ORIGINAL RESEARCH

Scope of dexmedetomidine as an adjuvant to 0.25% bupivacaine in femoral nerve block for postoperative analgesia after unilateral total knee replacement

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ABSTRACT

Background and objectives: To evaluate the efficacy of Dexmedetomidine as an adjuvant to 0.25% Bupivacaine in the femoral nerve block for postoperative analgesia following unilateral total knee replacement under spinal anaesthesia. **Methodology:** 60 patients who were posted for TKR taken up for our study after obtaining written informed consent. Femoral nerve block was administered under ultrasound guidance once the sensory level recedes to T12 dermatome. Here, patients were randomly allocated into two groups (A&B) using a computer-generated randomization chart. Patients in group A received 20ml of 0.25% Bupivacaine with Dexmedetomidine (0.5 mcg/kg) made up to 1ml (total 21ml). Patients in group B received 20ml of 0.25% Bupivacaine with 1ml normal saline (total 21ml). Pain was assessed using VAS, Motor power of lower limb was recorded with MBS and vitals are closely monitored. All the observations are tabulated and statistically analyzed. **Results:** In group A the mean duration of analgesia is $16.73(\pm 1.14)$ and in group B the mean duration of analgesia is $11.3(\pm 1.15)$, P value is statistically significant. **Conclusion:** Dexmedetomidine as an adjuvant to Bupivacaine prolongs theduration of analgesia in femoral nerve block after unilateral total kneereplacement.

Keywords: Total knee replacement, Femoral nerve block. Bupivacaine. Dexmedetomidine

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INTRODUCTION

Total knee replacement is successful procedure for treating patients with osteoarthritis to relieve joint pain, increase mobility, and improve quality of life.Patients undergoing total knee replacement surgery experience considerable postoperative pain. ^[1,2]It not only impairs early mobilization and rehabilitation but also prolongs the hospitalization.

Pain is typically the main component of patients with knee osteoarthritis. Pain is subjective and it involves peripheral and central neural mechanisms that are modulated by Neuro chemical, environmental, psychological, and genetic factors. Pain management after total knee replacement is still challenging, but is important due to good pain management can improve the outcome of patients.

The postoperative pain is caused by inflammation resulted from direct nerve injury or the tissue injury. Patients can perceive the pain through afferent pain pathway, this is the target of a variety of drugs. Direct local anaesthetics or the drugs that reduce the response of local hormones to injury (nonsteroidal anti-inflammatory drugs, such as ibuprofen or aspirin) can be utilized to block the activity of pain receptors, thereby reducing the activity of pain receptors.

Opioid is frequently used for postoperative pain management. However, it may be associated with many adverse effects, including headache, nausea, vomiting, respiratory depression, retention of urine, and constipation. Specific medical diseases related to the inadequate pain control involved myocardial infarction, coronary ischemia, venous thrombosis, and pneumonia. Effective postoperative analgesia can reduce opioid consumption and promote rehabilitation. Several methods have been applied to reduce postoperative pain after TKR including the peripheral nerve block and the local infiltration anesthesia, intravenous analgesics as well as the epidural anesthesia.Femoral nerve block (FNB) was reported to reduce postoperative pain and has increased in popularity because of its opioid sparing effects, and consistency with anticoagulatory therapy. FNBs can be performed as a single shot or as a continuous block using a catheter and an infusion. Continuous nerve blocks have the advantage of permitting the delivery of analgesia for a longer postoperative duration than single-shot nerve blocks. Nerve blocks have also been shown to result in a reduced need for parenteral or oral analgesia to control pain and in reported pain levels.

Bupivacaine is an amide local anesthetic that has shown high efficacy in terms of onset and duration of Femoral nerve block . To improve the quality of peripheral nerve blocks, many adjuvants to local anesthetic's are added. One such agent is Dexmedetomidine, and it is an alpha 2 agonist ^[5]. Dexmedetomidine (α_2 adrenoceptor agonist) is being used for intravenous (IV) sedation and analgesia for intubated and mechanically ventilated patients in

Intensive Care Units. Its use in peripheral nerve blocks has recently beendescribed. It has been reported to have a rapid onset time, to prolong the duration of local anesthetics, and is also reportedly safe and effective in peripheral nerve blocks.

MATERIALS AND METHODS

The present study was a single-center, Hospital based Prospective randomized double-blind Study conducted on patients scheduled for unilateral total replacement. The study was conducted after obtaining approval from the institutional ethics committee and informed written consent.60 patients were randomly allocated into two groups of 30 each.

INCLUSION CRITERIA

Patients scheduled for unilateral total knee replacement.

