www.jmscr.igmpublication.org
Impact Factor 5.84
Index Copernicus Value: 83.27
ISSN (e)-2347-176x ISSN (p) 2455-0450
crossref DOI: https://dx.doi.org/10.18535/jmscr/v5i7.210

IGM Publication
Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

Case Report

A comparative study of Ultrasound Guided Continuous Femoral Nerve Block Versus Local Infiltration Analgesia for management of postoperative Pain in Unilateral Total Knee Arthroplasty in an Indian scenario

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Abstract
Introduction: *Use of local infiltration in knee joint arthroplasty, provide postoperative analgesia and preserves motor power of quadriceps, which helps in early mobilisation, as compared to femoral nerve block which paralyses vastus medialis*
Aim: *To compare the application of postoperative analgesia provided by ultrasound guided femoral nerve block and local infiltration in unilateral total knee replacement*
Material and Methods: *A prospective study was conducted on 60 patients between 25 – 65years of ASA I and II, which were randomly(using random number table) divided into two groups – group 1-femoral nerve block (FNB) and group 2-local infiltration analgesia(LIA). Patients with chronic pain and on opioids were excluded. (power> 80%) Numeric rating scale (primary objective), sedation score, nausea vomiting score and motor power were analysed.*
Result: *Pain relief was better in FNB group (p value <.001) with less fentanyl demand (p value <.001) ,low sedation score and low nausea vomiting scoring but associated with low muscle power grading*
Conclusion: *FNB has better pain relief than LIA group but range of motion was reduced in FNB group.*
Keywords: *Local infliltration, inotrophy, opoids.*

Introduction and background

Pain from surgical sites can activate sympathetic efferent nerves and increase heart rate, inotropy and blood pressure. As sympathetic system activates it increases myocardial oxygen demand and reduced myocardial oxygen supply the risk of cardiac ischemia, particularly in patients with pre-existing cardiac diseases is increased [(1)].

Multi-interventional and rehabilitation strategy is therefore required, including very effective pain relief, if optimal outcomes are to be achieved, as outlined in the procedure –specific

recommendations from the PROSPECT group [2]. Recognition of these factors has led to the concept of 'fast Track' surgery [3]. A fast- track system also enabled early discharge (less than 3 days) after total hip and knee arthroplasty, although after total knee arthroplasty pain at 10 days after discharge was still significant (52% of patients with moderate pain and 16% with severe pain) increasing a need for improved post discharge analgesia [4] (Anderson et al,2009).

Local anesthetic wound infiltration reduced the proportion of patients with persistent pain and neuropathic pain. (Batoz etal 2009) [5].

Aims

To assess the quality of analgesia provided by femoral nerve block and local infiltration analgesia in unilateral TKR post operatively.

Objectives

Ease of technique, effectivity & side effects of one technique over other technique Our aim is to assess the quality of analgesia provided by the two techniques. The Numeric RATING Scale of 0-10 will be used to assess the pain. The other parameters we will be assessing are the dosage of rescue analgesia used in two groups and the associated side effects of the sedation, nausea-vomiting and respiratory depression associated with the use of opioids. Also the effect on other system like cardiovascular and motor power will be assessed.

Does LIA help in early ambulation as it does not cause any motor blockade and quadriceps weakness?

Does it reduce the usage of narcotics ?

Material & Methods

Study included patients in the age group 25-65 yrs, ASA grade I or II coming for unilateral total knee replacement of either gender.

Study excluded patients with Age<25 yrs or >65yrs, ASA grade III or IV, Patients with chronic pain or taking chronic opioid medication, known allergy to the medications used, contraindications to performing regional anaesthesia, unable to follow verbal or written instructions, Patients refusal

Each group had 30 patients. 60 patients of the age group 25 to 65 years of ASA grade I and II were randomly divided into two groups.

Measurement of outcomes

One group FB group had given Femoral Block with continuous infusion catheter placed and the second LIA group had given local infiltration during the surgery.

Primary outcome measured was the pain scores with two techniques. The secondary outcome were comparison of the rescue analgesics required and the associated complications. Also a record of the nausea & vomiting scores, muscle power grading and sedation scores were made.

Post-operative pain management was done by Numeric Rating Scale(0-10), the other parameters measured were Motor Power Grading on a 0-5 scale, nausea and vomiting score on a 0-3 scale, sedation score on a 0-3 scale as was done in our Acute Pain Service was being followed.

Both groups were received multimodal analgesia in the form of Inj Paracetamol 1 gram, eight hourly and SOS. Rescue analgesia with Inj Fentanyl was given. Record of the doses of the rescue analgesia and additional doses of Paracetamol was done.

Risks and benefits

The risk of neurological injury with neuraxial and peripheral blocks were avoided with the use of local infiltration. However the degree of pain relief with both techniques was determined by the rescue analgesics requirement and the associated side effects of nausea and vomiting, sedation and respiratory depression.

Satastical analysis

Satastical analysis was done by using the SPSS software. The comparison was made using the Chi square test and ANOVA.

National significance

Both techniques was being observed an effect on rapid recovery and thus reduces the cost of hospitalization. Also the minimum expenditure of LIA was further benefitted in cutting down the medical costs.

Methodology

After approval from indian spinal injuries centre's ethics committee, informed consent was taken from all patient entered into the study.

A total of sixty patients were included in the study and divided in two groups of 30 patients each, scheduled for elective surgery for unilateral total knee replacement. The study was carried out during the period extending from September 2014 to November 2015.On the basis of review of hospital 30 patients received FNB and 30 received LIA.

The patient were randomized in each group by serial assignment that is the first patient was assigned to group 1 and second patient to group 2, third patient to group 1 and henceforth, the pattern was followed.

All patient of group 1 assigned for Femoral nerve block received femoral nerve block post operatively with catheter in situ on continous infusion of 0.1 percent ropivicaine at 6 ml/hour.

