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Original Research Article

Effect of addition of low dose Dexmedetomedine to 0.5% Ropivacaine in single shot Ultrasonography guided Femoral Nerve Block in patients undergoing elective unilateral total knee arthroplasty: A double blinded randomized control study (RCT)

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Abstract

Background: Total Knee Replacement is an extremely painful condition. Many additives have been tried earlier, but all have some limitations & drawbacks. So, this led us to try low dose Dexmedetomine to study its possible benefits as an additive to 0.5% Ropivacaine in single shot Femoral Nerve Block for post operative analgesia in patients undergoing elective unilateral total knee arthroplasty.

Materials & Methods: 50 patients were randomized into 2 groups each. Group RD received low dose Dexmedetomidine (1 µg/kg) along with Ropivacaine 20 ml of 0.5% whereas Group RO received only Ropivaicaine 20 ml 0.5%. Results were studied in the form of VAS at rest & with movement, Duration of Block, First request of Rescue Analgesia, Its total consumption, Patients view of quality of analgesia, vitals & side effects, if any. Data was analyzed using SPSS 17.0 software, students't test & Pearson Chi square test.

Results: Statistically significant lower mean VAS were seen in group RD than in group RO on passive movement but not at rest. 64% RD Group patients did not demand rescue analgesia as opposed to 44 % in Group RO (p=0.156). For patients who requested for rescue analgesia, the mean duration of femoral nerve block was 562.29±165.27 minutes and 573±328.89 minutes, respectively for RO and RD group (p 0.918). Patients who did not demand rescue analgesia at all in the entire post-operative period, the duration of femoral nerve block was taken as 24 hours, the approximate mean duration of analgesia for the whole RO group was 936.88±463.672 minutes and for group RD 1120.44±465.521 minutes (p 0.17). Total Rescue Analgesia consumption & no of requests were less in RD than in RO group (p 0.705). Quality of analgesia (excellent & good) as per patients was better in RD group (p 0.07).

Conclusion: Addition of low dose Dexmedetomidine to local anesthetic produces longer lasting sensory block thus, more effective analgesia in terms of lower post operative VAS values and greater patient satisfaction with lesser adverse effects as compared to earlier Dexmedetomedine studies using higher doses than our study. It delayed the first request for rescue analgesia and decreased total 24 hour rescue analgesia consumption in the post operative period without any significant side effects.

Keywords: Low dose Dexmedetomidine, Ultrasonography, Single-shot Femoral Nerve Block.

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1. Introduction

Total knee replacement is an extremely painful condition which causes immobility related complications, prolonged hospital stay & interferes with optimal knee rehabilitation. Out of various post-operative pain control measures like IV analgesics, epidural analgesia & regional anaesthesia (femoral nerve block), the latter provide superior pain relief & faster post-operative knee rehabilitation. [1] With single shot peripheral nerve blocks, it is possible for the patient to remain ambulatory post-operatively as opposed to continous blocks. Femoral nerve block also avoids potential risks of urinary retention,

dizziness, nausea, vomiting & hypotension which may occur when epidural analgesia is used. [2,3]

Long acting local anaesthetics alone can provide excellent analgesia for only up to 9 to 14 hours. [4-7]. Many additives like Adrenaline, opioids, Clonidine, Dexamethasone, Sodium bicarbonate, etc. [8-22] all seem to have some limitation or drawback. So, this study is an attempt to see the possible benefits of using low dose Dexmedetomidine as an adjuvant to Ropivacaine in ultrasound guided single shot femoral nerve block for postoperative pain relief in patients undergoing elective unilateral total knee arthroplasty.

2. Materials & Methods

2.1 Ethics Committee Approval

After hospital & University ethics committee approval (BFUHS/2K13/P-Th/9715), this prospective double blinded Randomized control study (RCT) was conducted in the Department of Anesthesiology, Dayanand Medical College, Ludhiana, Punjab, India. Written informed consent was taken from all the patients before the procedure.

