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COMPARISON OF ANALGESIC EFFECT OF EPIDURAL ROPIVACAINE (0.2%) AND ROPIVACAINE (0.2%) WITH FENTANYL (4mcg/ml) IN POST OPERATIVE PATIENT OF TOTAL KNEE REPLACEMENT SURGERY

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Key words:

Analgesia, Ropivacaine, Fentanyl, Knee replacement surgery.

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ABSTRACT: Introduction: Epidural anesthesia is the most commonly used technique for providing not only peri-operative surgical anesthesia but post-operative analgesia in lower abdominal and limb surgeries. Our study aimed to assess the comparison between ropivacaine(Group A) and combination of ropivacaine with fentanyl (Group B) in terms of their analgesic effect, hemodynamic stability, side effects and requirement of rescue drug in post operative patient of total knee replacement surgery. **Materials and methods**: After surgery, Pulse rate, systolic and diastolic blood pressure, Sp02, visual analogue score and requirement of other analgesics was studied at every 30 minutes for 2 hrs, then hourly up to 12 hrs and every 2 hourly thereafter up to 24 hrs in group A and Group B. Patients were also observed for side effects. Statistically significant when the $p < 0.05$ and highly significant if $p < 0.001$. **Results:** In our study, there was no significant difference amongst the groups in respect to age, sex distribution, height and ASA physical status. There was no statistically significant difference in pulse rate, blood pressure and SpO2 at baseline between the two groups. In our study we observed that VAS scores were found to be better at all time during 24 hours observation in group B. No difference was found between the two groups, in terms of other side effects. **Discussion:** We observed that the need for rescue analgesia required higher in group A. So in our study requirement of rescue drug was significantly less with addition of fentanyl. In conclusion, our study has demonstrated that addition of fentanyl to ropivacaine decreased postoperative pain with stable vital signs in patients undergoing total knee replacement surgery, as compared to ropivacaine alone. Also the need for rescue analgesia was decreased with Group B.

INTRODUCTION: Management of postoperative pain is one of the most challenging and gratifying domains of anaesthesia. Any method of postoperative analgesia must meet three basic criteria: it must be effective, safe and feasible. Despite advances in knowledge of pathophysiology of pain, pharmacology of analgesics and development of effective techniques for postoperative pain control, many patients continue to experience considerable discomfort [1].

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The majority of patients after surgery managed with parenteral drugs are left with unrelieved pain[2]. Epidural anesthesia is the most commonly used technique for providing not only peri-operative surgical anesthesia but post-operative analgesia in lower abdominal and limb surgeries [3].

Total knee replacement is one of the most commonly performed surgeries. Epidural anesthesia provides dynamic analgesia, allowing patient to resume normal activities unlimited by pain [4].

Even though Bupivacaine, the ideal local anaesthetic, is popularly used in epidural space for analgesia the fear of inadvertent injection of the drug intravascular and it resulting in cardiac arrest which is difficult to resuscitate made us look at

other drugs [5, 6]. Ropivacaine, the recently introduced long acting amide local anaesthetic derived from Bupivacaine is claimed to have lesser cardiovascular side effects due to it being a S-enantiomer [5-8]. It is said to be better in its cardiovascular profile as patient can be revived from cardiovascular side effects much faster and with better outcome than when it occurs with Bupivacaine [8-10]. In the quest for searching the ideal drug for epidural space, Ropivacaine, an enantiomer of Bupivacaine was introduced recently [5, 6, 8, 9]. It is said to have similar pharmacological profile as that of Bupivacaine but with much better safety margin.

However, epidural local anaesthetic drugs administered alone have never become widely used for routine postoperative analgesia because of the significant failure rate resulting from regression of the sensory block and the unacceptable incidence of motor blockade and hypotension [11]. A variety of adjuvant may be added to epidural infusions to enhance analgesia while minimizing the side effects and these include mainly Opiates, Ketamine, Benzodiazepines etc. But no single drug has proved to be devoid of any side effect. So, search for an ideal adjuvant still continues that could result in reliable prolongation of postoperative pain relief without side effects[12].

Many a time for achieving desired peri-operative anaesthetic effect, invariably large volumes of local anaesthetic are used, thereby increasing the possibilities of local anaesthetic toxicity and deleterious hemodynamic consequences [9, 10]. The new amide local anaesthetic ropivacaine has minimal cardio-vascular and central nervous system toxicity as well as a lesser propensity of motor block during post-operative epidural analgesia [5, 9]. Opioids like fentanyl have been used traditionally as an adjunct for epidural administration in combination with a local anaesthetic to achieve the desired anaesthetic effect. The addition of opioid does provide a dose sparing effect of local anaesthetic and superior analgesia but there is always a possibility of an increased incidence of urinary retention, nausea, vomiting and respiratory depression.[13 14, 15]. So our study aimed to assess the comparison between ropivacaine and combination of ropivacaine with fentanyl in terms of their analgesic effect, hemodynamic stability, side effects and requirement of rescue drug in post operative patient of total knee replacement surgery.

MATERIALS AND METHODS:

This study titled by ―comparison of analgesic effect of epidural ropivacaine (0.2%) and ropivacaine (0.2%) with fentanyl (4mcg/ml) in post operative patient of total knee replacement surgery was conducted at sterling hospital, Ahmedabad which is a NABH (national accreditation board for hospitals and health care providers) 290 bedded tertiary care centre. This observational study conducted after obtaining approval from the institutional ethical and scientific committee and written informed consent. The study was done on 60 ASA I and II adult patients ranging from 45-75 years of age and from both sexes. Of the total 60 patients, we have used ropivacaine (0.2%) in 30 patients and ropivacaine (0.2%) with fentanyl (4mcg/ml) in rest of the 30 patients. Patients in whom ropivacaine was used are included in group A and ropivacaine with fentanyl in group B.

