ropivacaine has been recently introduced. This agent also provides differential blockade. The intensity of analgesia is more than that of Bupivacaine and the degree of motor blockade is less than that of Bupivacaine. At 0.75% concentration, Ropivacaine provides surgical anaesthesia. At 0.2% concentration, it provides pure analgesia. Another advantage of Ropivacaine over Bupivacaine is less cardiac toxicity [4].

This study purpose was to compare the postoperative analgesic effects between Ropivacaine with Fentanyl and Bupivacaine with Fentanyl in patients undergoing total knee replacement surgery.

Materials and Methods

Study population: ASA Grade 1 and 2 and patients of either sex

Study location: SVS Medical College, Mahabubnagar

Study period: 2016 – 2017

Type of study: Prospective randomized study

Number of groups: Two

Sample size: 30 in each group

Statistical test used: Student t-test unpaired.

Inclusion Criteria

1. Gender: Both Male and Female
2. ASA: I and II
3. Age group: 35-75 years of age.

Exclusion criteria

(a) Patients with coagulation abnormalities

(b) Systemic infection/ local infection at spinal site

(c) Neurological abnormalities

(d) Hypersensitivity to any of the drugs being used.

(e) Severe spinal deformity

(f) Increased ICP

(g) Patients who received intraoperative epidural top-ups and analgesics.

Study procedure: This study was conducted after getting due permission from the Institutional Ethical Committee and Scientific committee. Study sampling procedure and randomization to the two study groups: All consecutive patients undergoing Total knee replacement surgery during the study period were screened to evaluate if they met study inclusion criteria.

A study sample size of 60 patients (30 in each of the two study groups) was chosen as a convenience sample size as in patients undergoing total knee replacement.

Each patient was thoroughly assessed preoperatively to exclude the presence of any significant systemic illness other than the disease for which they had taken admission. The patients satisfying the study inclusion criteria were informed of the nature and purpose of the study, and written informed consent was obtained from the patients as in the informed consent form.

Preoperative assessment was done as per routine protocol for orthopaedic cases. A good history, thorough clinical examination and standard laboratory investigations were done

before proceeding further. For each patient a study proforma was completed as in.

Patients were randomly allocated to one of two treatment groups, each comprising 30 patients, by using computer-generated random numbers inserted into sealed envelopes marked 1–60. For each patient, an envelope was drawn randomly, and according to the number drawn, even numbers were allocated to study Group R and odd numbers were allocated to study Group B. The study solutions were prepared in a separate area by a person not involved in the patients' care, and the patients and anaesthesiologist were blinded to the study solutions.

Group R Ropivacaine (0.2%) 8 ml + 4 mcg/ml of Fentanyl was given epidurally.

Group B Bupivacaine (0.125%) 8 ml + 4 mcg/ml of Fentanyl was given epidurally.

Study epidural analgesia procedure

Prior to the procedure, a wide bore IV cannula was secured and patient were connected to standard monitors and vitals recorded. As per the hospital protocol, under aseptic conditions, in sitting position, after giving local infiltration with 5 ml of 2% Lignocaine in L2-L3 or L3-L4 space, epidural space identified using loss of resistance technique with 18G epidural needle. And with 25G Quincke's needle subarachnoid space identified and subarachnoid block given with 2.5 – 3 ml of 0.5% Bupivacaine Heavy. After subarachnoid block, epidural catheter was passed and fixed accordingly. Epidural test dose of 3 ml of 1.5% Lignocaine (45 mg) with 1 in 200000 Adrenaline was given to all patients in both groups to confirm the functioning status of epidural. Intraoperatively vitals were monitored and maintained. The patients who received intraoperative epidural top-ups and analgesics were also excluded from the study.

