International Journal of Current Advanced Research
ISSN: O: 2319-6475, ISSN: P: 2319-6505, Impact Factor: 6.614
Available Online at www.journalijcar.org
Volume 9; Issue 12 (A); December 2020; Page No.23417-23421
DOI: http://dx.doi.org/10.24327/ijcar.2020.23421.4636

Research Article

CURRENT STATUS AND FUTURE PROSPECTS OF ANESTHESIA IN PATIENTS UNDERGOING TOTAL KNEE REPLACEMENT SURGERY

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A R T I C L E I N F O

Article History:
Received 14th September, 2020
Received in revised form 29th October, 2020
Accepted 05th November, 2020
Published online 28th December, 2020

Key words:

TKR: Total Knee Replacement, Clonidine, Fentanyl, Intrathecal.

A B S T R A C T

Background: The armamentarium of local anesthetic adjuvants have evolved overtime from classical opiods to a wide array of drugs spanning several groups and varying mechanism of action, to avoid intra operative visceral and somatic pain, and to enhance post operative analgesia. Clonidine, an alpha 2 adrenergic agonist, has a variety of actions, including potentiating the effects of local anaesthetics. The aim of this study was to evaluate the differences in onset and duration of sensory and motor block, hemodynamic effects, post operative analgesia, and adverse effects of fentanyl versus clonidine when given intrathecally along with hyperbaric 0.5% bupivacaine in pateints undergoing total knee replacement (TKR). ***Method***: After approval from the institutional ethics committee and written informed consent from patient, 80 patients in the age group of 55-75 in ASA grade I and II undergoing elective total knee replacement surgeries were enrolled for the study. Patients were randomly allocated in two groups, group fentanyl (F) and group clonidine (C). Group F received bupivacaine 0.5% 3 ml, mixed with 25ug fentanyl to a total volume of 3.5 ml and group C received bupivacaine 0.5% 3ml with clonidine 50 ug . Statistical analysis were done using SAS 9.2, SPSS 15.0, Stata 10.1, medCalc 9.0.1 systat 12.0 and R environment Ver 2.11.1. ***Results***: Mean duration of motor block was significantly higher in group C (411.55± 82.38) as compared with group F (237.73±59.91). Significant difference in duration of sensory block was noted between group C (462.28±82.74) and group F (251.45±51.87). Duration of post operative analgesia was significantly longer in group C as compared to group F (mean duration of first request to rescue analgesia). In either of the groups we did not observe any side effects i.e bradycardia or hypotension, either during or after anesthesia that required intervention. ***Conclusions*:** Intrathecal clonidine is associated with prolonged motor and sensory block, hemodynamic stability and reduced need for rescue analgesia in 24 hours as compared to fentanyl.

INTRODUCTION

Currently total knee replacement is one of the most commonly performed orthopedic surgical procedure to improve mobility and patient quality of life especially in patients who are suffering from end stage osteoarthritis. [1,2] As the surgical techniques for TKR have evolved over times, so have the anesthetic techniques used for these procedures resulting in an improvement in patients outcomes.

The most common anaesthesia technique which is being performed during TKR is spinal anaesthesia (SA) not only because of its ease of administration but also because it being economical.

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However the greatest challenge with SA using only local anaesthesia is relatively shorter duration of action and therefore a need for early analgesic intervention in the post-operative period.

Numerous drug have been used in the recent past as an adjunct to local anaesthesia to increase the efficacy and duration of neuraxial block. Opioids were the first group of drug which were used along with Local anesthetic as an adjunct. Use of opioids resulted in increased duration of analgesia but were associated with undesirable side effects like nausea, vomiting, depression of ventilation and sedation. [3]

Fentanyl is a potent ,synthetic lipophilic mu receptor agonist, which has an analgesic effects at supraspinal level acting through opioid receptors situated in dorsal horn of spinal cord.[4] Intrathecal fentanyl is an established method for intraoperative anaesthesia and to supplement post-operative

analgesia. Clonidine is an imidazole derivative with selective partial agonist properties which inhibits nociceptive impulses by activation of post junctional alpha-2 adrenoceptor in the dorsal horn of spinal cord. In neuraxial block, it has a local effects on blockage of sympathetic outflow while in peripheral nerve blocks it prolongs duration of analgesia by hyperpolarization of cyclic nucleotide gated cation channel.[5]

The aim of the present study was to compare the duration of analgesia, duration of motor and sensory block, intraoperative hemodynamics caused by intrathecal Bupivacaine combined with fentanyl versus Bupivacaine combined with clonidine.