EXCLUSION CRITERIA

Patient refusal

- Infection at the local site
- Allergy to local anesthetics

RESULTS

During the present study a total of 60 subjects were taken into study Group A and B were comparable with regard to their age, weight, sex.

| Age (Years) | GROUPA | | GROUP B | | | | |
|--|--------|-------|----------------|-------|--|--|--|
| | (n=30) | n (%) | (n=30) | n (%) | | | |
| 40-50 | 5 | 16.7% | 5 | 16.7% | | | |
| 50-60 | 9 | 30.0% | 12 | 40.0% | | | |
| 60-70 | 6 | 20.0% | 6 | 20.0% | | | |
| 70-80 | 6 | 20.0% | 7 | 23.3% | | | |
| 80-90 | 4 | 13.3% | 0 | 00.0% | | | |
| Mean | 2.83 | | 2.50 | | | | |
| SD | 1.31 | | 1.04 | | | | |
| Chi-Square Test, P Value=.342, not significant | | | | | | | |

 Table1: Association between Study Group and Age (N=60)
 Page (N=60)

• Bleeding disorders **METHOD OF STUDY**

60 Patients posted for total knee replacement surgery, during their pre-anaesthetic checkup (PAC), were explained about all the modalities of anaesthesia and analgesia feasible to them and those patients who are willing to participate in the study were evaluated for the inclusion and exclusion criteria. Patients satisfying the inclusion criteria were enrolled for the study after taking written informed consent. After surgery patients were shifted to post anaesthesia care unit (PACU) and were monitored until the resolution of subarachnoid blockade to T12 dermatome, and FNB administered under ultrasound guidance. Here, patients are randomly allocated into two groups A & B using a computer-generated randomization chart.Patients in group A received 20ml of 0.25% Bupivacaine with Dexmedetomidine (0.5 mcg/kg) made up to 1ml (total 21ml).Patients in group B received 20ml of 0.25% Bupivacaine with 1ml normal saline (total 21ml). Pain was assessed using visual analog scale(VAS), Motor power of lower limb was recorded with modified bromage scale (MBS) and vitals are closely monitored. All the observations are tabulated and statistically analyzed.

STATISTICAL ANALYSIS

All the quantitative data was tested using student t-test and qualitative data by chi square test.

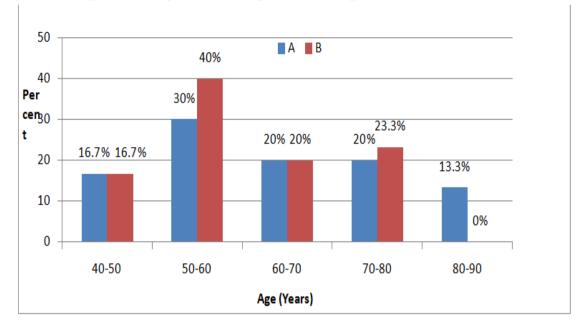
P<0.05 were statistically significant.

When variables are continuous variables for equivalence design, the formula is

$$n > 2 \left[\frac{\left(z_{1-\alpha/2} + z_{1-\beta} \right) \sigma}{\delta} \right]^2.$$

Where n= size per group

 $Z_{1-\alpha/2}$ & $Z_{1-\beta}$ =standard normal deviation σ = clinically acceptable margin δ = standard deviation of both comparison groups n = 2265.99/81 = 27.97 approx. 30 for each group

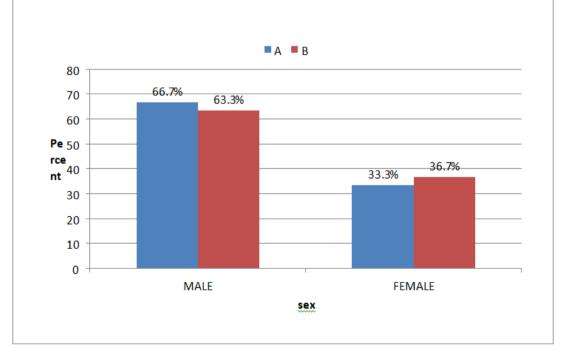


Graph 1: Bar diagram for comparison of Groups A & B with Age

The patients are now divided into two groups based on their sex in the following table. Table 2: Association between Study Group and Sex (N=60)

| Sex | GROUPA | | GROUP B | | |
|---|--------------|-------|----------------|-------|--|
| | (n=30) n (%) | | (n=30) | n (%) | |
| 1 | 20 | 66.7% | 19 | 63.3% | |
| 2 | 10 | 33.3% | 11 | 36.7% | |
| Chi-Square Test, P Value=0.5, not significant | | | | | |

Graph 2: Bar diagram for comparison of Groups A & B with SEX

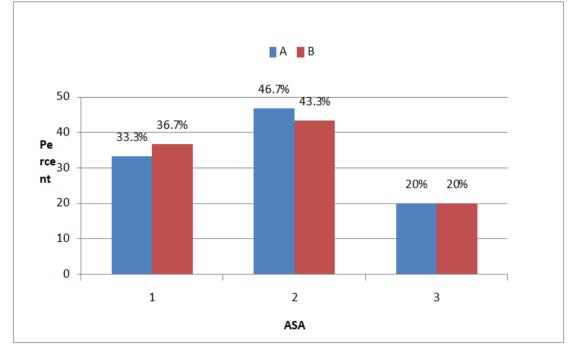


The patients are compared for the association between study groups and ASA in the following table Table 3: Association between Study Group and ASA (N=60)

| I | ASA | GROUPA | | GROUPB | |
|---|-----|----------------|-------|----------|-------|
| | | A (n=30) n (%) | | B (n=30) | n (%) |
| | 1 | 10 | 33.3% | 11 | 36.7% |

| 3 Chi-Squa | 20.0% | | | |
|---------------|-------|----------------|----|-------|
| 2 | 14 | 46.7% 20.0% | 13 | 43.3% |