Group A	epidural ropivacaine (inj. Ropivacaine 0.2%) at 6 ml/hr
Group B	epidural ropivacaine with fentanyl (inj. ropivacaine 0.2% plus 4mcg/ml fentanyl) at 6 ml/hr

All patients were subjected to pre-anesthetic assessment in detail through history taking and physical examination day before surgery. The patient‘s age, sex, height, and vital data including pulse rate, systolic and diastolic blood pressure and spo2 were noted. Relevant investigations were carried out and recorded in all cases. Patients were informed in general terms regarding the procedure of the study. The informed consent was obtained from patient preoperatively as per hospital rules and regulations. All patients were fasted for 8 hrs.

Exclusion criteria:

1. Patient‘s refusal for procedure
2. Infection at puncture site
3. Bleeding disorders
4. Allergy to study drugs

5. A history of opioid dependence or sedative drugs.

Anaesthetic technique:
Under due aseptic and antiseptic precautions and with patient in sitting position, a skin wheal was raised at L3-L4 inter space with 2cc of 1% lignocaine. The epidural space was identified using a 18G touhy needle in the midline with loss of resistance to air technique. Subarachnoid block was performed by removal of spinal needle stilette and with appearance of free flowing and clear CSF, Inj. Bupivacaine 0.5 % heavy 3 ml (15mg) was given slowly. The anesthesiologists performing the block recorded the intra-operative data and a nurse followed the patients post-operatively until discharged from the post-anesthesia care unit (PACU).

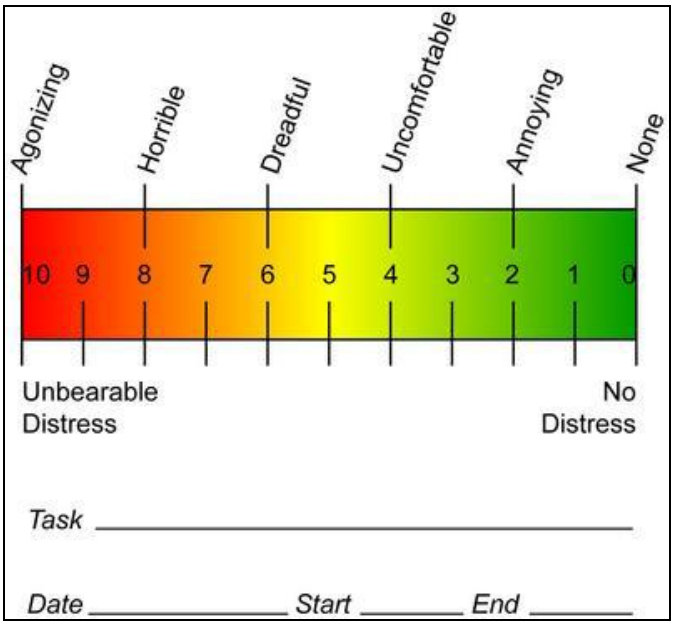
Postoperative observation:
After completion of surgery all patients were shifted to the recovery room, supplemental intravenous fluid was continued. Pulse rate, blood pressure, Sp02, regression time for sensory and motor block were recorded in PACU.

Epidural infusion with inj. ropivacaine 0.2% (6ml/hr) in group A and inj. ropivacaine 0.2% plus 4mcg/ml fentanyl (6 ml/hr) in group B was started once sensory level of the subarachnoid block regresses to T12 dermatome level. The regression of the sensory block was assessed by the loss of pinprick method using a blunt 21-gauge needle in a cephalic-to-caudal fashion along the left anterior axillary line.

Pulse rate, systolic and diastolic blood pressure, Sp02, visual analogue score and requirement of other analgesics was studied at every 30 minutes for 2 hrs, then hourly up to 12 hrs and every 2 hourly thereafter up to 24 hrs. Patients were also observed for side effects like nausea, vomiting, bradycardia, hypotension, sedation, shivering, motor blockade, respiratory depression, and urinary retention.

Pain assessment:
Visual Analogue Scale (VAS) was used to assess the intensity of pain and pain relief. This scale consisted of a 10 cm line, marked at 1cm each, on which patient expresses the degree of pain by placing a point. Mark ―0‖ represents no pain and mark ―10‖ represents worst possible pain. It was assessed initially at every 30 minutes for 2 hrs, then hourly up to 12 hrs and every 2 hourly thereafter up to 24 hrs.

Visual analogue scale:



0—No pain 1, 2, 3—Mild pain 4, 5, 6—Moderate pain 7, 8, 9—Severe pain 10—worst pain ever felt.

Modified Bromage scale used to assess any motor block.

Scale		Degree of block
0	Free movement of legs and feet with ability to raise extended legs	None
1	Inability to raise extended leg and knee flexion is decreased, but full flexion of feet and ankle present	Partial – 33 %
2	Inability to raise legs or flex knee, flexion of ankle and feet is present	Partial - 66%
3	Inability to raise leg, flex knee or ankle or move toes	Complete paralysis

Fall of >20% in the systolic Blood Pressure & pulse rate from the baseline value were considered as hypotension and bradycardia respectively.

Limitations and ethical issues:
The study being an observational study, randomization of data and blinding of observer could not be conducted. This may have led to bias

like observer bias or selection bias thus decreasing the validity of the study.

The study was conducted at a single centre only so results cannot generalize as the sample size is small.

Statistical analysis:

The sample size was determined based on the ability to detect a difference in the primary outcome variable and pain score was assessed with VAS. Various article published in journals were also considered for deciding appropriate sample size. Data are presented as mean and standard deviation for continuous values or median with inter quartile range for discontinuous values. For continuous variables, independent sample unpaired t test or Mann-Whitney rank sum test was employed to compare the inter group differences, and chi square test was adopted for categorical variables. The difference was regarded as statistically significant when the $p < 0.05$ and highly significant if $p < 0.001$.

The statistical software namely statistical package for social sciences (SPSS) 15.0 and software EPI INFO 7.0 Data Entry: Student's *t*-test was used for analysis of data.

Observation and results:

After obtaining approval from the institutional ethical and scientific committee and written informed consent from all patients, 60 patients of ASA grade 1 and 2 undergoing total knee replacement surgery at Sterling hospital, Ahmedabad were studied. They were divided into two groups and received following drugs.