MATERIAL AND METHODS

This was a randomized prospective study carried out in the Dept of Anaesthesia at a tertiary care teaching hospital between Jan 2019 to Jan 2020.After institutional ethics committee approval and obtaining written informed consent from the patients.80 patients in the age group of 55 to 75 years in ASA I and II undergoing elective surgery were enrolled for the study. Patients were randomly divided into two group(n=40) namely group F which received 3.0 ml of 0.5% Inj bupivacaine(heavy) mixed with 25 mcg of Inj fentanyl to volume of 3.5 ml and the second group namely group C received 3.0 ml of 0.5% Inj bupivacaine(heavy) mixed with 50 mcg of Inj clonidine to volume of 3.5 ml.

Exclusion criteria

1. Patients less than 55 years and more than 75 years
2. Patients with comorbid conditions and who were using alpha 2 adrenergic receptors antagonists, calcium channel blocker, angiotensin converting enzyme inhibitors.
3. Patients with psychiatric and neurological illness.
4. Patients on anticoagulant.

RESULTS

The groups were comparable with respect to gender distribution in both groups.

Table 1 Gender distribution in the two groups

Gender	Group I (F)		Group II (C)	
	No	%	No	%
Female	24	60.0	17	42.5
Male	16	40.0	23	57.5
Total	40	100.0	40	100.0

Sample are gender matched with p= 0.117

Table 2 Age distribution in the two groups. The groups were comparable with respect to age distribution in both groups.

Age in years	Group I (F)		Group II (C)	
	No	%	No	%
41-50	1	2.5	2	5.0
51-60	11	27.5	11	27.5
61-70	23	57.5	24	60.0
>70	5	12.5	3	7.5
Total	40	100.0	40	100.0
Mean ± SD	64.13 ± 6.38		62.33 ± 6.39	

Sample are age matched with p=0.211

Table 3 Weight (kg) distribution in the two groups. The groups were comparable with respect to weight(kg) distribution in both groups.

Gender	Group I (F)		Group II (C)	
	No	%	No	%
<50	1	2.5	4	10.0
50-60	7	17.5	6	15.0
61-70	17	42.5	19	47.5
71-80	6	15.0	10	25.0
81-90	8	20.0	1	2.5
>90	1	2.5	0	0.0
Total	40	100.0	40	100.0
Mean ± SD	69.68 ± 11.11		66.20 ± 10.74	

Table 4 ASA grade distribution in the two groups.

ASA grade	Group I (F)		Group II (C)	
	No	%	No	%
Grade 1	23	57.5	1	2.5
Grade 2	17	42.5	39	37.5
Total	40	100.0	40	100.0

ASA grade 1 distribution is more in group 1 compared to group 2 which is statistically significant with $p<0.001^{**}$ however there is no statistically significant difference in the distribution of ASA grade 2 in either groups.

Table 5 Surgery distribution in the two groups. The groups were comparable with respect to distribution of surgery in both groups.

Sugery	Group I (F)		Group II (C)	
	No	%	No	%
TKR LT	20	50.0	26	65.0
TKR RT	20	50.0	14	35.0
Total	40	100.0	40	100.0

Distribution of surgery is statistically not significant in two groups with p= 0.175

Table 6 Duration of motor block distribution in the two groups

Duration of motor block (min)	Group I (F)		Group II (C)	
	No	%	No	%
<250	25	62.5	0	0.0
250-450	15	37.5	26	65.0
>450	0	0.0	14	35.0
Total	40	100.0	40	100.0
Mean	237.73 ± 59.91		411.55 ± 82.38	

Mean duration of motor block is significantly less in group 1 (F) compared to group 2 (C) with $p< 0.001^{**}$.