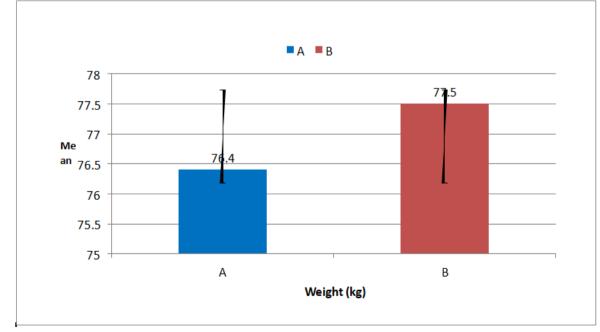
Graph 3: Bar diagram for comparison of Groups A & B with ASA



The patients are compared for the association between study group and weight in the following table **Table4: Association between Study Group and Weight (N=60)**

| Weight(kg) | GROUP | A (n=30) | GROUP B (n=30) | | | |
|---|-------|----------|----------------|-----------|--|--|
| | Mean | SD(±) | Mean | $SD(\pm)$ | | |
| | 76.40 | 6.015 | 77.50 | 8.784 | | |
| Unpaired t Test, P Value=0.574, not significant | | | | | | |

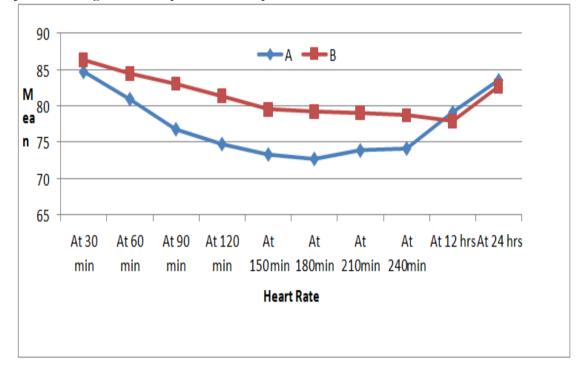
Graph 4: Bar diagram for comparison of Groups A & B with Weights (kg)



| | GROUPA (n=30) | | GROUP | GROUPA (n=30) | | |
|-------------|-----------------|-------------|-------|---------------|----------|--|
| HR | Mean | SD(±) | Mean | SD(±) | P-value | |
| At 30 min | 84.70 | 9.66 | 86.30 | 9.50 | 0.520 | |
| At 60 min | 80.93 | 10.99 | 84.43 | 10.01 | 0.202 | |
| At 90 min | 76.77 | 11.14 | 83.03 | 10.76 | < 0.031* | |
| At 120 min | 74.73 | 8.75 | 81.33 | 9.91 | <0.013* | |
| At 150min | 73.30 | 8.75 | 79.53 | 9.32 | < 0.010* | |
| At 180min | 72.67 | 6.86 | 79.20 | 9.22 | < 0.003* | |
| At 210min | 73.87 | 7.26 | 79.00 | 8.85 | < 0.017* | |
| At 240min | 74.13 | 6.76 | 78.70 | 8.76 | < 0.028* | |
| At 12 hrs | 79.10 | 7.46 | 77.90 | 7.52 | 0.537 | |
| At 24 hrs | 83.53 | 7.41 | 82.67 | 7.25 | 0.649 | |
| Unpaired T- | Test, P Value * | Significant | | | | |

The patients are compared for the association between study group and HR Table 5: Association between Study Group and HR (N=60)

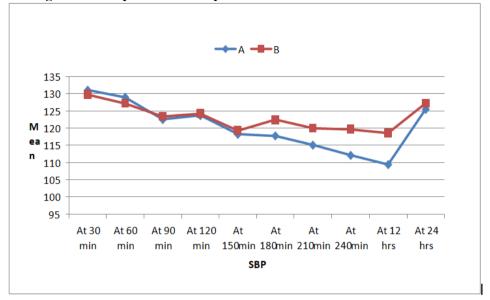
Graph 5: Line diagram for comparison of Groups A & B with HR



Patients are compared for the association between study group and SBP in the following table **Table 6: Association between Study Group and SBP (N=60)**

| tion between Study Group and SDI (N=00) | | | | | | | | |
|---|--------|---------------|--------------|----------------|----------|--|--|--|
| | GROUP | -A (n=30) | GROUP- | GROUP-B (n=30) | | | | |
| SBP | Mean | $SD(\pm)$ | Mean | $SD(\pm)$ | P-value | | | |
| At 30 min | 131.07 | 7.839 | 129.70 | 7.747 | 0.500 | | | |
| At 60 min | 128.93 | 8.706 | 127.17 | 8.292 | .424 | | | |
| At 90 min | 122.53 | 19.744 | 123.37 | 18.758 | 0.867 | | | |
| At 120 min | 123.70 | 7.475 | 124.20 | 8.306 | 0.807 | | | |
| At 150min | 118.23 | 18.425 | 119.27 | 21.190 | 0.841 | | | |
| At 180min | 117.73 | 7.515 | 122.43 | 9.066 | < 0.033* | | | |
| At 210min | 115.07 | 8.191 | 119.97 | 8.556 | < 0.027* | | | |
| At 240min | 112.13 | 8.740 | 119.63 | 9.008 | < 0.002* | | | |
| At 12 hrs | 109.40 | 8.418 | 118.53 | 9.486 | < 0.000* | | | |
| At 24 hrs | 125.47 | 5.380 | 127.20 | 6.661 | 0.272 | | | |
| | Unpair | ed T- Test, I | Value *Signi | ficant | | | | |