Group A	epidural ropivacaine (inj. ropivacaine 0.2%) at 6 ml/hr
Group B	epidural ropivacaine with fentanyl (inj. ropivacaine 0.2% plus 4mcg/ml fentanyl) at 6 ml/hr

All the patients were observed for up to 24 hours post operatively and the following results were recorded.

TABLE 1: DEMOGRAPHIC CHARACTERISTICS OF PATIENTS AMONG THE GROUPS

Variable	Group A	Group B	p value
Age (yrs)	64.1±7.89	62.9±6.82	0.52
Sex (M/F)	14/16	13/17	0.629
Height (cm)	164±6.23	163±5.74	0.72
ASA grade (1/2)	8/22	10/20	0.273

P value is >0.05- not significant

There was no significant difference amongst the groups in respect to age, sex distribution, height and ASA physical status (P > 0.05%).

TABLE 2: CHANGES IN PULSE RATE

	Group A	Group B		
Time	Mean ± SD	Mean ± SD	p Value	Inference
Baseline	84.2±5.5	83.9±6.25	0.86	NS
15min.(intraop)	80.8±4.92	81.1±5.40	0.82	NS
30 min.	79.13±4.57	78.9±5.35	0.84	NS
45 min.	79.5±4.26	78.2±4.42	0.28	NS
1 hr.	79.4±4.69	80.03±5.16	0.62	NS
30 min.(postop)	80.7±4.31	79.7±5.40	0.43	NS
1 hr.	80.57±4.91	80.3±4.68	0.82	NS
1.30 hr.	81.1±4.86	81.7±5.86	0.68	NS
2 hr.	82±5.04	82.47±5.20	0.73	NS
3 hr.	83.2±5	81.97±5.01	0.33	NS
4 hr.	83.4±5.23	81.43±6.29	0.20	NS
5 hr.	82.37±4.36	80.63±5.97	0.20	NS
6 hr.	82±4.03	80.2±6.46	0.20	NS
7 hr.	83.1±4.45	80.8±6.15	0.10	NS
8 hr.	83.47±5.41	81.1±6.41	0.13	NS
9 hr.	82.5±4.58	79.8±6.57	0.07	NS

10 hr.	81.97±4.26	81.17±5.03	0.53	NS
11 hr.	82.6±5.42	80.5±5.98	0.14	NS
12 hr.	82.43±5.26	79.6±6.33	0.064	NS
14 hr.	82.9±5.29	80.37±5.76	0.081	NS
16 hr.	81.63±5.39	79.07±6.03	0.087	NS
18 hr.	81.8±4.75	79.2±5.86	0.064	NS
20 hr.	80.73±5.37	79.17±6.06	0.29	NS
22 hr.	80.27±5.50	78.8±6.16	0.33	NS
24 hr.	81.5±5.45	79.5±6.43	0.18	NS

NS – Not significant

As shown in **Table 2** there was no statistically significant difference in pulse rate at baseline between the two groups. Postoperatively also there was no statistically significant difference observed for 24 hours (p >0.05).

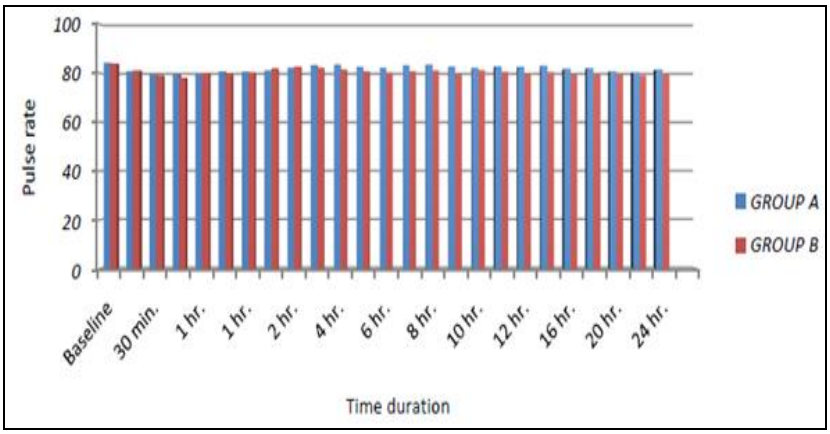


FIG. 1: CHANGES IN PULSE RATE

TABLE 3: CHANGES IN SYSTOLIC BLOOD PRESSURE

	Group A	**Group B**		
Time	Mean ± SD	Mean ± SD	p Value	Inference
Baseline	127.3±5.99	128.1±5.98	0.61	NS
15min.(intraop)	117.73±6.65	120.2±6.44	0.16	NS
30 min.	114.93±6.33	117.07±5.84	0.18	NS
45 min.	116±5.14	118±4.54	0.24	NS
1 hr.	119.4±4.19	120.6±5.09	0.31	NS
30 min.(postop)	122±4.26	121.6±4.26	0.43	NS
1 hr.	123±3.24	122.5±4.02	0.60	NS
1.30 hr.	124±3.69	123.4±3.54	0.78	NS
2 hr.	126±4.03	125±4.36	0.30	NS
3 hr.	126.6±4.8	125.6±3.65	0.38	NS
4 hr.	126±4.72	124.4±5.28	0.16	NS
5 hr.	125±4.42	123.7±5.57	0.18	NS
6 hr.	124.5±4.35	122.37±5.14	0.093	NS
7 hr.	125.1±4.64	122.8±6.00	0.093	NS
8 hr.	123.5±4.24	121.57±5.62	0.14	NS
9 hr.	123±3.89	121±5.73	0.10	NS
10 hr.	124±5.61	121.8±6.13	0.17	NS
11 hr.	124±5.58	122±6.89	0.093	NS
12 hr.	122±5.53	120.3±6.20	0.27	NS
14 hr.	121.8±6.09	120.8±5.19	0.50	NS
16 hr.	121±6.04	119.47±5.85	0.22	NS
18 hr.	120.6±6.21	119.2±5.98	0.39	NS
20 hr.	122±6.43	119.8±5.86	0.28	NS
22 hr.	121±6.54	120±5.91	0.29	NS
24 hr.	121±6.33	119±6.49	0.18	NS