Table 7 Duration of sensory block distribution in the two groups

Duration of sensoryblock (min)	Group I (F)		Group II (C)	
	No	%	No	%
<250	20	50.0	0	0.0
250-450	20	50.0	16	40.0
>450	0	0.0	24	60.0
Total	40	100.0	40	100.0
Mean ± SD	251.45± 51.87		462.28± 82.74	

Mean duration of sensory block is significantly less in group 1 (F) compared to group 2 (C) with $p< 0.001^{**}$.

Table 8 Comparision of heart rate (bpm) in the two groups.

Heart rate (bpm)	Group 1 (F)	Group 2 (C)	P value
Pre operative	75.95± 6.63	74.00± 4.05	0.117
At spinal	79.35± 5.79	66.35± 3.89	≤0.001
3 min	86.90± 5.38	87.70± 5.01	0.493
6 min	76.90± 6.06	77.95± 4.24	0.372

9 min	78.10± 5.96	79.10± 4.46	0.398
12 min	77.75± 5.98	79.80± 5.08	0.102
15 min	77.20± 5.81	79.38± 4.90	0.074+
30 min	79.30± 4.95	77.10± 5.80	0.72+
45 min	79.55± 5.34	76.35± 5.97	0.014
60 min	79.83± 4.48	75.60± 6.19	0.001**
75 min	79.79± 4.48	74.54± 6.40	≤ 0.001**
90 min	80.45± 4.23	74.74± 6.40	0.001**
105 min	80.60± 5.42	73.86± 6.50	0.006**
120 min	80.89± 5049	75.24± 6.15	0.025**
135 min	80.44± 4.88	75.78± 6.50	0.070+
Immediate post operative	75.25± 6.80	75.20± 6.81	0.974
1 hr	78.80± 5.99	78.85± 5.97	0.970
2 hr	86.50± 5.54	86.45± 5.54	0.968
3 hr	76.15± 5.93	76.00± 5.97	0.911
4 hr	93.95± 105.60	77.30± 6.17	0.323
5 hr	76.85± 6.22	76.85± 60.12	1.000
6 hr	76.35± 5.62	76.55± 5.47	0.872
7 hr	76.00± 5.71	75.78± 5.45	0.857
8 hr	75.50± 5.41	75.00± 5.28	0.677

There were no reports of bradycardia in either group.

Table 9 Comparision of SBP (mm of Hg) in the two groups

SBP (mm of Hg)	Group 1 (F)	Group 2 (C)	P value
Pre operative	119.85± 5.23	122.25± 6.87	0.083+
At spinal	104.35± 4.48	110.60± 4.51	≤ 0.01**
3 min	130.60± 2.98	131.65± 5.34	0.281
6 min	122.80± 5.06	123.85± 6.80	0.436
15 min	124.75± 4.87	125.00± 5.75	0.834
60 min	124.05± 6.63	123.85± 4.21	0.873
90 min	123.19± 7.05	122.34± 5.60	0.588
120 min	121.33± 7.19	121.24± 5.53	0.969
Immediate post operative	131.68± 5.34	119.35± 4.63	≤ 0.001**
2 hr	124.40± 6.41	129.30± 3.78	≤ 0.001**
4 hr	125.00± 5.75	122.60± 4.92	0.048**
6 hr	124.60± 6.03	123.90± 4.77	0.566
8 hr	124.10± 6.37	123.69± 5.42	0.760

There were no reports of hypotension in either group.

Table 10 Comparision of DBP (mm of Hg) in the two groups

DBP (mm of Hg)	Group 1 (F)	Group 2 (C)	P value
Pre operative	79.30± 2.58	78.80± 5.04	0.578
At spinal	71.45± 3.20	71.90± 4.32	0.598
3 min	87.10± 3.07	86.30± 3.47	0.278
6 min	80.15± 4.19	80.90± 2.02	0.311
15 min	80.10± 3.23	80.40± 2.04	0.621
60 min	79.30± 2.62	79.48± 3.94	0.816
90 min	79.14± 3.73	78.92± 3.89	0.805
120 min	78.38± 4.58	78.06± 4.46	0.775
Immediate post operative	86.30± 3.47	78.65± 4.33	≤ 0.001**
2 hr	80.75± 3.13	86.60± 3.74	≤ 0.001**
4 hr	79.95± 3.46	78.65± 3.12	0.546
6 hr	80.25± 3.57	80.70± 3.06	0.547
8 hr	80.00± 3.65	80.31± 2.66	0.670

There were no reports of hypertension ineither group.