Technique

Group 1

After cleaning with betadine and sterile draping and preparation using the bony landmarks that is on medial side of thigh when the patient under general anaesthesia with the help of USG . After localization of artery, vein and nerve ,the touhy needle inserted along the long axis of USG probe and tracing the tip of needle which was counter checked by normal saline and drug had been given accordingly.

After localization of artery, vein and nerve, we used to insert the catheter which was fixed at the skin.

Catheter attached to infusion pump which consisted of 0.1% of ropivicaine at 6 ml/hr

Group 2

Preparing an injectant mixture consisted of ropivacaine HCl, 2.0 mg/mL mixed with 30 mg ketorolac and 10 µg/mL adrenaline. Dividing the mixture in three equal parts and administering each of them at the time when surgeon were ready to put implant we had infiltrated medial and lateral collateral ligaments and posterior capsule before putting implant. When surgeon used to start closing the inscision then the drug was being infiltrated at wound edges and subcutaneous tissues. Then catheter placed between posterior capsule and medial condyle. The catheter was secured for further infiltration. Subsequently at 20 hours and 48 hours drugs were infiltrated via catheter.

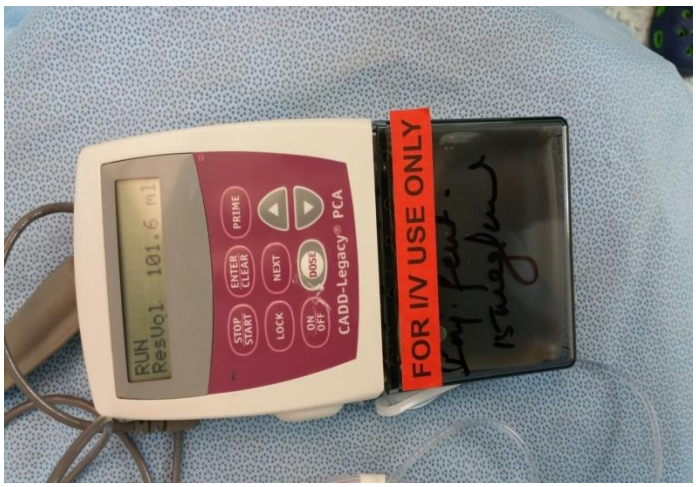

Figure.a) CADD pump for I/V PCA (used for fentanyl infusion)

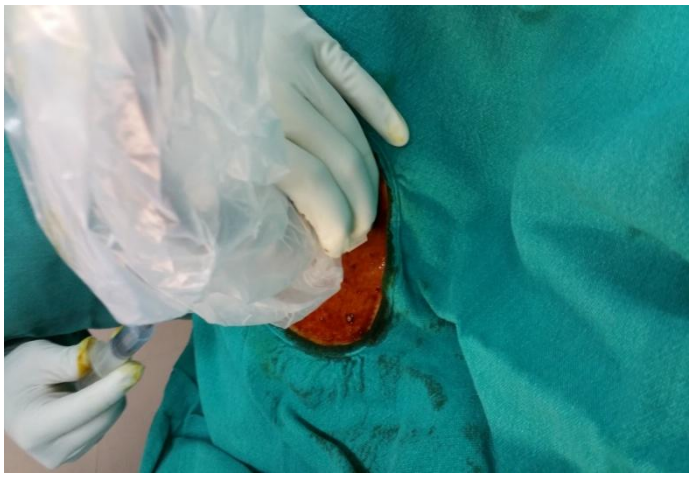

Figure b) A USG linear high frequency (8–12 MHz) probe placed perpendicular to the course of the femoral nerve block.

Figure c) Fornia continuous infusion balloon pump used for ropivicaine perineural infusion.

Patients of group 2 received local infiltration analgesia in perioperative period. Constituent of local anesthetic: the ropivacaine-ketorolac adrenaline (RKA) mixture.

Postoperatively

Group 1 was given continous ropivicaine infusion via fornia infusion balloon pump perineurally.

Group 2 received two times bolus of ropivicaine ketorolac and adrenaline mixture after 15-20 hours and 48 hours of surgery with 15-20 ml of RKA mixture.

4. Method of measurement of outcome of interest:

Post-operative assessment was done by

- Numeric Rating Scale (0-10)
- Motor Power Grading on a (0-5) scale,
- Early mobilization time,
- Free mobilization time,
- Nausea and vomiting score on a 0-3 scale
- Sedation score on a 0-3 scale

All above are used to be done in our APS were being followed.

Observation

Numeric rating scale

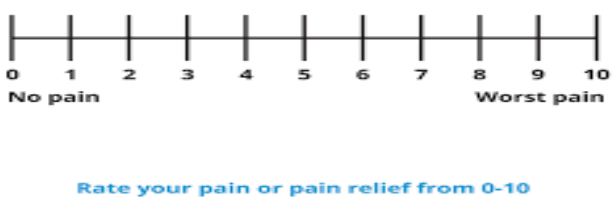

Figure d)

Instruct the patient to point to the position on the lines between the faces to indicate how much pain they are currently feeling. The far the most left indicates

'No pain' and the far right end indicates 'worst pain ever'

Nausea and vomiting score -:

0 – No nausea/vomiting .

1- Nausea <10 min or vomiting once

2- Nausea > 10 min or vomiting twice.

3- Nausea > 10 min vomiting >2 times or uncontrolled.

Sedation Score :

Sedation Score	Response
0	Awake
1	Mild sedation,easy to rouse
1S	Asleep,easy to rouse
2	Moderate sedation,unable to emin awake
3	Difficult to rouse

Muscle power grading

SCORE	RESPONSE
0	No movement
1	Flicker is perceptible in the muscle
2	Movement only if gravity eliminated
3	Can move limb against gravity
4	Can move against gravity &some resistance exerted by examiner.
5	Normal power

Result

This study was conducted for total 60 patients, thirty in each of two groups.