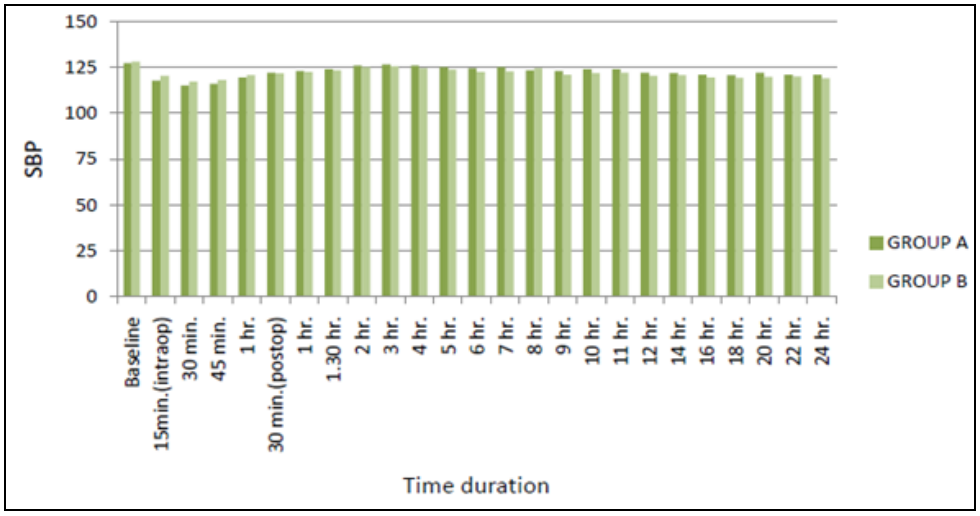


FIG.2: CHANGES IN SYSTOLIC BLOOD PRESSURE

NS – Not significant

Systolic blood pressure was comparable between groups before intrathecal injection of drugs and intraoperatively. In postoperative period for 24 hours observation systolic blood pressure was comparable between two groups. The mean systolic blood pressure was not significantly different between two groups, though ropivacaine with fentanyl group showed slight fall in blood pressure at all time points.

TABLE 4: CHANGES IN DIASTOLIC BLOOD PRESSURE

	Group A	**Group B**		
Time	Mean ± SD	Mean ± SD	p Value	Inference
Baseline	82.3±6.49	82.37±6.11	0.98	NS
15min.(intraop)	75.6±4.84	75.3±5.98	0.83	NS
30 min.	73.3±4.32	72.13±5.24	0.35	NS
45 min.	74.4±4.16	73.7±4.34	0.53	NS
1 hr.	76.4±4.70	76.1±6.02	0.83	NS
30 min.(postop)	78.3±4.59	77.13±4.64	0.35	NS
1 hr.	78.9±3.85	78.57±4.49	0.78	NS
1.30 hr.	79.6±4.03	79.67±4.13	0.97	NS
2 hr.	82±4.3	81±4.68	0.40	NS
3 hr.	82.3±4.64	82±4.89	0.46	NS
4 hr.	81.7±4.38	79.77±5.39	0.13	NS
5 hr.	80.5±3.74	78.77±5.48	0.16	NS
6 hr.	79.83±4.08	77.83±5.42	0.11	NS
7 hr.	81.17±4.53	78.83±6.07	0.097	NS
8 hr.	79.23±4.26	77.63±5.29	0.2	NS
9 hr.	78.8±3.85	76.4±5.56	0.06	NS
10 hr.	79.6±4.43	77.3±5.74	0.09	NS
11 hr.	79.8±5.43	77.2±5.84	0.072	NS
12 hr.	77.6±5.12	76.23±5.89	0.34	NS
14 hr.	76.97±5.86	76.2±5.32	0.60	NS
16 hr.	76.5±5.58	75.23±5.56	0.38	NS
18 hr.	76.8±5.29	75.37±5.63	0.31	NS
20 hr.	77.6±5.95	75.47±5.59	0.66	NS
22 hr.	77.3±5.65	75.3±5.68	0.18	NS
24 hr.	77.4±5.49	75±5.86	0.11	NS

As shown in **Table 4** diastolic blood pressure was comparable between two groups. There were no statistically significant differences observed in diastolic blood pressure between two groups.