Table 11 Comparision of first request to rescue analgesia (min) in the two groups

Rescue analgesia (min)	Group I (F)		Group II (C)	
	No	%	No	%
≤ 250	22	55.00	0	0.0
250-500	18	45.0	32	80.0
≥ 500	0	0.0	8	20.0
Toal	40	100.0	40	100.0
Mean ± SD	241.80± 40.43		478.33± 33.10	

Mean duration of first request to rescue analgesia is significantly earlier in group 1 (F) (241.80± 40.43 min) as compared to group 2 (C) (478.33± 33.10 min) with p= ≤ 0.001**

Table 12 Highest pain score on VAS scale (0-10) in 24 hrs in the two group

Highest pain score in VAS scale (0-10)	Group I (F)		Group II (C)	
	No	%	No	%
≤ 3	0	0.0	2	5.0
3-6	26	65.0	38	95.0
≥ 6	14	35.0	0	0.0
Total	40	100.0	40	100.0
Mean ± SD	5.93± 1.38		4.25± 0.84	

Highest pain score on VAS Scale (0-10) is significantly less in group 2 (C) (4.25± 0.84) as compared to to group 1 (F) (5.93± 1.38) with p= ≤ 0.001**

Procedure and Data Collection

Patients in both the groups were administered Tab Aprax 0.25mg Per orally given at 2200 hrs night before the surgery. Pre operatively all patients were subjected to standard monitoring, including an electrocardiogram (5 lead), nonintravenous blood pressure , pulse oximeter and baseline vital parameter were noted. An intravenous (IV) access with a 16-gauge IV cannula was established in all patients and they were preloaded with 500 ml of Ringer Lactate. Spinal anaesthesia was performed with the patient in the sitting position, using a 25-gauge Lumbar Puncture needle with a midline approach at L3-4 interspace. After intrathecal injection, patients were immediately placed in the supine position for 5mins after which, they were placed in the required position for the start of the surgey.

Heart rate and noninvasive arterial blood pressure were measured every 3 min for 15 min and then every 15 min till 2 hours of surgery and thereafter every 30 min till completion of surgery, whereas peripheral oxygen saturation was monitored continuously by pulse oximeter. The onset of sensory block was defined as the time between injection of intrathecal anesthetic and the absence of pain at the T8 dermatone assessed by sterile pinkprick every 2 min till T8 dermatone was achieved. The highest level of sensory block was evaluated by pin prick at midclavicular line anteriorly every 5 min for 20 min after the injection, therafter every 15 min.

Motor block was assessed using the Modified Bromage Scale.

Grade	Definition
0	No motor block
1	Inability to raise extended leg; able to move knees and feet
2	Inability to raise extended leg and move knee; able to move feet
3	Complete block of motor limb

The data was collected every hourly till there was complete regression of block.

Postoperatively, the pain score was recorded in 24 hrs by using visual analog pain scale (VAS) between 0 and 10 (0= no pain, 10 = most sever pain). The patient was asked to point to the position on the line between the faces to indicate how much pain they were currently feeling. Once the patient had indicated how much pain they had, the clinician reviewed the reverse side of the ruler, which indicated a number 0-10. The number that correlated with the position on the VAS the patient pointed to the rating was recorded. IV PCM was given as rescue analgesia when VAS was>4.

Statistical Methods

Descriptive and inferential statistical analysis was been carried out in the present study. Results on continuous measurements

are presented on Mean ± SD (Min- Max) and results on categorical measurments are presented in Number(%). Significance was assessed at 5% level of significance. Student t test (two tailed, independent) has been used to find the significance of study parameters. Chi-square/ Fisher Exact test was used to find the significance of study parameters on categorical scale between two or more groups. The Statistical software namely SAS 9.2, SPSS 15.0, Stata 10.1, MedCalc 9.0.1, Syastat 12.0 and R environment ver.2.11.1 were used for the analysis of the data and Microsoft Word and Excel have been used to generate graphs, tables etc.