Statistical analysis was done by applying independent T-test for those variables which are continous in nature (NRS).These all variables are normally distributed and sample size is adequate that is why we have aaplied parametric test .If p value is < .05 that means there is a significant difference between the two groups. The other four variables (NVS, SS, Rescue analgesia, Number of night stay) are categorical in nature.To see the association between the two groups, we have applied chi square test. If p- value <.05 that means there is a significant difference between two groups.

In order to obtain linear trend within a group for those variables which are continuous in nature

(NRS), we have applied repeated measurement analysis test followed by post op Bon frienni test. In order to see the linear trend in case of categorical variables we have applied friedmann test followed by Newman-kallis test.

This table showing age distribution among two groups as we can see there is no statistical significance in the distribution, the maximum number of patients are falling under the group of age 50-60 years i.e, 15 in femoral nerve block and 18 in local infiltration analgesisa .This is followed by age group 61-70 years.

The graph of gender distribution is showing female preponderance in both the group. This may be due to the fact that randomization was done by serial assignment of patients to groups without gender randomization ,as discussed above.

		type of analgesia		Total	Pearson Chi-sqr value	p-value
		FNB	LIA			
AGE GROUP	30-40 Yrs	1	1	2	0.518	0.915
	41-50 Yrs	6	4	10		
	51-60 Yrs	16	18	34		
	61-70 Yrs	7	7	14		
Total		30	30	60		

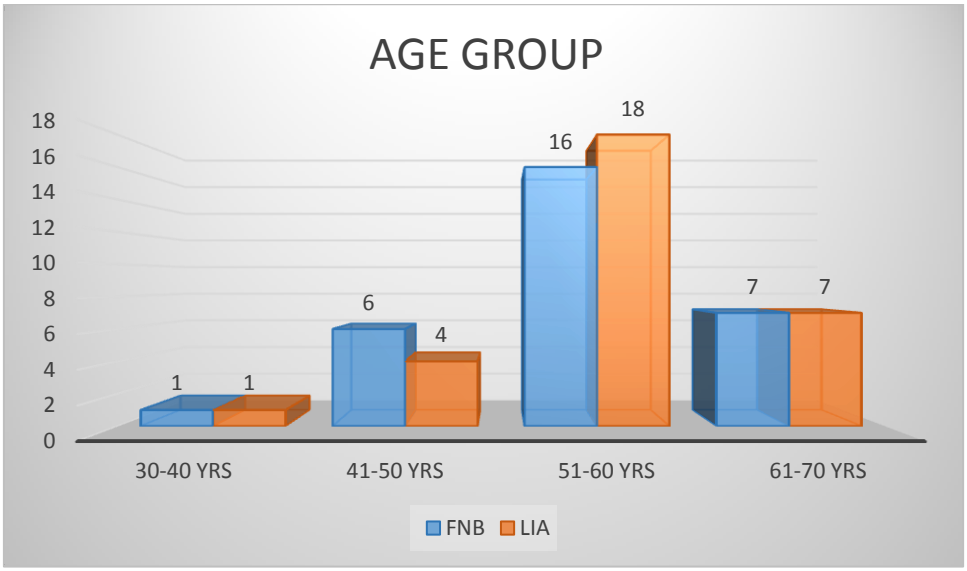

Figure 1. Distribution of age among the two groups.

Chi-Square Tests					
	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	4.406[a]	1	0.036		
Continuity Correction[b]	3.237	1	0.072		
Likelihood Ratio	4.542	1	0.033		
Fisher's Exact Test				0.07	0.035
Linear-by-Linear Association	4.33	1	0.037		
N of Valid Cases[b]	58				
a. 0 cells (.0%) have expected count less than 5. The minimum expected count is 7.50.					
b. Computed only for a 2x2 table					

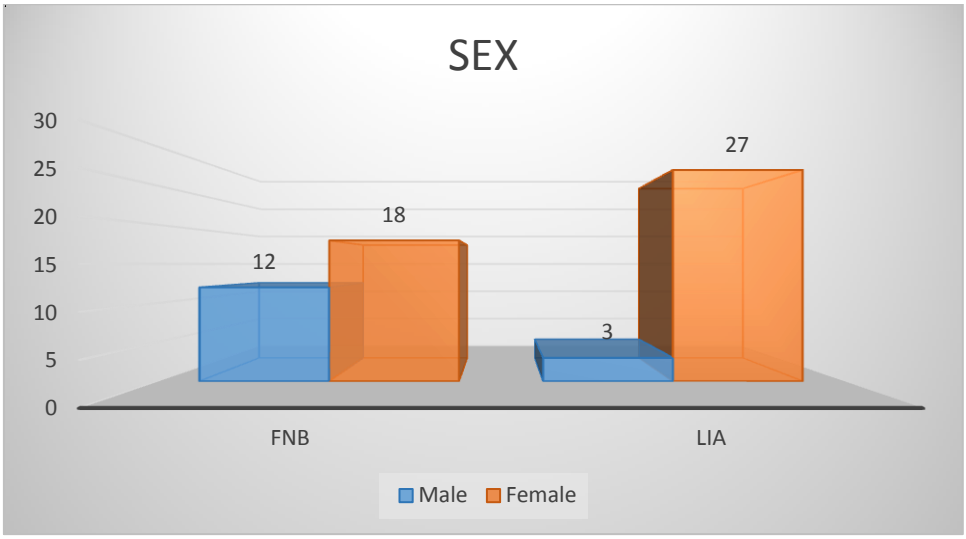

Figure 2. Distribution of gender among two groups

Interference from the (table 3 and figure 3), we can conclude that there is a gradual decreasing trend in NRS scoring in both the group FNB and LIA. But we can see at 16 hours there is slightly higher NRS scoring in LIA group.The NRS scoring was significant lower with FNB group.