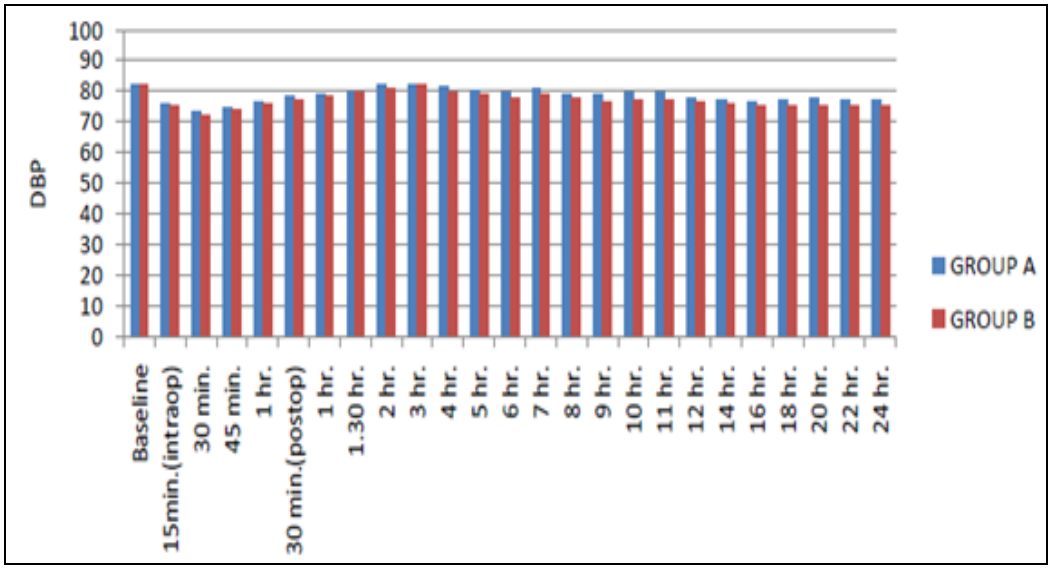


FIG.4: CHANGES IN DIASTOLIC BLOOD PRESSURE

NS – Not significant

TABLE 5: CHANGES IN SpO_2

	Group A	Group B		
Time	**Mean ± SD**	**Mean ± SD**	**p Value**	**Inference**
Baseline	98.2±0.76	98.1±0.73	0.73	NS
15min.(intraop)	98.3±0.70	98.0±0.83	0.14	NS
30 min.	98.0±0.74	98.1±0.78	0.74	NS
45 min.	97.9±0.81	97.9±0.88	0.88	NS
1 hr.	97.9±0.80	98.0±0.89	0.76	NS
30 min.(postop)	97.87±0.86	98.0±0.86	0.37	NS
1 hr.	98.0±0.87	98.03±0.89	0.88	NS
1.30 hr.	98.37±0.76	98.23±0.82	0.52	NS
2 hr.	98.07±0.94	97.9±0.97	0.52	NS
3 hr.	98.1±0.94	97.8±0.92	0.27	NS
4 hr.	98.0±0.91	97.9±0.9	0.57	NS
5 hr.	98.1±0.88	98.0±0.87	0.66	NS
6 hr.	97.8±0.80	97.93±0.87	0.54	NS
7 hr.	98.0±0.79	97.86±0.73	0.50	NS
8 hr.	98.03±0.85	97.93±0.78	0.64	NS
9 hr.	98.0±0.83	97.8±0.85	0.36	NS
10 hr.	98.1±0.80	97.93±1.0	0.39	NS
11 hr.	98.1±0.78	98.0±0.76	0.87	NS
12 hr.	98.23±0.68	97.96±0.81	0.17	NS
14 hr.	97.83±0.74	97.7±0.78	0.62	NS
16 hr.	98.2±0.87	97.86±0.93	0.20	NS
18 hr.	98.13±0.97	97.7±0.97	0.11	NS
20 hr.	98.07±0.90	97.73±0.86	0.15	NS
22 hr.	98.0±0.85	97.7±0.87	0.24	NS
24 hr.	98.1±0.86	97.8±0.81	0.09	NS

NS- Not Significant

As shown in **Table 5** SpO_2 was comparable between two groups. There was no statistically significant difference observed in pulse oxymetry (SpO_2) between two groups.

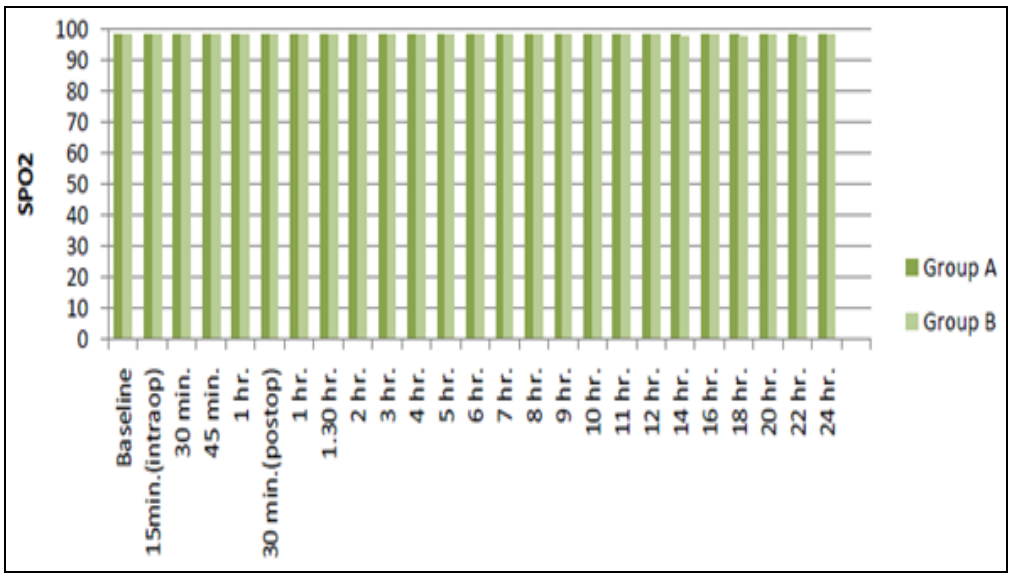


FIG. 4: CHANGES IN SpO_2

TABLE 6: CHANGES IN VISUAL ANALOGUE SCALE

	Group A	Group B		
Time	**Mean ± SD**	**Mean ± SD**	**p Value**	**Inference**
Baseline	--	--	--	--
15min.(intraop)	--	--	--	--
30 min.	--	--	--	--
45 min.	--	--	--	--
1 hr.	--	--	--	--
30 min.(postop)	0	0	--	--
1 hr.	0	0	--	--
1.30 hr.	0	0	--	--
2 hr.	0	0	--	--
3 hr.	2.0±1.05	1.63±0.89	0.15	NS
4 hr.	2.67±1.09	2.23±0.93	0.10	NS
5 hr.	2.60±1.38	1.93±0.94	0.03	S
6 hr.	2.40±1.35	1.73±1.11	0.042	S
7 hr.	2.30±1.24	1.7±0.95	0.04	S
8 hr.	2.23±1.14	1.67±0.88	0.035	S
9 hr.	2.03±0.93	1.63±0.96	0.11	NS
10 hr.	2.10±1.09	1.50±1.07	0.036	S
11 hr.	1.97±0.89	1.53±0.77	0.049	S
12 hr.	1.83±0.83	1.43±0.86	0.072	NS
14 hr.	1.93±0.98	1.43±0.86	0.04	S
16 hr.	1.87±1.25	1.23±1.01	0.035	S
18 hr.	1.6±0.86	1.13±0.78	0.031	S
20 hr.	1.57±0.77	1.07±0.78	0.016	S
22 hr.	1.47±0.68	1.17±0.70	0.098	NS
24 hr.	1.40±0.56	1.1±0.80	0.099	NS