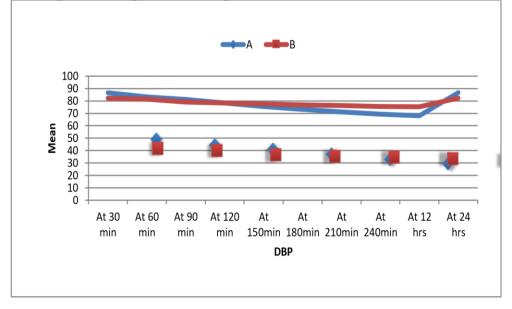
Graph 6: Line diagram for comparison of Groups A & B with SBP



The patients are now compared for the association between study group and DBP in the following table **Table 7: Association between Study Group and DBP (N=60)**

| | GROUP | PA (n=30) | GROUP B (n=30) | | |
|------------|--------|---------------|----------------|-----------|----------|
| DBP | Mean | $SD(\pm)$ | Mean | $SD(\pm)$ | P-value |
| At 30 min | 86.47 | 10.827 | 82.27 | 13.159 | 0.182 |
| At 60 min | 83.33 | 9.607 | 81.33 | 12.645 | 0493 |
| At 90 min | 81.07 | 9.461 | 79.03 | 13.389 | 0.500 |
| At 120 min | 78.37 | 9.835 | 78.30 | 11.891 | 0.981 |
| At 150min | 75.63 | 8.880 | 77.63 | 12.923 | 0.488 |
| At 180min | 73.23 | 8.943 | 76.83 | 12.839 | 0.213 |
| At 210min | 71.23 | 8.537 | 76.20 | 11.633 | 0.064 |
| At 240min | 69.27 | 8.733 | 75.63 | 12.113 | < 0.023* |
| At 12 hrs | 68.07 | 8.509 | 75.33 | 12.053 | < 0.009* |
| At 24 hrs | 86.70 | 9.319 | 82.30 | 10.780 | 0.096 |
| | Unpair | ed T- Test, I | Value *Si | gnificant | |

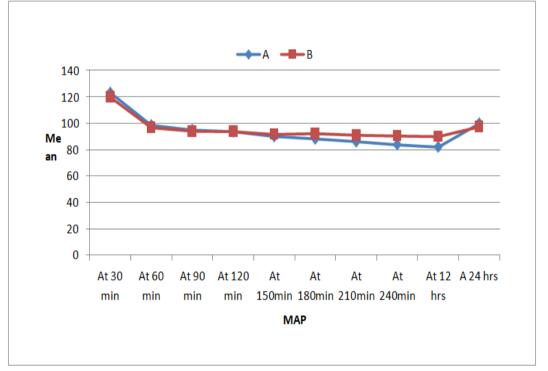
Graph 7: Line diagram for comparison of Groups A & B with DBP



| MAP | GROUP | - A (n=30) | GROUP- | B (n=30) | |
|------------|--------|----------------|--------------|-----------|----------|
| | Mean | SD(±) | Mean | $SD(\pm)$ | P-value |
| At 30 min | 123.18 | 9.821 | 119.69 | 11.408 | 0.210 |
| At 60 min | 98.53 | 8.536 | 96.61 | 10.320 | 0.435 |
| At 90 min | 94.89 | 9.754 | 93.81 | 12.491 | 0.711 |
| At 120 min | 93.48 | 8.026 | 93.60 | 9.589 | 0.957 |
| At 150min | 89.83 | 10.397 | 91.51 | 12.169 | 0.568 |
| At 180min | 88.07 | 7.176 | 92.03 | 10.347 | 0.90 |
| At 210min | 85.84 | 7.222 | 90.79 | 9.362 | < 0.026* |
| At 240min | 83.56 | 7.675 | 90.30 | 10.151 | < 0.005* |
| At 12 hrs | 81.84 | 7.699 | 89.73 | 10.219 | < 0.001* |
| A 24 hrs | 99.62 | 7.174 | 97.27 | 8.662 | 0.256 |
| | Unpai | red T- Test, I | P Value *Sig | gnificant | |

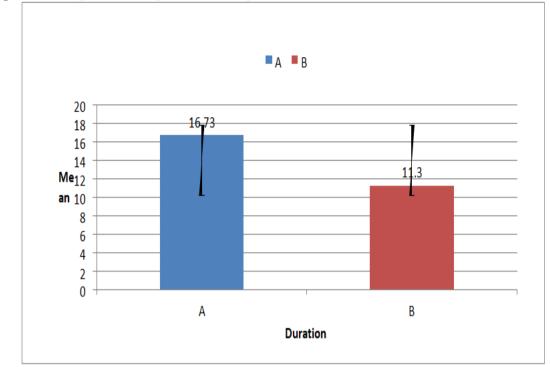
The patients are compared for the association between study group and MAP in the following table **Table 8: Association between Study Group and MAP (N=60)**