Table 3. Comparision of NRS score

	Group	N	Mean	Std. Deviation	t-value	p-value	Significane
NRS 4	FNB	30	4.40	1.52	6.64	0.001	S
	LIA	30	6.57	0.94			
NRS 8	FNB	30	4.30	1.37	7.05	0.001	S
	LIA	30	6.43	0.94			
NRS 12	FNB	30	4.13	1.22	6.89	0.001	S
	LIA	30	5.93	0.74			
NRS 16	FNB	30	3.57	0.73	11.74	0.001	S
	LIA	30	6.00	0.87			
NRS 20	FNB	30	3.30	0.60	12.27	0.001	S
	LIA	30	5.40	0.72			
NRS 24	FNB	30	3.37	0.49	13.93	0.001	S
	LIA	30	5.37	0.61			
NRS 48	FNB	30	3.47	0.68	9.42	0.001	S
	LIA	30	5.10	0.66			

NS - non significant , S - significant

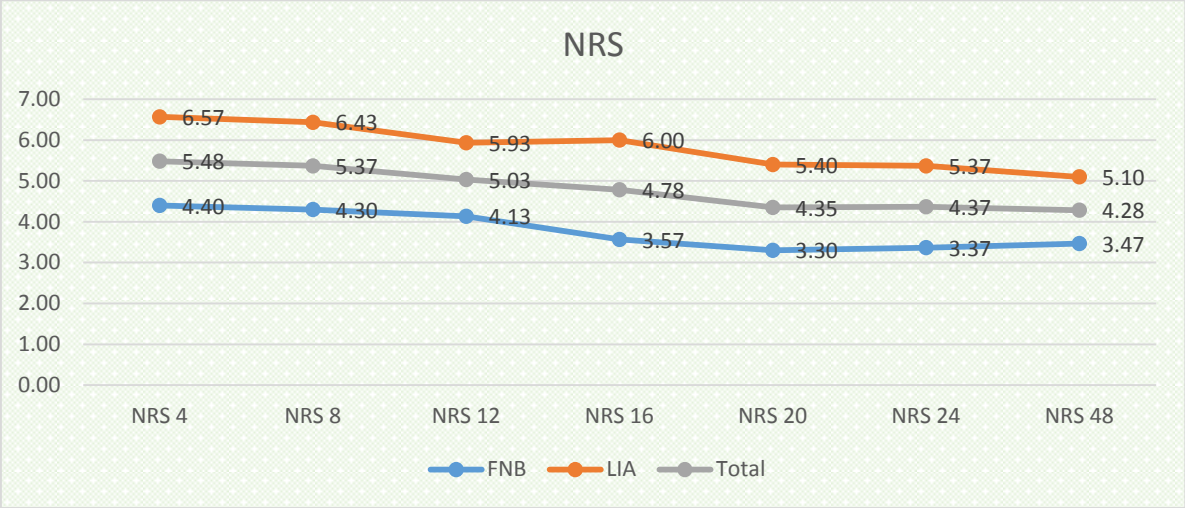

Figure 3. Comparision of NRS score:

From the table 4 and figure 4 we can conclude that at 4 hours,12 hours and 48 hours the value were significant. As we can see in the given figure that NVS score were falling upto 20 hours of duration thereafter that there is a gradual increase in NVS scoring.

Table 4. Comparision of NVS

Group	Score	NVS4	NVS8	NVS12	NVS16	NVS20	NVS24	NVS48
FNB	0	17	21	26	27	28	27	25
	1	13	9	4	3	2	3	4
	2	0	0	0	0	0	0	1
	3	0	0	0	0	0	0	0
LIA	0	3	15	19	24	27	24	15
	1	26	14	11	6	3	6	14
	2	1	1	0	0	0	0	1
	3	0	0	0	0	0	0	0
FNB vs LIA	chi-square	15.13	3.09	4.36	1.17	0.218	1.17	8.05
	p-value	0.001	0.214	0.037	0.278	0.64	0.278	0.018
	Significance	S	NS	S	NS	NS	NS	S

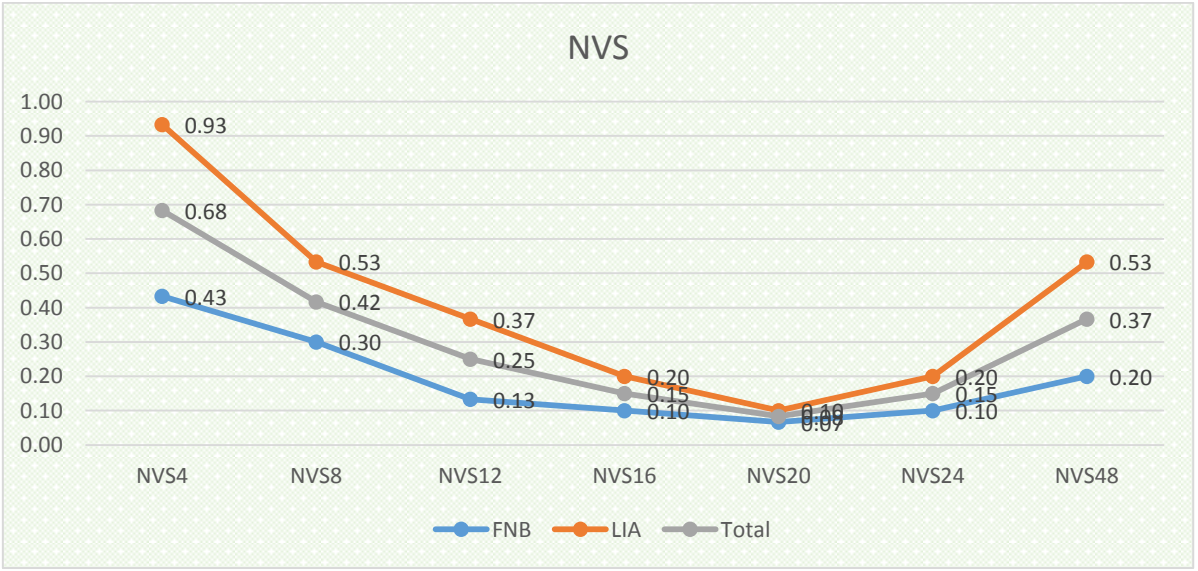

Figure 4. Comparision of NVS :

SS score

We can conclude from table 5 and figure 5 at 4 hours,12 hours and at 48 hours the SS score were significant .Up to the duration of 16 hours there was a gradual decrease in sedation score in both the groups there after there was gradual increase in sedation score upto 48 hours which was still lower than the early 12 hours sedation score.