Study procedure in the postoperative period for measuring study outcomes In the postoperative period, whenever the patient complained of pain, study solutions were given accordingly and parameters recorded. Baseline pulse, heart rate, blood pressure, pain score, motor power were noted before the epidural injection. Thereafter heart rate (HR) and noninvasive mean arterial blood pressure (MAP) were measured at 5 min intervals initially for first 20 min and for every 15 min thereafter.

Study definitions

1. Clinically relevant bradycardia was defined as a decrease in HR of 50 bpm and was treated with atropine 0.5 mg IV.

2. Clinically relevant hypotension constituted a decrease of 20% or more in systolic blood pressure from baseline values and was treated with ephedrine 5 mg or mephentiramine 5 mg IV.

3. Arterial oxygen saturation was registered continuously by pulse oximetry.

4. Pain score noted using Wong-Baker's facies scale and Visual Analogue Scale.

5. Motor power was also recorded as per the Modified Bromage scale.

Modified Bromage Scale

Grade 1 was considered when the motor block was complete. Grade II when near to complete motor block and the patient was able to move only his feet. Grade III when the motor block was partial and the patient could move the knees. Grade IV when patient was able to raise leg but could not keep in that position. Grade V when patient could keep the leg raised for minimum of 10 seconds. Grade VI when there was no weakness.

Time was taken as zero i.e. at the time when epidural infusion was complete. Pain scale was used to note the time of onset of analgesia. Score was 0 or 1 when there was no pain. This time was taken as peak action time. In case the patient complained of pain, 50 µg of fentanyl was given.

Statistical analysis:

The data was presented as means and standard deviation. Students t test was used to compare the means between the two groups.

Observations and Results

Table 1 shows patient demographic characteristics. The mean age in Group R was 59.73 ± 7.04 with a range of 35–75 years, where as in Group B it was 61.13 ± 7.89, with a range of 35 - 75 years. There was no statistically significant difference between the two groups when compared by student's t- test (p value = 0.3580). Out of the 30 patients in Group R, 16 were males and 14 were females where as in Group B, out of 29, 16 were males and 13 were females. So total 32 out of 59, i.e. 54.23% were males and 27 out 59, i.e. 45.76% were females and the same was represented in the piediagram. Among the population selected, the mean weight was 70.56 ± 8.50 kg in group R; 70.82 ± 9.83 kg in group B. The difference between the two groups was not significant by student's t –test. (p value = 0.9135).

Table 2 shows study outcomes on Epidural Analgesic effects. The mean time of onset of analgesia in group R was 5.53 min when compared to group B which was 6.96 min. This is statistically significant when compared with student's t-test (p value = 0.0001). The peak of action that is "0-1" on pain score was 16.30 min in Group R and 17.03 min in Group B (p value = 0.1836). The average duration of action in group R was 74.17 min whereas in group B it was 71.51 min (p value = 0.3878). Both peak of action and duration of action are not significant when compared with student's t-test.

Table 3 shows comparison of pain score between the two groups. The pain score was assessed using Visual analogue scale and Wong Baker's facies scale. The mean value for Group R in VAS was 0.23 and in Facies scale it was 0.46 where as in Group B in VAS scale was 0.62 and in Facies scale it was 0.44. When compared using student's t-test, there was a significant difference between two groups with VAS (p value = 0.0042) and insignificant with facies scale (p value = 0.8883).

Table 4 shows comparison of additional need for analgesic supplementation with fentanyl in two groups. Among the 30 patients studied in each group, in group R no patients required fentanyl as additional supplementation while one required in group B. There was no statistical difference between the two groups as assessed by the unpaired student's t-test.