2.2 Inclusion Criteria & Randomization

50 ASA grade I-III patients were randomized to two groups of 25 patients each according to random envelope generated allocations made by anesthesiologist uninvolved in study. Group RO 20 ml Ropivacaine 0.5% Group RD 20 ml Ropivacaine 0.5% & low dose Dexmedetomidine (1 µg/kg). An envelope was chosen randomly for each patient.

2.3 Aims & Objectives: 1) Quality & 2) Duration of Post-operative analgesia, 3) 24 hour rescue analgesic consumption 4) side effects, if any.

2.4 Exclusion Criteria

Patients with psychiatric problems (uncooperative patients) & communication difficulties, Peripheral neuropathies on the operative limb, Myopathies, Severe liver & kidney disease, history of allergy to any drug being used in our study, vascular disease i.e. Raynaud's disease, Bleeding diathesis or coagulation abnormalities, local cutaneous infection were excluded.

2.5 Pre-Anesthetic Check Up

After complete and thorough pre-anaesthetic check up, patients were instructed about Visual Analogue Scale (VAS) as a tool for measuring post-operative pain. They were educated about post-operative pain relief plan & informed about their abilities to request rescue analgesic if needed.

2.6 Analgesia Technique

Spinal anaesthesia was given with a 26-gauge Quincke's spinal needle, 10 mg of hyperbaric Bupivacaine 0.5% (2ml) + 25 micrograms Fentanyl (final volume 2.5 ml) was injected. Vitals were monitored. Sensory block duration of subarachnoid block was calculated by regression to T12 and motor block by return of modified Bromage Score 6 in the non-operated limb. Patients were assessed for pain two hours after the subarachnoid block i.e. at the time of execution of femoral nerve block which was given 2 hrs after the subarachnoid block under ultrasound guidance by an experienced blinded anesthesiologist who was unaware of nature of study drug solution and was not involved with further monitoring of the patient., All findings in PACU were recorded by a blinded anesthesiologist who was not aware of the type of drug solution used in femoral nerve block.

Diclofenac 75 mg Q8H was given with the first dose at the commencement of femoral nerve block. At any time VAS $\geq$ 5 or rescue analgesia demand by the patient was marked as the termination of the femoral nerve block. Tramadol 50 mg intravenous bolus was given as rescue analgesic repeated up to a maximum of 100 mg in continuous 4 hours or 400 mg in 24 hours. Total rescue analgesia used in 24 hours was recorded.

2.7 Statistical Analysis

17.0 SPSS software was used. Mean values and SDs were analyzed using unpaired Student's t-test and proportions using Pearson Chi-square test. P value < 0.05 was taken as statistically significant.

3. Observation & Results

3.1 Post Operative Pain Assessment

3.1.1 At Rest

Though, overall mean VAS in RD group at rest was lower than that of the RO group at rest, it could not achieve any statistical significance.

3.1.2 On Passive Movement

Statistically significant lower mean VAS was seen in group RD than in group RO on passive movement at the following observation times.

1st to 3rd hour,5th to 8th hour,11th hour,15th hour,16th hour, 19th hour, 20th hour and 48th hour ($p<0.05$)*

3.2 Demand for Rescue Analgesia

16 patients in RD group (64%) did not demand for rescue analgesia as compared to only 11 patients in RO group (44%). This difference was statistically insignificant (p value 0.156).

3.3 Duration of Femoral Nerve Block

No statistically significant difference was noted among the 14 patients from RO group (56%) and 9 patients from RD group (36%) who demanded for rescue analgesia. For patients who requested for rescue analgesia, the mean duration of femoral nerve block was 562.29±165.27 minutes and 573±328.89 minutes, respectively for RO and RD group which was not statistically significant (p value 0.918). The patients who did not demand rescue analgesia at all in the entire post-operative period, the duration of femoral nerve block was taken as 24 hours, the approximate mean duration of analgesia for the whole RO group comes out to be 936.88±463.672 minutes and for group RD 1120.44±465.521 minutes with p value of 0.17.