Table 5. Comparision of SS score

Group	Score	SSS4	SSS8	SSS12	SSS16	SSS20	SSS24	SSS48
FNB	0	12	20	25	28	29	27	26
	1	17	9	4	1	1	3	4
	2	1	1	1	0	0	0	0
LIA	0	3	13	15	24	26	24	19
	1	27	16	14	4	2	5	11
	2	0	1	1	2	2	1	0
FNB vs LIA	chi-sqr	8.67	3.45	8.05	4.09	2.497	1.67	4.36
	p-value	0.013	0.179	0.018	0.129	0.287	0.432	0.037
	Significance	S	NS	S	NS	NS	NS	S

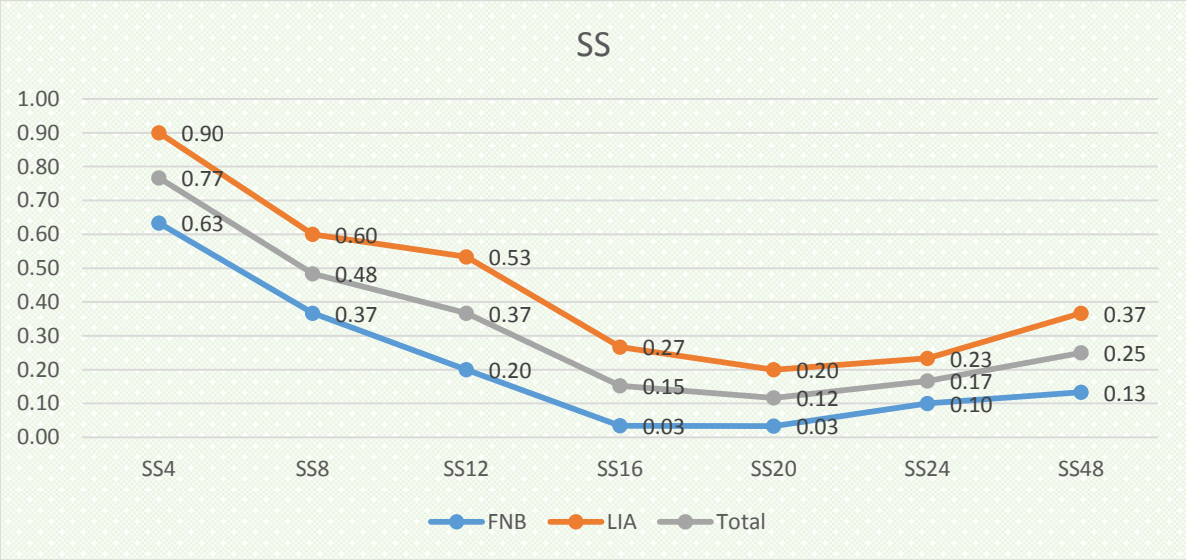

Figure 5. Comparision of sedatiuon score

Table 6. Comparision of MPG

Group	MPG	MPG4	MPG8	MPG12	MPG16	MPG20	MPG24	MPG48
FNB	0	0	0	0	0	0	0	0
	1	0	0	0	0	0	0	0
	2	14	8	2	1	0	1	1
	3	15	20	25	23	21	16	15
	4	1	2	3	6	9	13	14
	5	0	0	0	0	0	0	0
LIA	0	0	0	0	0	0	0	0
	1	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0
	3	28	20	13	7	1	0	0
	4	2	10	17	23	29	30	30
	5	0	0	0	0	0	0	0
FNB vs LIA	chi-sqr	18.26	13.33	15.59	19.5	28.71	23.72	21.82
	p-value	<0.001	0.001	<0.001	<0.001	<0.001	<0.001	<0.001

MPG

From the above table 6 and figure 6 we can conclude that the MPG value in both the group had significant difference that is LIA group had high MPG scoring as compared to FNB group.But there was a gradual increase in MPG scoring in both the group in the duration of 48 hours.