Graph 8: Line diagram for comparison of Groups A & B with MAP



The patients are compared for the association between the study groups and the duration of analgesia in the following table

| Duration | GROUP | A (n=30) | GROUP B (n=30 | | | |
|---|------------|-----------|---------------|-----------|--|--|
| | Mean | $SD(\pm)$ | Mean | $SD(\pm)$ | | |
| | 16.73 1.14 | | 11.3 | 1.15 | | |
| Unpaired t Test, P Value=0.000, significant | | | | | | |

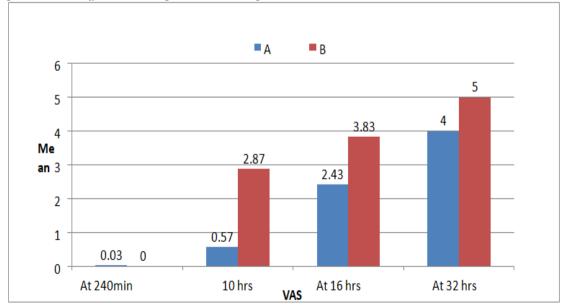


Graph 9: Bar diagram for comparison of Groups A & B with Duration

The patients are compared for the association between study groups and VAS in the following table **Table 10: Association between Study Group and VAS (N=60)**

| VAS | GROUPA | | | GROUPB | | P-value | | |
|-----------|---------------------------------------|-----------|--------|--------|-------|---------|----------|--|
| | Mean | $SD(\pm)$ | Median | Mean | SD(±) | Median | | |
| At 240min | 0.03 | 0.183 | 0.00 | 0.00 | 0.000 | 0.00 | < 0.5* | |
| 10 hrs | 0.57 | 0.728 | .00 | 2.87 | 0.346 | 3.00 | < 0.000* | |
| At 16 hrs | 2.43 | 0.568 | 2.00 | 3.83 | 0.379 | 4.00 | < 0.000* | |
| At 32 hrs | 4.00 | 0.000 | 4.00 | 5.00 | 0.000 | 5.00 | < 0.000* | |
| | Chi-square Test, P Value *Significant | | | | | | | |

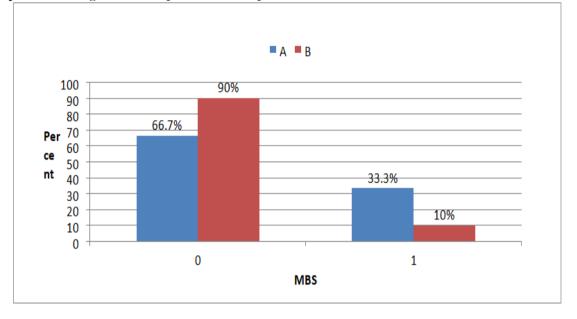
Graph 10: Bar diagram for comparison of Groups A & B with VAS



The patients are compared for the association between study group and MBS in the following table **Table 11: Association between Study Group and MBS (N=60)**

| MBS | GROUP- A | | GROUP- B | | | |
|--|-----------------|-------|----------|--------|--|--|
| | (n=30) | n (%) | (n=30) | n (%) | | |
| 0 | 20 | 66.7% | 27 | 90.0% | | |
| 1 | 10 | 33.3% | 3 | 10.0% | | |
| Chi-Square Test, P Value=0.05, Significant | | | | | | |

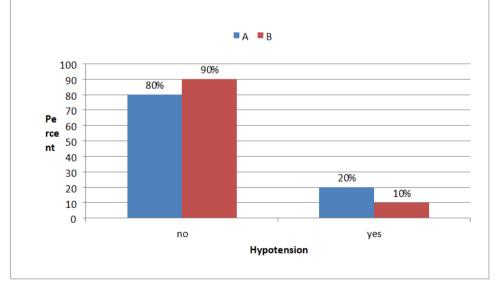
Graph 11: Bar diagram for comparison of Groups A & B with MBS



The patients are now compared for the association between study group and hypotension in the following table Table 12: Association between Study Group and Hypotension (N=60)

| | GROUP -A | | GROUP -B | | | | |
|---|-----------------|-------|-----------------|-------|--|--|--|
| Hypotension | (n=30) | n (%) | (n=30) | n (%) | | | |
| no | 24 | 80.0% | 27 | 90.0% | | | |
| yes | 6 | 20.0% | 3 | 10.0% | | | |
| Chi-Square Test, P Value=0.28,not Significant | | | | | | | |

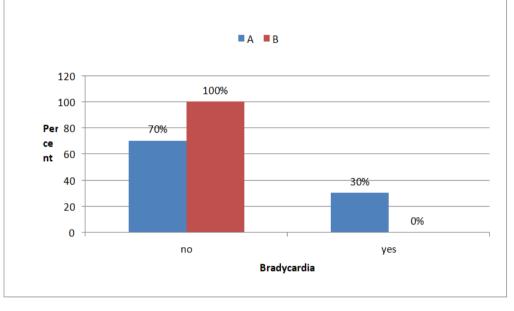
Graph 12: Bar diagram for comparison of Groups A & B with Hypotension