VAS scores were found to be better at all time during 24 hours observation in ropivacaine with fentanyl group and these scores were significantly lower than ropivacaine group ($P<0.05$) at most of the time

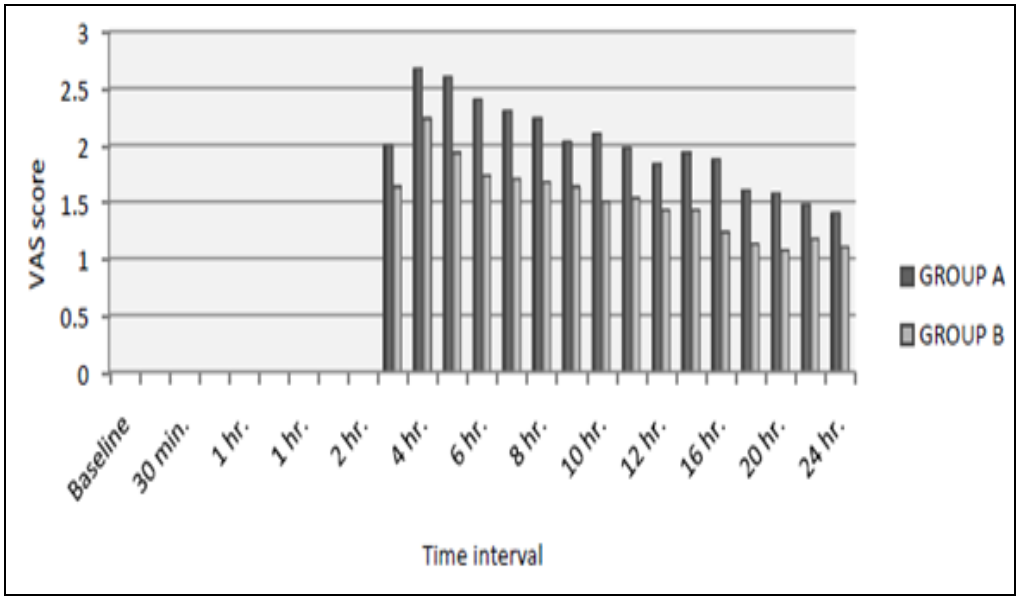


FIG. 5: CHANGES IN VISUAL ANALOGUE SCALE

TABLE 7: REQUIREMENT OF RESCUE ANALGESICS

Rescue analgesia given	Group A No. of patients	Group B No. of patients	P value
Yes	12 (40%)	5 (16.7%)	
No	18 (60%)	25 (83.3%)	0.044
Total	30	30	

We observed that the need for rescue analgesia in the form of inj. Diclofenac sodium 75 mg I.M. required in 12 (40%) patients in Group A and in 5 (16.7%) patients in Group B (P 0.044). So in our study requirement of rescue drug was significantly less with addition of fentanyl. And also patient in group B has enhanced pain control than group A.

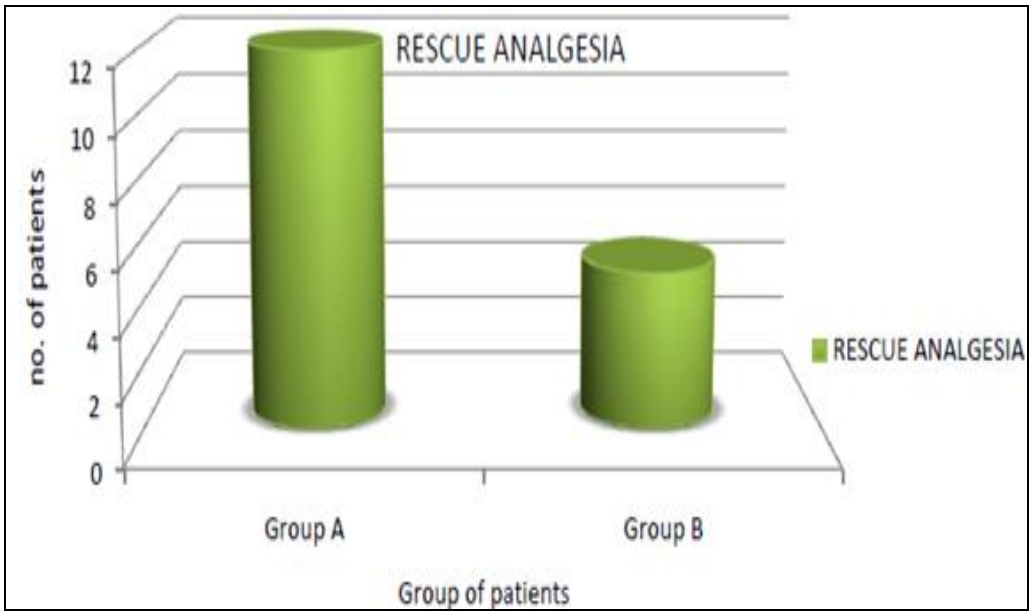


FIG. 6: REQUIREMENT OF RESCUE ANALGESICS

TABLE 8: SIDE EFFECTS

	Group A	Group B
Side effects	**No. Of Patients**	**No. Of Patients**
Nausea & vomiting	0	6 (20%)
Bradycardia	0	0
Hypotension	0	0
Pruritus	0	8 (26%)
Resp. depression	0	0
Urinary retention	0	0
Shivering	0	0
Sedation	0	0
Motor blockade	0	0

Nausea and vomiting was observed in 6 patients (20%) in Group B and none of the patients in Group A. Nausea and vomiting treated with ondensatron 0.06 mg/kg. Pruritus was observed in 8 patients (26%) in Group B and in none of the patients in Group A, pruritus was treated with naloxone 1-2 mcg/kg. Side effects like nausea-vomiting and pruritus was significantly higher in group B. No difference was found between the two groups, in terms of other side effects.