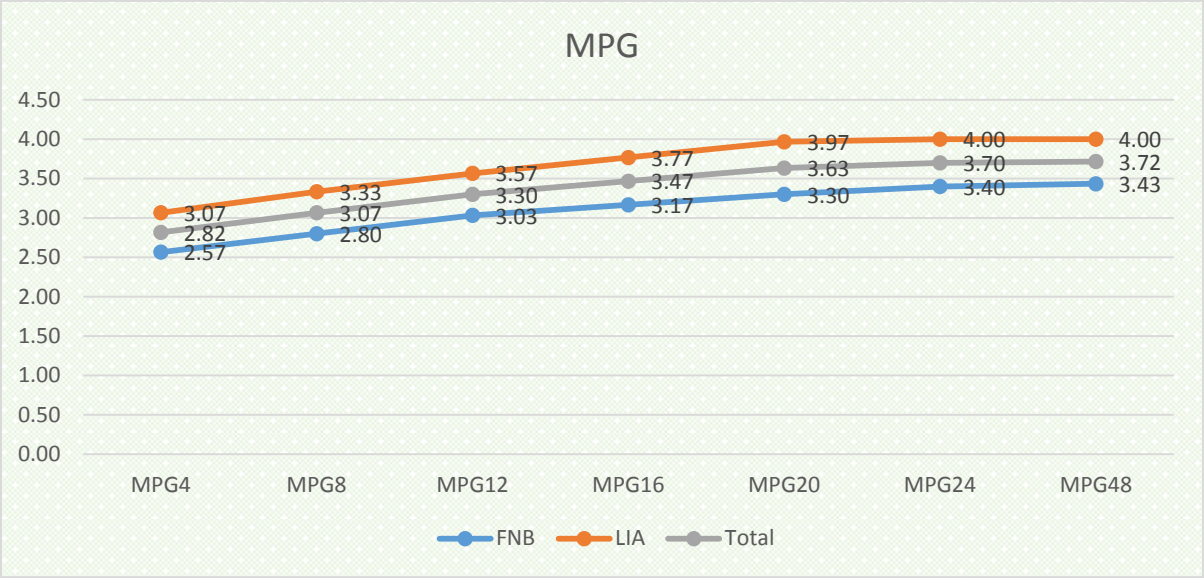

Figure .6. Comparision of MPG

Early mobilization time

Early mobilisation were affected in three patients of femoral nerve block and 27 patients of LIA .The result was significant with p value of <0.001.We found that the motor was on rising trend from 4 hours to 48 hours in both the group.

Table 7. Comparision Of Early mobilization

Early mobilization time		type of analgesia		Total	Pearson Chi-sqr value	p-value
		FNB	LIA			
	Affected	3	27	30	38.4	<0.001
	Unaffected	27	3	30		
Total		30	30	60		

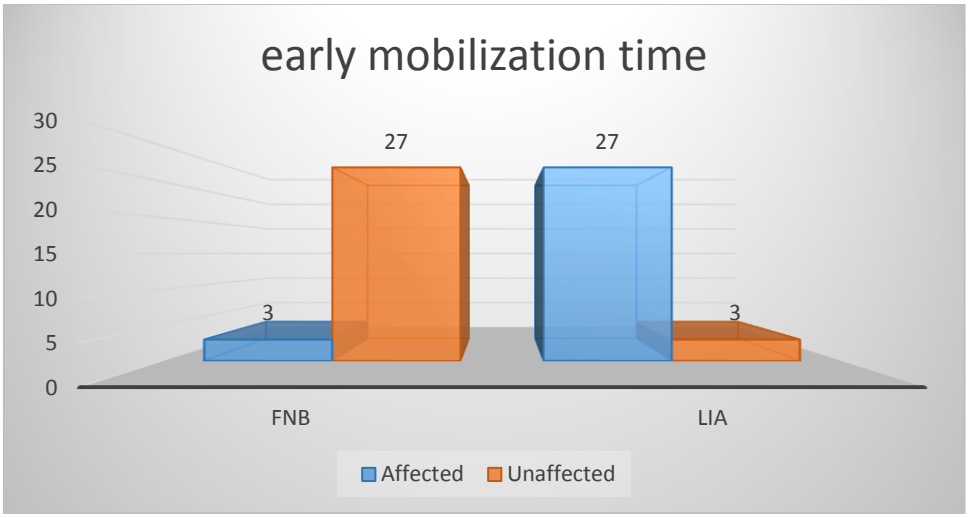

Figure 7 Distribution of early mobilisation in group

Free mobilization time

Free mobilisation time had been compared in both group we found there is no significant difference between the two group p value was <0.79 as we can see in the table and figure 8 .12 patients of FNB and 11 patients of LIA had been affected.

Table 8. Comparision of Free mobilization time

free mobilization time		Type of analgesia		Total	Pearson Chi-sqr value	p-value
		FNB	LIA			
	Affected	12	11	23	0.071	0.791
	Unaffected	18	19	37		
Total		30	30	60		

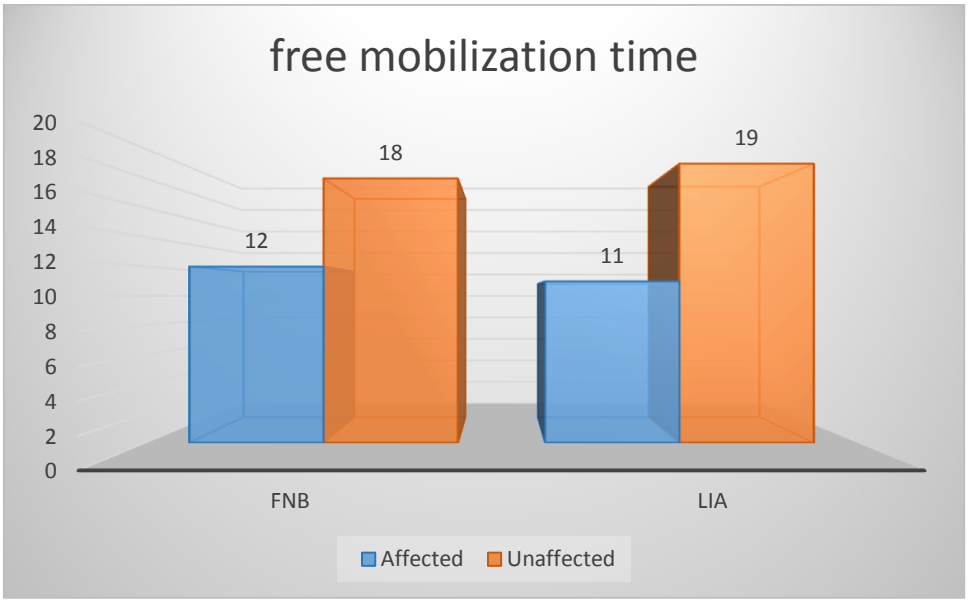

Figure 8. Comparision of Free mobilization time

Rescue analgesia

Patient of LIA had required more rescue analgesia than FNB.The p-value was highly significant <0.001.