The patients are compared for the association between study group and Bradycardia in the following table **Table 13: Association between Study Group and Bradycardia** (N=60)

| | GROUPA | | GROUP B | | | | |
|---|-----------------|-------|----------------|--------|--|--|--|
| Bradycardia | (n=30) | n (%) | (n=30) | n (%) | | | |
| no | 21 | 70.0% | 30 | 100.0% | | | |
| yes | 9 | 30.0% | 0 | 00.0% | | | |
| Chi-Square Test, P Value=0.001, Significant | | | | | | | |

Graph 13: Bar diagram for comparison of Groups A & B with Bradycardia



DISCUSSION

With a P value of 0.342 Age distribution has no statistical significance. With a a P value of 0.5 Gender distribution has no statistical significance. With a P value of 0.959ASA physical status has no statistical significance.With a P value of 0.574 Weight distribution has no statistical significance. Adverse events like Hypotension with P value of 0.28 has no statistical significance.

Heart rate (HR)- In Group-A among 30 patients, the HR is maximum at 30 minutes with a mean (SD) of 84.70 (\pm 9.66). in Group-B among 30 patients, the HR is maximum at 30 minutes with a mean (SD) of 86.30 (\pm 9.50). P value is statistically significant.

Systolic blood pressure (SBP) - In Group-A among 30 patients, the SBP is maximum at 30 minutes with a mean (SD) of 131.07 (\pm 7.839). In Group-B among 30 patients the SBP is maximum at 30 minutes with a mean (SD) of 129.07 (\pm 7.747). P value is statistically significant.

Diastolic blood pressure (DBP) - In Group-A among 30 patients, the maximum DBP is observed at 30 minutes with a mean (SD) of 86.47 (\pm 10.827). In Group-B among 30 patients, the maximum DBP is observed at 30 minutes with a mean (SD) of 82.27 (\pm 13.159). P value is statistically significant.

Mean arterial pressure (MAP)- In Group-A among 30 patients the maximum MAP is observed at 30 minutes with a mean (SD) of 123.18 (±9.821). In Group-B among 30 patients, the maximum MAP is

observed at 30 minutes with a mean (SD) of 119.69 (± 11.408) . P value is statistically significant.

Visual analog scale (**VAS**)- In Group-A among 30 patients, VAS is maximum at 16 hours with a mean (SD) of 2.43 (± 0.568) and a median of 2.00. In Group-B among 30 patients, VAS is maximum at 16 hours with a mean (SD) of 3.83 (± 0.379) with a median of 4.00. P value is statically significant.

Modified bromage scale (**MBS**) - In Group-A among 30 patients, the MBS score is 0 in 20 (66.7%) patients and 1 in 10 (33.3%) patients. In Group-B the MBS score is 0 in 27 (90.0%) patients and 1 in 3 (10%) patients. P value is statistically significant.

Bradycardia- In Group-A among 30 patients, 21 (70%) patients reported no signs of bradycardia and 9 (30%) patients developed bradycardia. In Group-B among 30 patients, 30 patients (100%) patients reported no signs of bradycardia.

From the above observations and inferences, it is demonstrated that equivalent doses of Dexmedetomidine is a better adjuvant to Bupivacaine in femoral nerve block forPostoperative analgesia after unilateral total knee replacement.

CONCLUSION

In conclusion, all these above results suggest that adding Dexmedetomidine as an adjuvant to 0.25% Bupivacaine in femoral nerve block prolongs duration of analgesia without significant increase in the degree of motor blockade during postoperative period in unilateral total knee replacement. Although bradycardia, hypotension are associated with dexmedetomidine, they were easily reversed. It also decreased the use of opioids and other modes of rescue analgesia.