DISCUSSION

As the population ages and remains physically active through their sixth decade, major orthopedic joint repacement procedures are becoming increasingly more common. The most important risk factor for major adverse events after TKR is advanced age. The most common complications after TKR includes cardiac events, pulmonary embolism (PE), pneumonia and respiratory failure, and infection.[6,7] Older patients with major comorbidities, including cardiac disease, pulmonary disease, and diabetes, should have a complete preoperative medical evaluation.

In addition, Obesity can be a problem in the postoperative period, with regard to OSA and infections. Many of these patients require prolonged postoperative monitoring in the post anaesthesia care unit or ICU. Although general anaesthesia can be safely provided for TKR, a prospective case-controlled study found general anaesthesia with endotracheal intubation to be a major risk for nonsurgical complications after TKR.[8] Regional anaesthesia in the form of a neuraxial block (spinal or epidural) or a combination of a femoral and scaiatic block can be provide for the surgery.

Patients who have undergone TKR have sever postoperative pain, and several studies have reported a reduction in postoperative complications and improved outcomes when this pain is managed with regional anaesthesia. [9-11] On the other hand fentanyl, a lipophilic μ-receptor agonist opioid, is being used as an adjuvant for a long time with no major complications.[12] In the present study, an attempt was made to compare the analgesic effects and side-effects of Clonidine and Fentanyl for total Knee Replacement surgery when used as an adjuvant with Bupivacaine.

In our study, we added additives 25 μg Fentanyl in group F and 50 Microgram Clonidine in group C respectively to 3ml of 0.5% Bupivacaine (Heavy) intrathecally, of 40 patients each. Intra operative haemodynamics, in terms of heart rate and blood pressure however remained fairly constant in patients from boththe groups. We found that in group C patients the duration of motor blocade was significantly longer (411.55 ± 82.38) as compared to group F (237.73 ± 59.91 minutes) with P < 0.001 and then duration of sensory blockade was longer (462.28 ± 82.74 minutes) when compared to group 1 (251.45 ± 51.87 min) with statistacally significant p value <0.001. Also mean duration of first request to rescue analgesia is significantly earlier in group F (241.80 ± 40.43 min) as compared to group C (478.33± 33.10 min). These results are consistant with the results obtained by Khan, Aamir Laique *et al* [13] in 2015 where in the duration of motor and sensory blockade and mean duration of first request to rescue analgesia was higher in patients receving dexmitidomedine as compared to fentanyl when given intrathecally this shows that alpha agonists be it clonidine or dexmitidomidine is more effective in producing motor and sensory block compared to opiods.

The findings in our study suggested that the use of intrathecal clonidine as an adjuvant to bupivacaine provides a longer sensory and motor blockade and also prolongs the postoperative analgesic effect than the use of fentanyl with bupivacaine. Side effects like bradycardia and hypotension were not noticed in our study. No patient had residual neurologic deficit, postdural puncture headache or transient neurologic symptoms. The average duration of surgery lasted from 90 to 120 min. However, the potential risk of hypotension and bradycardia should be kept in mind and adequate care should be taken in the operation room.

Summary

Spinal anaesthesia is the prefered choice of anaesthesia in lower limb surgeries over the decades. However problem with this technique is its limited duration of action. So for long duration surgeries alternatives like epidural anaesthesia or general anaesthesia are required. Clonidine is a selective alpha-2-adgeneric agonist and has property to potentiate the action of local anaesthetic used in spinal anaesthesia. Fentanyl is an opioid and it has also the same property.Use of intrathecal clonidine as adjuvant to bupivacaine provides a longer sensory and motor blockade and also prolong the postoperative analgesic effect than the use of fentanyl with bupivacaine. It adds on to the patient comfort and results in early ambulation.

In conclusion the choice of anesthetic adjuvant to local anesthetic solely determines the outcomes listed in this study. This study gives credence to other studies in the literature that supports the use of alpha 2 agonist over opiods as an adjunt to local anesthetics when given intrathecally in patients undergoing elective TKR surgeries.

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How to cite this article:

Satish Kumar Mishra *et al* (2020) 'Current Status And Future Prospects of Anesthesia In Patients Undergoing Total Knee Replacement Surgery', *International Journal of Current Advanced Research,* 09(12), pp. 23417-23421.
DOI: http://dx.doi.org/10.24327/ijcar.2020. 23421.4636

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