Table 9. Comparsion of rescue analgesia

		type of analgesia		Total	Pearson Chi-sqr value	p-value
		FNB	LIA			
Rescue analgesia	NIL	20	0	20	56.33	<0.001
	<=5 times	7	0	7		
	6-10 times	2	0	2		
	11-15 times	1	11	12		
	16-20 times	0	19	19		
Total		30	30	60		

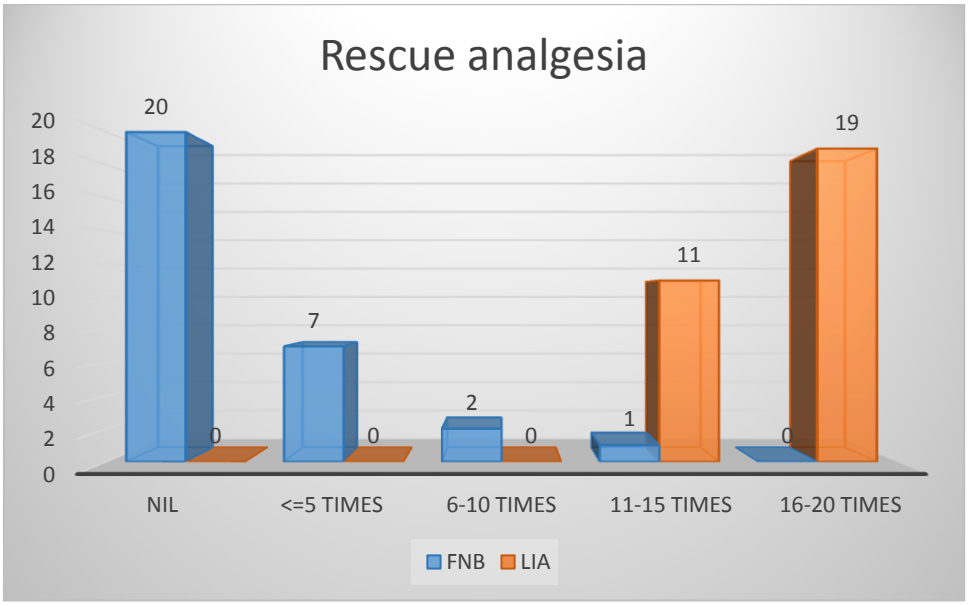

Figure 9. Comparision of rescue analgesia

Discussion

Pain is one of commonest manifestation of surgery as a result of tissue damage at the surgical site.It has been found that the cause of pain ,the time of onset, the site of its generation and its likely duration are all known outcome in elective surgery.

Nalini et al have studied pain management for orthopaedic procedures and found that success of regional anaesthesia for orthopaedic surgery will depend on how anaesthesiologists use current available medication and techniques in finding the appropriate analgesia drug mixtures, appropriate concentrations, and route of administration for each type of surgery .

NRS scoring

Various studies have been done comparing femoral nerve block with local infiltration analgesia, some studies have shown almost comparable result ,few studies have shown local infiltration analgesia is better than femoral nerve block and few are showing FNB is better than LIA . Both femoral block and LIA resulted in low average pain intensity during the first two postoperative day but in our study there is a significant difference between the two groups when we compared the NRS scoring where pain relief was lesser in LIA group. We compared two routinely used methods both are effective for postoperative pain relief in TKA. None of the patients in this study were given an analgesic other than intravenous fentanyl, administered through a PCA pump, and paracetamol (4 g in 24 h).

As we have discussed graph of NRS showing the decreasing trend of pain in both group but obviously the NRS scoring is remarkably low in FNB.

Fan L et al had conducted a study on Nerve Block for Total Knee Arthroplasty: A Prospective, Randomized Clinical Trial the group who had received local anaesthetic had less VAS score. Morphine consumption, VAS at rest, range of motion, and Knee Society Score were similar between the two groups. This study showed group B, the local anesthetic group had less VAS with movement on postoperative day 1 (P = .01) than that of group A, which means a better pain control.

Busch CA et al., Kehlet H et al, Andersen LØ et al ,Parvataneniet al, Kerr DR et al. Toftdahl K et al all had conducted the study to see efficacy of periarticular multimodal drug injection in total knee arthroplasty and they found remarkable decrease in NRS scoring in case of LIA.

NVS scoring

Femoral nerve block and LIA have been compared by Fan L et al in which they enrolled

157 patients out of which they found eighteen patients (11 percent) in group A (FNB) and twenty one(13 percent) patients in group B(LIA) experienced mild-to-medium nausea or vomiting.

In our study in 48 hours of duration the nausea vomiting scoring at 4 hours ,12 hours and 48 hours t was significantly higher in LIA group which may be correlated with total rescue analgesia i.e, fentanyl demand which was more in LIA in my study. Kerr DR et al., also conducted study Local infiltration analgesia:

MPG

Toftdahl and collaborators (2007) presented data suggesting that LIA with ropivacaine, ketorolac, and epinephrine results in faster postoperative activation, as indicated by being better able to walk on the first postoperative day as compared to femoral block in our study the motor power of patients in FNB group were significantly low as compared to LIA in 48 hours. In our study we have found that motor power has been affected in FNB group. In case of LIA group the MPG score was high as it doesnot result in muscle weakness.