Table 5 shows comparison of Haemodynamic parameters and other complications in both the groups. The mean value of baseline pressure (MAP) before giving the topup/bolus in both the groups

Table 1: Patient demographic characteristics

Demographic characteristics	Group R	Group B	p value
Age (years)	59.73 + 7.04	61.13 + 7.89	0.3580
Sex (M/F)	16/14	16/13	
Weight (kg)	70.56 + 8.50	70.82 + 9.83	0.9135

Table 2: Study outcomes on Epidural Analgesic effects

Outcome	Group R	Group B	p value
Time of onset of analgesia (min)	5.53 + 1.13	6.96 + 1.34	0.0001
mean time of peak action (min)	16.3 + 1.46	17.03 + 2.57	0.1836
Mean time of duration of action (min)	74.17 + 12.04	71.51 + 11.35	0.3878

Table 3: Comparison of pain score between the two groups

Pain score	Group R	Group B	p value
Mean VAS	0.23+0.5	0.62+0.49	0.0042
Mean Facies scale	0.46+0.5	0.44+0.5	0.8883

Table 4: Comparison of additional need for analgesic supplementation with fentanyl in two groups

	Group R	Group B	p value
Requiring fentanyl	0	1 + 0.61	0.3142

Table 5: Comparison of Haemodynamic parameters and other complications in both the groups

Time intervals	Heart rate (mean + SD)			Mean arterial pressure (mean + SD)		
	Group R	Group B	P value	Group R	Group B	p value
Baseline	75.56 + 8.48	81.34 + 10.9	0.0267	94.73 + 12.76	91.86 + 10.88	0.0014
5 min	78.3 + 11.05	87.03 + 13.98	0.3525	87.03 + 13.61	89.34 + 11.44	0.4838
10 min	75.3 + 8.12	77.34 + 9.59	0.3879	79.36 + 11.27	83.06 + 10.91	0.2058
15 min	74.03 + 8.97	75.65 + 9.71	0.5079	71.36 + 9.35	79.86 + 9.96	0.0013
20 min	73.76 + 9.83	73.72 + 9.79	0.9868	71.73 + 9.45	73.75 + 6.89	0.3525
30 min	73.93 + 9.49	73.31 + 9.86	0.8056	73.1 + 8.49	72.31 + 7.69	0.07099
45 min	73.8 + 9.76	74.51 + 8.66	0.7668	75.06 + 8.81	72.13 + 8.9	0.2094
60 min	74.5 + 9.11	74.4 + 7.5	0.9811	77.23 + 8.52	76.31 + 6.9	0.6567
90 min	74.96 + 8.72	75.96 + 6.78	0.6262	80.13 + 6.78	77.37 + 6.85	0.2148
120 min	77.23 + 9.95	75.96 + 6.74	0.5705	81.9 + 10.34	78.65 + 6.28	0.1524

Table 6: Comparison of motor activity

	Group R	Group B	p value
Peak Modified Bromage score (mean)	5.06 + 0.44	4.75 + 0.51	0.0169

was calculated. There was significant difference in both the groups p value = 00.14. Then mean values for every 5 min till first 20 min later on for every 15 min for up to 120 min were recorded by using Student's t-test, the mean value of mean arterial pressure in both groups was found insignificant except at 15 min interval where it was significant (p value = 0.0013.)

The mean basal heart rate (at time 0) was compared between the two groups. There was significant statistical difference between the two groups p = 0.0267. The mean values of the heart rate calculated thereafter showed no significant difference throughout the procedure.

Table 6 shows comparison of motor activity. The mean of the peak Modified Bromage score in group R was 5.06 and in group B was 4.75. By Student's t-test, there was significant difference between the two groups (p = 0.0169).

Discussion

As compared to other surgeries, the early mobility is more desirable in knee replacement surgeries in order to avoid quadriceps weakness which can lead to prolonged immobilisation and its complications. In this series of studies, we compared 0.2% Ropivacaine with 4 mcg/ml of Fentanyl with 0.125% Bupivacaine with 4 mcg/ml of Fentanyl. The selection of the concentrations of drug depend on the pharmacodynamic properties of these drugs. At this concentration, these drugs selectively block the sensory nerve fibers sparing the motor fibers totally or partially. This selective blockade of sensory fibers is called differential blockade. When time of onset is compared, there is extremely significant difference between the two groups. Time of onset of action in Ropivacaine with fentanyl is 5.53 min whereas in Bupivacaine with Fentanyl is 6.96 min (p value = 0.0001).