Table 1: Rescue Analgesia Consumption Comparison among the 2 Groups

Rescue analgesia (Tramadol) consumed	Group RO (n=14)	Group RD (n=9)	p value
50 mg	4 (29%)	3 (33%)	0.502
100 mg	9 (64%)	4 (45%)	
150 mg	1 (7%)	2 (22%)	

Table 2: Rescue Analgesia Consumption Time Course

Time period during which Rescue Analgesia was demanded	Group RO (total requests made)	Group RD (total requests made)	p value
0-8 hour	9	5	0.705
9-16 hour	10	9	
17-24 hour	6	3	

3.4 Patient's View of Analgesia Quality

Post operative pain relief was classified as Excellent (no pain/discomfort), Good (minor pain/discomfort which was tolerable), Moderate (pain/discomfort which was not tolerable but relieved with intervention) and Poor (pain/discomfort that was neither tolerable nor relieved with intervention) after explaining them in their own simple vernacular language.

Table 3: Analgesia Quality Comparison

Quality	Group RO (n=25)	Group RD (n=25)	p value
Excellent	11(44%)	17 (68%)	0.07
Good	4 (16%)	6 (24%)	
Moderate	6 (24%)	1 (4%)	
Poor	4 (16%)	1 (4%)	

3.5 Vital Signs

At the 24th hour which recorded a mean heart rate of 79 in group RO and 70.84 in group RD which was statistically significant (p value 0.032)*

*Statistically significant higher mean SBP was seen for group RO from the 10th minute to 9th hour, at 11th hour, 15th hour, 16th hour, 21st hour and 22nd hour.

*For DBP, statistically significant higher mean DBP was seen for group RO 10th minute to 5th hour, 7th hour, 8th hour, 11th hour and 16th to 18th hour.

*Significantly higher mean MAP for group RO was observed from 10th minute to 90th minute, 2.5th -3.5th hour, 5th -9th hour, 11th hour, 15th -17th hour and 23rd hour.

Statistically significant lower respiratory rate in group RD (p value <0.05) was seen at 40th minute, 9th hour, 11th hour and 48th hour of observation.

3.6 Adverse Effects

Nausea, Bradycardia & Hypertension was statistically significant as seen.

4. Discussion

4.1 Dexmedetomidine as an Adjuvant

All the adjuvants have limitations or disadvantages. Dexmedetomidine Dexmedetomidine, a highly selective α_2 adreno-receptor agonist with sedative, anxiolytic, analgesic & neuroprotective properties has shown promising result till now.[23] High dose Dexmedetomidine attenuates the acute Bupivacaine & Ropivacane induced perineural inflammation and safely improves the duration of antinociception following sciatic nerve blockade in rat [23,24].

There are only a few human studies that have proven Dexmedetomidine efficacious as an adjuvant to local anaesthetics in peripheral nerve block. [25-32]

4.2 Duration of Analgesia

The duration of analgesia in group RO in our study was longer as compared to a study by Theodosidas P *et al* [33] who performed 3-in-1block following total knee arthroplasty using Ropivacaine (398 minutes) and Bupivacaine (367 minutes) (p=0.62). This could be due to the difference in the blind block technique (3-in-1 block) v/s single shot ultrasound guided femoral nerve block.

In a double-blind fashion by Weber *et al*. [34], total of 84 patients received either 15, 20, 25 or 30 ml of Ropivacaine 0.5% with block duration being 534 ± 379 min for 15 ml, 799 ± 364 min for 20 ml, 624 ± 342 min for 25 ml and 644 ± 266 min for 30 ml. Thus, it is seen that the duration of analgesia with different volumes of the same concentration of Ropivacaine as ours was comparable to our results. But because of better sensory spread, 20 ml of Ropivacaine 0.5% appears to be the most appropriate dose for peripheral analgesia after TKR.