REFERENCES

- Puolakka Pa, Rorarius MG, Roviola M, Puolakka Tj, Nordhausen K, Lindgren L. Persistent pain following knee arthroplasty. Eur J Anaesthesiology. 2010; 27:455-60.
- American society of Anesthesiologists Task Force on Acute pain management. IN the perioperative setting: An updated report by the American Society of Anesthesiologists. Task Force on Acute pain Management. Anesthesiology. 2012; 116:248-73.
- Singh J, Yu S, Chen L, Cleveland J.Rates of Total Joint Replacement in the United States: Future Projections to 2020–2040 Using the National Inpatient Sample. The Journal of Rheumatology. 2019;46(9):1134-1140.
- Ravi B, Croxford R, Reichmann W, Losina E, Katz J, Hawker G.The changing demographics of total joint arthroplasty recipients in the United States and Ontario from 2001 to 2007.Best Practice & Research Clinical Rheumatology. 2012;26(5):637-647.
- Kandasami M, Kinninmonth AW, Sarungi M, Baines J, Scott NB. Femoral nerve block for total knee replacement - a word of caution. Knee. 2009 Mar;16(2):98-100. doi: 10.1016/j.knee.2008.10.007. Epub 2008 Nov 28.
- Gaffney CJ, Pelt CE, Gililland JM, Peters CL. Perioperative pain management in hip and knee arthroplasty. Orthop Clin North Am, 2017, 48: 407– 419.
- Moucha CS, Weiser MC, Levin EJ. Current strategies in anesthesia and analgesia for total knee arthroplasty. J Am Acad Orthop Surg, 2016, 24: 60–73.
- Dimaculangan D, Chen JF, Borzio RB, Jauregui JJ, Rasquinha VJ, Maheshwari AV. Periarticular injection and continuous femoral nerve block versus continuous femoral nerve block alone on postoperative opioid consumption and pain control following total knee arthroplasty: randomized controlled trial. J Clin Orthop Trauma, 2019, 10: 81–86.
- Li JW, Ma YS, Xiao LK. Postoperative Pain Management in Total Knee Arthroplasty. Orthop Surg. 2019;11(5):755-761.
- Rosenblatt RM. Continuous femoral anesthesia for lower extremity surgery. Anesthesia and Analgesia 1980;59(8):631-2.
- Sharma S, Iorio R, Specht LM, Davies-Lepie S, Healy WL. Complications of femoral nerve block for total knee arthroplasty. Clin Orthop Relat Res. 2010;468(1):135-140.
- 12. Singelyn FJ, Deyaert M, Joris D, Pendeville E, Goureweur JM. Effects of intravenous patientcontrolled analgesia with morphine, continuous epidural analgesia, and continuous three-in-one block on postoperative pain and knee rehabilitation after unilateral total knee arthroplasty. Anesth Analg. 1998; 87:8
- 13. Li J, Duan R, Zhang Y, Zhao X, Cheng Y, Chen Y, Yuan J, Li H, Zhang J, Chu L, Xia D, Zhao S. Betaadrenergic activation induces cardiac collapse by aggravating cardiomyocyte contractile dysfunction in

bupivacaine intoxication. PLoS One. 2018;13(10):e0203602.

- Iskander A, Gan TJ. Novel analgesics in ambulatory surgical patients. Curr cpin Anaesthesiol. 2018 Dec;31(6):685-692.
- Prabhakar A, Lambert T, Kaye RJ, Gaignard SM, Ragusa J, Wheat S, Moll V, Cornett EM, Urman RD, Kaye AD. Adjuvants in clinical regional anesthesia practice: A comprehensive review. Best Pract Res Clin Anaesthesiol. 2019 Dec;33(4):415-423.
- 16. Barrington MJ, Uda Y. Did ultrasound fulfill the promise of safety in regional anesthesia? Curr Opin Anaesthesiol. 2018 Oct;31(5):649-655.
- Wolfe RC, Spillars A. Local Anesthetic Systemic Toxicity: Reviewing Updates From the American Society of Regional Anesthesia and Pain Medicine Practice Advisory. J Perianesth Nurs. 2018 Dec;33(6):1000-1005.
- Petrikas AZh, Ol'khovskaia EB, Medvedev DV, Diubaĭlo MV. [Disputable issues of Malamed's "Handbook of local anesthesia" (2004)]. Stomatologiia (Mosk). 2013;92(2):71-6.
- 19. Grewal A. Dexmedetomidine: New avenues. J AnaesthClinPharmacol 2011; 27:297-302.
- 20. Abramov D, Nogid B, Nogid A. Drug forecast. PandT 2005 Mar; 30(3): 158.
- 21. Haselman A M. Dexmedetomidine: A useful adjunct to consider in some high risk situation. AANA Journal 2008 Oct;76(5).
- Aho M, Erkola O, Kallio A, Scheinin H, Korttila K. Comparison of Dexmedetomidine and midazolam sedation and antagonism of Dexmedetomidine with atipamazole. J Clin Anaesth; 1993;5:194-203.
- Jones MEP, Maze M. Can we characterize the central nervous system actions of alpha-2 adrenergic agonists? Br J Anaesth 2001;86(1):1-3.
- 24. Maarouf M. Evaluation of effect of Dexmedetomidine in reducing shivering following epidural anaesthesia. ASA annual meeting Abstract AA-49.
- El-HennawyAM, Abd-Elwahab. Addition of clonidine or Dexmedetomidine to bupivacaine prolongs caudal analgesia in children. Br J Anaesth 2009; 103; 268-74.
- Allen HW, Liu SS, Ware PD, Nairn CS, Owens BD. Peripheral nerve blocks improve analgesia after total knee replacement surgery. Anesth Analg. 1998 Jul 1;87(1):93-7.
- 27. Singelyn FJ, Deyaert M, Joris D, Pendeville E, Goureweur JM. Effects of intravenous patientcontrolled analgesia with morphine, continuous epidural analgesia, and continuous three-in-one block on postoperative pain and knee rehabilitation after unilateral total knee arthroplasty. Anesth Analg. 1998;87:8
- Horn JL, Pitsch T, Salinas F, Benninger B. Anatomic basis to the ultrasoundguided approach for saphenous nerve blockade. Reg Anesth Pain Med. 2009 SepOct;34(5):486-9.
- Sharma S, Iorio R, Specht LM, Davies-Lepie S, Healy WL. Complications of femoral nerve block for total knee arthroplasty. Clin Orthop Relat Res. 2010 Jan;468(1):135-40.
- 30. Ilfeld BM, Duke KB, Donohue MC. The association between lower extremity continuous peripheral nerve blocks and patient falls after knee and hip arthroplasty. Anesth Analg. 2010 Dec;111(6):1552-4.