When duration of action is compared, in this study duration of action in ropivacaine with fentanyl is 74.17 min and in bupivacaine with fentanyl group it is 71.51 min which is statistically insignificant (p value = 0.3878). McGlade DP et al. [7] reported that duration of action in their comparative study between 0.5% ropivacaine and 0.5% bupivacaine in lumbar epidural anaesthesia for lower limb orthopaedic surgeries was statistically insignificant. The duration of action in Ropivacaine group is 3.5 hrs and in Bupivacaine group is 3.4 hrs. Manjushree et al. [8] also stated that there is no statistically significant difference in duration of action in their studies when 0.25% of Bupivacaine is compared with 0.25% of Ropivacaine in caudal epidural analgesia.

When potencies and motor blockade are compared, in this study in both groups, Ropivacaine with fentanyl group is more potent and causes less motor blockade when compared with the other group. Visual analogue scale in Ropivacaine group is 0.23 whereas in Bupivacaine group it is 0.62 indicating that ropivacaine group is more potent (p value = 0.0042). This was supported by other studies. McGlade et al. [7] reported that in Ropivacaine group, sensory blockade is 78% satisfactory when compared to 71% in Bupivacaine group. Pitimana-aree et al. [9] showed in their comparative studies between 0.0625% Bupivacaine with 3 mcg/ml of fentanyl and 0.15% ropivacaine in total knee replacement surgeries, there is no statistical significant difference between two groups when degree of analgesia is compared. Manjushree et al. [8] also stated that there is no statistical difference between the two groups when degree of analgesia is considered.

Fernandez et al. [10] in their study, when compared between epidural 0.0625% bupivacaine with 2 mcg/ml of fentanyl and 0.1% Ropivacaine in labor analgesia stated that the degree of analgesia and patient satisfication is more in bupivacaine and fentanyl group. When degree of motor blockade is compared, in this study using Modified Bromage scale, the score is high i.e. 5.06 when compared to the score in bupivacaine group i.e. 4.75 indicating that Ropivacaine with Fentanyl group produces less motor blockade but statistically insignificant (p value = 0.0169). This was supported by studies like McGlade et al. [7] and Manjushree et al. [8] In these studies, it was proven that the motor blockade is less with ropivacaine group when compared to bupivacaine group.

When hypotension is compared, there is statistical significant difference present between the two groups, when mean arterial pressure at baseline and at 15 min interval mark is considered. The mean value of mean arterial pressure at baseline in Group R is 87.03 mmHg and in Group B it is 97.86 mmHg with p value equals to 0.0014. The mean value of mean arterial pressure at

baseline in Group R is 71.36 mmHg and in Group B it is 79.86 mmHg with p value = 0.0013. When complications like bradycardia, nausea, vomiting, pruritis, etc are compared, there is no statistically significant difference between the two groups. This was supported by studies like McGlade et al. [7] and Manjushree et al. [8] Only one study contradicted this finding.

Pitimana-aree et al. [9] in their studies found that complications like pruritis, nausea, vomiting are more in Bupivacaine and Fentanyl group in comparison to Ropivacaine group. The p value in this study is equal to 0.015. The reason for this contradiction is in that study they compared bupivacaine with Fentanyl and plain Ropivacaine. McGlade et al. [7] Pitimana-aree et al. [9], Fernández-Guisasola J et al. [10], Manjushree et al. [8] gave similar findings.

Conclusion

Ropivacaine with Fentanyl appears to be more rapid in onset of action, produces more potent analgesia, less motor blockade. These study findings can be confirmed, explored further by increasing the sample size and to the patients undergoing other surgical procedures.

Key Messages

Ropivacaine in combination with fentanyl can be used among patients who undergo total knee replacement.

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