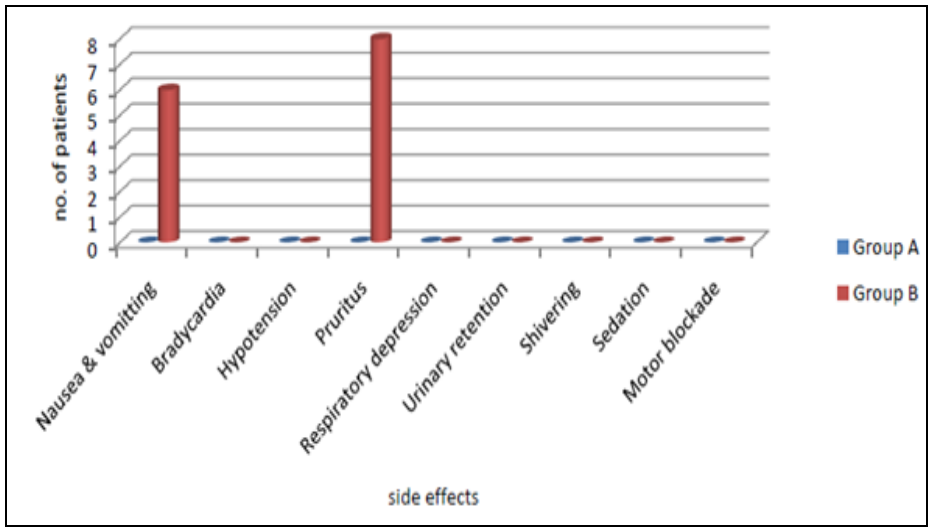


FIG.7: SIDE EFFECTS

DISCUSSION: Effective pain control is essential for optimal care of surgical patients. Surgery produces tissue injury with consequent release of histamine and inflammatory mediators. The release of inflammatory mediators activates peripheral nociceptors, which initiate transduction and transmission of the nociceptive information to the central nervous system (CNS) and the process of neurogenic inflammation in which release of neurotransmitters in the periphery induces vasodilatation and plasma extravasations.

Fentanyl has emerged as a suitable opioid for infusion into epidural space. Advantages of fentanyl over other opioids are that, it is more lipophilic, easily crosses lumbar Dura and quickly penetrates the lipid phase of underlying tissue of the cord. This study was undertaken with idea of providing effective pain free recovery period in patient undergoing total knee replacement surgery with the purpose was to compare the analgesic effect of epidural ropivacaine (0.2%) and ropivacaine (0.2%) with fentanyl (4mcg/ml) in post operative patient.

Hemodynamic parameters like pulse rate, blood pressure, SpO_2, pain score as per Visual Analogous scale, side effects and requirement of rescue drugs compare between these two groups.

Demographic variables: The two groups were comparable with respect to age, sex distribution, height and ASA physical status as per **Table 1**.

Cardiovascular parameters:
There was no statistically significant difference in pulse rate, blood pressure and SpO_2 at baseline between the two groups. Mean Pulse rate was 84.2±5.5 min for Group A and 83.9±6.25 for Group B and p >0.05(0.86). In same study there was no significant difference in mean blood pressure for both groups. For Group A 127.3±5.99 and for Group B is 128.1±5.98 and p > 0.05(0.61). SpO_2 was comparable between two groups. For Group A mean SpO_2 was 98.2±0.76 and Group B 98.1±0.73 (0.73).There was no statistically significant difference observed in SpO_2 between two groups.

In postoperative period for 24 hours observation systolic and diastolic blood pressure in all patients was comparable between two groups. The mean systolic and diastolic blood pressure was not significantly different between two groups, though ropivacaine with fentanyl group showed slight fall in blood pressure at all time points.

Quality of analgesia:
In our study we observed that VAS scores were found to be better at all time during 24 hours observation in ropivacaine with fentanyl group and these scores were significantly lower than ropivacaine group (P<0.05) at most of the times. Addition of fentanyl to ropivacaine can enhance this analgesic effect.

Comparison with other studies:
Kanai a *et al* thirty-six patients were randomized to one of the three postoperative epidural infusion groups: bupivacaine 0.125%, ropivacaine 0.2%, or ropivacaine 0.2% with 2.2 mcg/ml of fentanyl. Pain was assessed using a visual analog scale (VAS). The maximal VAS in patients receiving 0.2% ropivacaine + fentanyl was significantly less compared to that in the other two groups. The regression of sensory blockade was significantly prolonged in patients treated with ropivacaine + fentanyl. They concluded that epidural injection of ropivacaine with fentanyl decreased postoperative pain with stable vital signs in patients undergoing leg orthopedic surgery, as compared to bupivacaine or ropivacaine alone, possibly because of the maintenance of sensory blockade by ropivacaine and enhancement of this sensory blockade by fentanyl.[16]

We also found that vital signs were **not** significantly different between two groups, though ropivacaine with fentanyl group showed stable vital signs during postoperative period for 24 hours observation. In our study VAS scores were significantly better in ropivacaine with fentanyl group.

Scott DA, Blake D *et al* this prospective, randomized, double-blinded study was conducted in 1999 to compare the analgesic effectiveness and side effects of epidural infusions with ropivacaine 2 mg/ml alone and in combination with fentanyl 1 mcg/ml, 2 mcg/ml, and 4 mcg/ml after major abdominal surgery. The median of individual visual analog scale score with coughing was significantly lower (P < 0.01) for Group R4F at rest and with coughing. For all groups, >90% of patients had no detectable motor block after 24 h. Hypotension, nausea, and pruritus were more common with the larger dose of fentanyl. They conclude that, an epidural infusion of ropivacaine 2 mg/ml with fentanyl 4 mcg/ml provided significantly more effective pain relief.[17]

In our study of 60 patients nausea and vomiting was observed in 6 patients (20%) and pruritus was observed in 8 patients (26%) of the patients in Group B and in none of the patients in Group A. Side effects were significantly higher in group B (ropivacaine 0.2% with fentanyl 4mcg/ml). No difference was found between the two groups, in terms of other side effects. Our study corroborates with the findings Scott DA.

We observed that the need for rescue analgesia required in 12 (40%) patients in Group A and in 5 (16.7%) patients in Group B (p 0.044). So in our study requirement of rescue drug was significantly less with addition of fentanyl (opioids).