In a study by Wulf *et al*, [35] 21 male adults received 60 ml Ropivacaine 0.5% as regional anaesthesia (ilioinguinal-iliohypogastric blocks) in inguinal hernia repair. 12 patients had block duration >24 hours and 5 patients had 5-12 hours. These results were comparable to our group RO which received the same concentration of Ropivacaine but one-third of the total volume i.e. 20 ml. In our study, in 11 out of 25 patients in RO group the duration of analgesia was more than 24 hours and mean duration of analgesia in the rest 14 patients was around 9 hours (562.29±165.274 minutes).

In studies with Dexmedetomidine were reviewed, the one by Esmaoglu *et al* [30] for axillary block, the duration of analgesia was (887.14±260.82) minutes in group Levobupivacaine while it was (1008.69±164.04) minutes in group Levobupivacaine with Dexmedetomidine, hence about 13.7% prolongation of duration of analgesia. The duration of analgesia with Dexmedetomidine as an adjuvant to 0.25% Bupivacaine (35ml) was (456±97.99) minutes in a study by Swami *et al* [32] . Obayah *et al* [31] showed an increase in the time to first analgesic request following greater palatine nerve blocks cleft palate repair in children when Bupivacaine plus Dexmedetomidine

(1µg/kg) was compared with Bupivacaine alone (22 hr vs. 14.2 hr, p <0.001), a prolongation by about 55%. In patients who did not demand any rescue analgesia, if we take duration of analgesia as 24 hours, then the approximate duration of analgesia in RO group is 936.88±463.672 minutes and 1120.44±465.521 minutes in RD group showing approximately 20% prolongation of analgesia due to the addition of Dexmedetomidine (1µg/kg) to 20 ml of 0.5% Ropivacaine.

4.3 Effect of Dexmedtomidine on VAS (Visula Analogue Scale)

Group RD had overall lower mean VAS than group RO both at rest and on passive movement. Though the differences during rest were statistically insignificant, mean VAS recorded during passive movement showed more promising results in RD group with most of the readings being statistically significantly less as compared to patients of RO group (p<0.05). The reason for the fluctuation of VAS both during rest and on passive movement is explained by the fact that the femoral nerve block was applied 2 hours after subarachnoid block. This was the time when surgery got completed and the body had suffered maximal tissue damage and pain and inflammation was at its peak. Thus the application of femoral nerve block immediately post operatively served to control the pain resulting from inflammation when the effect of subarachnoid block almost wore off. This is clinically significant as the early post operative hours are the one which are more painful due to tissue damage and are of utmost concern to the patient and the attending physician. With time, the effect of femoral nerve block started wearing off which is when the mean VAS levels started rising. But, they were kept in check by the multimodal analgesia i.e. Injection Diclofenac 75 mg intravenous every 8 hours, in addition to femoral nerve block. At the end of 24 hour period, the mean VAS levels again started falling due to various factors like the residual effect of femoral nerve block, multimodal analgesia being administered round the clock and more importantly, the inflammation started subsiding and healing of the tissues started. Thus, the femoral nerve block covered the period of maximal pain perception very efficiently. Thus, when low dose Dexmedetomidine was added to 20 ml of Ropivacaine 0.5% in a dose of 1mcg/kg, it had beneficial effect on the quality of analgesia imparted as is evident by the overall lower mean VAS in group RD than in group RO with insignificant differences at rest, but statistically significant differences on passive movement at the following observation hours: 1st to 3rd hour, 5th to 8th hour, 11th hour, 15th hour, 16th hour, 19th hour, 20th hour, 48th hour.

These results were consistent with the human study on Dexmedetomidine done by Obayah *et al* [31] which showed significantly lower pain scores and increase in the time to first analgesic request in 24 hours following greater palatine nerve block Similarly our findings were also corroborated by decreased pain scores noted in other human studies on Dexmedetomidine done by Esmaoglu *et al* [30] and Swami *et al* [32].