- Paul JE, Arya A, Hurlburt L, Cheng J, Thabane L, Tidy A, Murthy Y. Femoral nerve block improves analgesia outcomes after total knee arthroplasty: a meta-analysis of randomized controlled trials. Anesthesiology. 2010 Nov;113(5):1144-62.
- 32. Gupta R, Varma R, Dexmedetomidine as an intrathecal adjuvant for postoperative analgesia Deepika Shukla, Anil Verma, Apurva Agrawal, Comparative study of intrathecal dexmedetomidine with intrathecal magnesium sulfate used as adjuvants to bupivacaine, Journal of Anaesthesiology, Volume 27, Issue 4, 2011 ISSN 2320- 5407 International Journal of Advanced Research (2016), Volume 3, Issue 1, 1024- 1045 1043
- Bauer M, Wang L, Onibonoje OK, Parrett C, Sessler DI, Mounir-Soliman L, et al. Continuous Femoral Nerve Block Decreasing Local Anesthetic Concentration to Minimize Quadriceps Femoris Weakness. Anesthesiology. 2012 Mar 1;116(3):665-72.
- 34. Kwofie MK, Shastri UD, Gadsden JC, Sinha SK, Abrams JH, Xu D, et al. The effects of ultrasoundguided adductor canal block versus femoral nerve block on quadriceps strength and fall risk: a blinded, randomized trial of volunteers. Reg Anesth Pain Med. 2013 Jul-Aug;38(4):321-5.
- Andersen HL, Gyrn J, Moller L, Christensen B, Zaric D. Continuous saphenous nerve block as supplement to single-dose local infiltration analgesia for postoperative pain management after total knee arthroplasty. Reg Anesth Pain Med. 2013 Mar-Apr;38(2):106-11.
- 36. Spalevic M, Dimitrijevic L, Kocic M, Stankovic I, Zivkovic V. AB1124 The Importance of the Early Rehabilitation after Total Knee Replacement in Osteoarthritis and Rheumatoid Arthritis Patients. An Rheum Dis. 2014 Jun 1;73(Suppl 2):1173-4.
- 37. Kim DH, Lin Y, Goytizolo EA, Kahn RL, Maalouf DB, Manohar A, et al. Adductor Canal Block versus Femoral Nerve Block for Total Knee ArthroplastyA Prospective, Randomized, Controlled Trial. Anesthesiology. 2014 Mar 1;120(3):540-50.
- Kaur A, Singh RB, Tripathi RK, Choubey S. Comparision Between Bupivacaineand Ropivacaine in Patients Undergoing Forearm Surgeries Under Axillary Brachial Plexus Block: A Prospective Randomized Study. J Clin Diagn Res. 2015 Jan; 9(1): UC01–UC06. DOI: 10.7860/JCDR/2015/10556.5446.

- 39. Vanita Ahuja et al, Role of dexmedetomidine as adjuvant in postoperative sciatic popliteal and adductor canal analgesia in trauma patients: a randomized controlled trial, the Korean journal of pain, Volume 11, Issue 4, page 320-24, 2018.
- 40. Sinhaet al, Comparison of two doses of dexmedetomidine for supraclavicular brachial plexus block: a randomized controlled trial. Journal of Anesthesia Essays, Volume-12, Issue-2, Page: 470-4, 2018.
- 41. L Vorobeichik, Evidence basis for using perineural dexmedetomidine to enhance the quality of brachial plexus nerve blocks: a systematic review and metaanalysis of randomized controlled trials, British Journal of anesthesia, Volume 118, Issue 2, Page: 167-181, 2017.
- 42. Aathira Suresh et al, A prospective, randomized controlled, double-blinded study comparing dexmedetomidine and clonidine as an adjuvant to ropivacaine in femoral nerve block for postoperative analgesia in patients undergoing total knee arthroplasty, Ain-Shams Journal of Anesthesiology, Volume 13, Article no.44, 126-130, 2021
- 43. Senthil K. Packiasabapathy, Effect of dexmedetomidine as an adjuvant to bupivacaine in femoral nerve block for perioperative analgesia in patients undergoing total knee replacement arthroplasty: A dose–response study, Saudi journal of anesthesia, volume 11, issue-3, page: 293-98, 2017
- 44. Swain A, et al. Adjuvants to local anesthetics: Current understanding and future trends. World Journal of Clinical Cases, volume 5, issue-8, page: 307-323, 2017
- 45. Thomas M. Halaszynski, Dexmedetomidine: A look at a promising new avenue of use, Saudi journal of anesthesia, Volume 6, Issue-2, Page:104-106, 2012
- 46. Jing-wen Li, Post operative pain management in total knee arthroplasty, Journal of orthopedic surgery, Volume-8, Issue-4, page: 102-108, 2019
- 47. Hilary Wallace et al, Effect of intra-articular alphaagonists on post-operative outcomes following arthroscopic knee surgery: A systematic review and metaanalysis, Egyptian journal of anesthesia, Volume 33 issue 2, Page: 195-201, 2017
- 48. Reuben et al, Postoperative analgesia for outpatient arthroscopic knee surgery with intraarticular clonidine, Journal of anesthesia and analgesia, Volume 88, issue 11, page:729-733, 2000.