Early mobilization time and free mobilization time

Carli F et al have conducted Analgesia and functional outcome after total knee arthroplasty: periarticular infiltration vs continuous femoral nerve block. Patients in Group F(femoral nerve block) used the PCA less (P=0.02) to achieve adequate analgesia. Postoperative 2Minute Walking Test was similar in both groups (P=0.27).In our study we found that the patients of FNB group were able to cooperate for early mobilization after 24 hours of surgery significantly more than the LIA. In case free mobilization we found that patients of both the group affected and there is no significant difference in groups. By applying chi square test p value was 0.791 which was insignificant . Kerr DR et al., conducted study Local infiltration analgesia: a technique for the control of acute postoperative pain following knee and hip surgery: a case study of 325 patients. Pain control was generally satisfactory (numerical rating scale pain score range 0-3). No morphine was required for postoperative pain control in two-thirds of the patients. Most patients were able to walk with assistance between 5 and 6 h after surgery and independent mobility was achieved 13-22 h after surgery

Rescue analgesia

Few study has shown that femoral nerve block has remarkable decrease in opioids dose. Paul JE et al., Carli F et al Analgesia and functional outcome after total knee arthroplasty: periarticular infiltration vs continuous femoral nerve block.In our study we categorised rescue analgesia according to their demand in a day less than 5 times ,6-10 times,11-15 times,16-20 times. None of the patient of LIA group had such a low demand but in FNB group 7 patients(23 percent) were there in whom less than 5 times fentanyl required .In two patients (6 percent of FNB and none of the LIA group patients required 6-11 times of rescue analgesia. One patient (3 percent) of FNB and 11 patients (36 percent) of LIA required 11 -15 times rescue analgesia. No patient of FNB group and 19 (63 percent) patients of LIA group had required more than 16 times. So from above we can conclude that the rescue analgesia requirement is remarkably low in FNB.

Number of night stay

Number of night stay in our hospital is 10 days for every patient so we couldnot be able to calculate the duration of night stay. But in few studies it has been found that number of night stay has been reduced in LIA groups even upto 2 days.

Conclusion

From the above data we can conclude the following

- Pain relief was better in FNB group
- Motor power grading was low in FNB group.
- Early mobilization was affected in LIA group.
- Free mobilization remained insignificant in both the group .

- LIA technique was easy to administer but as we can conclude that it relieved pain and decreased rescue analgesia demand but less than FNB group.
- There were no infection found at local site.
- The other parameters like sedation, nausea were significantly high in both the groups.
- Further studies on LIA required and looking forward for continuous local anaesthetics delivery via wound catheter along with intermittent bolus delivery.

Source(s) of support: Nil
Presentation at a meeting: Nil
Conflicting Interest: Nil

References

1. Ropivacaine: A review of its pharmacology and clinical use Gaurav Kuthiala and Geeta Chaudhary Gaurav Kuthiala and Geeta Chaudhary IJR Vol 55 Mar-Apr 2011(2) 105-109.
2. Hansen TG Expert Rev Neurother. 2004 Sep; 4(5):781-91
3. Toxicological and local anesthetic effects of optically active isomers of two local anaesthetic compounds. Aberg G Acta Pharmacol Toxicol (Copenh). 1972; 31(4):273-86.
4. McClure JH Br J Anaesth. 1996 Feb; 76(2):300-7.
5. Kindler CH, Paul M, Zou H, Liu C, Winegar BD, Gray AT, Yost CS J Pharmacol Exp Ther. 2003 Jul; 306(1):84-92.
6. Graf BM, Abraham I, Eberbach N, Kunst G, Stowe DF, Martin E Anesthesiology. 2002 Jun; 96(6):1427-34
7. Dony P, Dewinde V, Vanderick B, Cuignet O, Gautier P, Legrand E, Lavand'homme P, De Kock M The comparative toxicity of ropivacaine and bupivacaine at equipotent doses in rats.Anesth Analg. 2000 Dec; 91(6):1489-92.
8. Knudsen K, Beckman Suurküla M, Blomberg S, Sjövall J, Edvardsson N .[Central nervous and cardiovascular effects of i.v. infusions of ropivacaine, bupivacaine and placebo in volunteers. Br J Anaesth. 1997 May; 78(5):507-14.
9. Graf BM Curr The cardiotoxicity of local anesthetics: the place of ropivacaine Top Med Chem. 2001 Aug; 1(3):207-14.
10. Cederholm I, Evers H, Löfström JB Skin blood flow after intradermal injection of ropivacaine in various concentrations with and without epinephrine evaluated by laser Doppler flowmetry.Reg Anesth. 1992 Nov-Dec; 17(6):322-8.
11. Porter J, Crowe B, Cahill M, Shorten G The effects of ropivacaine hydrochloride on platelet function: an assessment using the platelet function analyser (PFA-100).Anaesthesia. 2001 Jan; 56(1):15-8.
12. Simpson D, Curran MP, Oldfield V, Keating GM Drugs. 2005; 65(18):2675-717.
13. Burm AG, Stienstra R, Brouwer RP, Emanuelsson BM, van Kleef JW Anesthesiology. 2000 Aug; 93(2):395-403location]
14. Ekström G, Gunnarsson UBDrug Metab Dispos. 1996 Sep; 24(9):955-61.
15. Selander D, Sjovall J, Waldenlind L. Accidental i.v injections of ropivacaine: Clinical experience of six cases [abstract] Reg Anaesth. 1997;22:70
16. Jokinen MJ, Olkkola KT, Ahonen J, Neuvonen PJ Clin Pharmacol Ther. 2001 Oct; 70(4):344-50.
17. Cpogna G,Celleno D,Fusco P,Lyons G,Columb M.Relative potencies of bupivicaine and ropivicaine for analgesia in labour Br J Anaesth 1999;82:371±3.
18. Polley LS ,Columb MO,Naughton NN ,Wagner DS, CosmasJM Relative analgesic potencies of ropivicaine and bupivicaine for epidural analgesia in labour.Anaesthesiology 1999;90 944±50.

19. Crosby E, Sandler A, Finucane B, Writer D, Reid D, McKenna J, Friedlander M, Miller A, O'Callaghan-Enright S, Muir H, Shukla R Can J Anaesth. 1998 Nov; 45(11):1066-71.
20. Peduto VA, Baroncini S, Montanini S, Proietti R, Rosignoli L, Tufano R, Casati A Eur J Anaesthesiol. 2003 Dec; 20(12):979-83.