4.4 Rescue Analgesia Consumption

Total rescue analgesia consumption was 1250 mg in group RO and 850 mg in group RD which also shows that addition of low dose Dexmedetomidine has beneficial effect on pain control, though it was statistically insignificant. Similar results were seen in a study conducted by Gerhard *et al* [36] where they added Dexmedetomidine to Ropivacaine to see its effect on the duration of interscalene brachial plexus block for elective shoulder surgeries. The total piritramide (opioid analgesic) dose for the first 24 hours was lower in the Dexmedetomidine group when compared to the Ropivacaine group, but this result was not statistically significant (19.4[15.7] v/s 23.3 [19.8] mg, p=0.39).

The total numbers of requests made for rescue analgesia were far more in RO group (25) than in RD group (17). This also supports beneficial role of adding Dexmedetomidine.

4.5 Quality of Block

It is seen that more excellent results were observed in RD group i.e. 68% as compared to 44 % in RO group and so were the moderate results (24% in group RD and 16% in group RO). Thus addition of Dexmedetomidine produced far number of patients reporting excellent quality of femoral nerve block as compared to only Ropivacaine.

4.6 Vital Signs

4.6.1 Heart Rate

In the study by Esmaoglu *et al* [30] heart rate levels in group LD (Levobupivacaine and Dexmedetomidine), except basal measurements, were significantly lower than those in group L (Levobupivacaine) (p value < 0.05). In group LD, bradycardia was observed in 7 patients, and all of these patients were treated with atropine. There were no episodes of bradycardia in group L.

In the study by Esmaoglu *et al* [30] SAP and DBP levels in group LD at 10, 15, 30, 45, 60, 90, and 120 minutes were significantly lower than those in group L (p value < 0.05).

4.6.2 Mean Arterial Pressure

The incidence of postoperative bradycardia has been reported as high as 40% in healthy surgical patients who received intravenous Dexmedetomidine, especially high doses. [37] These hemodynamic changes are caused by the inhibition of the central sympathetic outflow overriding the direct stimulating effects [38]. Another possible explanation is the stimulation of the presynaptic α_2 adreno-receptor, leading to a decreased Norepinephrine release [39]. The release of Epinephrine is also reduced by the same amount [40]. Similar effect was shown in a study

by Bloor *et al* [41]. But in our study, the acute hemodynamic changes were not seen as the route of administration was not intravenous. Dyck *et al* [42] also concluded similar findings.

4.6.3 Respiratory Rate

Patients receiving Dexmedetomidine as a primary therapy experienced clinically effective sedation yet were still easily arousable.[43] At clinically effective doses, Dexmedetomidine has been shown to cause much less respiratory depression than other sedatives [44]. However, co-administration of Dexmedetomidine with anaesthetic agents, sedatives, hypnotics, or opioids is likely to cause additive effects [45]. Also, addition of Dexmedetomidine caused better pain alleviation which leads to greater comfort level of the patient and thus decreased respiratory rate.

4.6.4 Adverse Effects

Bradycardia in group RD, is explained by the effect Dexmedetomidine has on the cardiovascular system.[38-40,45] This was seen by Swami *et al* [32] where lower pulse rate and blood pressure didn't require treatment, as it happened in our study too. Nausea, vomiting and anxiety were also noted in our study which was in contrast to the study done by Esmaoglu *et al* [30]. Also no neurologic deficit was observed in our study on study limb (data not shown). Thus, use of Dexmedetomidine is safe in peripheral nerve blocks. Supporting our finding is the study by Esmaoglu *et al* [30] and Swami *et al* [32] and also animal studies [23,24].

5. Summary & Conclusion

Thus, we conclude that the addition of Dexmedetomidine as an adjuvant to 0.5% Ropivacaine in femoral nerve block following total knee arthroplasty produces more effective analgesia in terms of lower post operative VAS values and greater patient satisfaction. It delayed the first request for rescue analgesia and decreased total 24 hour rescue analgesia consumption in the post operative period without any significant side effects.

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