In conclusion, our study has demonstrated that addition of fentanyl (4mcg/ml) to ropivacaine (0.2%) decreased postoperative pain with stable vital signs in patients undergoing total knee replacement surgery, as compared to ropivacaine alone, possibly because of the maintenance of sensory blockade by ropivacaine and enhancement of this sensory blockade by fentanyl. Also the need for rescue analgesia was decreased with addition of

fentanyl 4mcg/ml with ropivacaine 0.2% (Group B). However use of epidural fentanyl along with ropivacaine causes opioid-related side effects, particularly pruritus and nausea-vomiting.

CONCLUSION: Addition of FENTANYL in doses of 4mcg/ml with 0.2% ROPIVACAINE (GROUP B) in the epidural analgesia improves the postoperative analgesic efficacy. The mean Visual analog scale scores were significantly lower for patients in whom epidural Ropivacaine 0.2% with Fentanyl 4mcg/ml (Group B) compare with ropivacaine 0.2% alone with stable hemodynamic parameters. The mean rescue analgesic requirement was lower for patients in whom fentanyl added to ropivacaine (Group B). However use of epidural fentanyl along with ropivacaine causes opioid-related side effects, particularly pruritus and nausea-vomiting. No difference was found between the two groups, in terms of other side effects.

CONFLICTS OF INTEREST: There are no conflicts of interest.

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REFERENCES:

1. Rony RY, Fortier MA, Chorney JM, Perret D, Kain ZN. Parental postoperative pain management: attitudes, assessment, and management. Pediatrics. 2010 Jun; 125(6):e1372-8. PubMed PMID: 20498177. Epub 2010/05/26. eng.
2. Dahl V, Raeder J. Non-opioid postoperative analgesia. Acta Anaesthesiol Scand. 2000; 44(10):1191-203.
3. Grass JA. The role of epidural anesthesia and analgesia in postoperative outcome. Anesthesiology clinics of North America. 2000 Jun; 18(2):407-28, viii. PubMed PMID: 10935017. Epub 2000/08/10. eng.
4. Choi P, Bhandari M, Scott J, Douketis J. Epidural analgesia for pain relief following hip or knee replacement. Cochrane Database Syst Rev. 2003; 3(3).
5. Hansen TG. Ropivacaine: a pharmacological review. Expert Rev Neurother. 2004 Sep; 4(5):781-91. PubMed PMID: 15853505. Epub 2005/04/28. eng.
6. McClure JH. Ropivacaine. Br J Anaesth. 1996 Feb; 76(2):300-7. PubMed PMID: 8777115. Epub 1996/02/01. eng.
7. Stienstra R. The place of ropivacaine in anesthesia. Acta Anaesthesiol Belg. 2003; 54(2):141-8. PubMed PMID: 12872430. Epub 2003/07/23. eng.
8. Kuthiala G, Chaudhary G. Ropivacaine: A review of its pharmacology and clinical use. Indian J Anaesth. 2011 Mar; 55(2):104-10. PubMed PMID: 21712863. Pubmed Central PMCID: PMC3106379. Epub 2011/06/30. eng.
9. Leone S, Di Cianni S, Casati A, Fanelli G. Pharmacology, toxicology, and clinical use of new long acting localanesthetics, ropivacaine and levobupivacaine. Acta Bio Medica Atenei Parmensis. 2008; 79(2):92-105.
10. Graf BM, Abraham I, Eberbach N, Kunst G, Stowe DF, Martin E. Differences in cardiotoxicity of bupivacaine and ropivacaine are the result of physicochemical and stereoselective properties. Anesthesiology. 2002 Jun; 96(6):1427-34. PubMed PMID: 12170056. Epub 2002/08/10. eng.
11. Mogensen T, Hjortso NC, Bigler D, Lund C, Kehlet H. Unpredictability of regression of analgesia during the continuous postoperative extradural infusion of bupivacaine. Br J Anaesth. 1988 Apr; 60(5):515-9. PubMed PMID: 3377927. Epub 1988/04/01. eng.
12. Tsukada S, Wakui M, Hoshino A. Pain control after simultaneous bilateral total knee arthroplasty: a randomized controlled trial comparing periarticular injection and epidural analgesia. J Bone Joint Surg Am. 2015 Mar 4; 97(5):367-73. PubMed PMID: 25740026. Epub 2015/03/06. eng.
13. Kaya T, Buyukkocak U, Basar H, Sagsoz N. Comparison of epidural ropivacaine 0.2% and ropivacaine 0.2% in combination with sufentanil 0.75 microg mL-1 for postcaesarean analgesia. Agri : Agri (Algoloji) Dernegi'nin Yayin organidir = The journal of the Turkish Society of Algology. 2008 Oct; 20(4):30-7. PubMed PMID: 19117154. Epub 2009/01/02. eng.
14. Pitimana-aree S, Visalyaputra S, Komoltri C, Muangman S, Tiviraj S, Puangchan S, et al. An economic evaluation of bupivacaine plus fentanyl versus ropivacaine alone for patient-controlled epidural analgesia after total-knee replacement procedure: a double-blinded randomized study. Reg Anesth Pain Med. 2005; 30(5):446-51.
15. Lorenzini C, Moreira L, Ferreira M. Efficacy of ropivacaine compared with ropivacaine plus sufentanil for postoperative analgesia after major knee surgery. Anaesthesia. 2002; 57(5):424-8.
16. Kanai A, Kinoshita S, Suzuki A, Okamoto H, Hoka S. [Advantage of ropivacaine for postoperative epidural analgesia following leg orthopedic surgery]. Masui The Japanese journal of anesthesiology. 2005; 54(1):8-13.
17. Scott DA, Blake D, Buckland M, Etches R, Halliwell R, Marsland C, et al. A Comparison of Epidural Ropivacaine Infusion Alone and in Combination with 1, 2, and 4 [micro sign] g/mL Fentanyl for Seventy-Two Hours of Postoperative Analgesia After Major Abdominal Surgery. Anesth Analg. 1999; 88(4):857-64.

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