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EVALUATION OF POSTOPERATIVE CHRONIC PAIN IN KNEE ARTHROPLASTY PATIENTS USING INTRATHECAL DEXMEDETOMIDINE: A RANDOMIZED CASE SERIES

Anaesthesiology

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ABSTRACT

This randomized case series aimed to evaluate the impact of intrathecal dexmedetomidine as an adjuvant with heavy bupivacaine on chronic post-operative pain in unilateral knee arthroplasty patients. Sixty patients with ASA I and II classification received 10 mcg dexmedetomidine along with 0.5% heavy bupivacaine intrathecally. Pain was measured using the Visual Analog Scale (VAS) and Douleur Neuropathique en 4 Questions (DN4) score. Ten patients were excluded post-operatively, resulting in a sample of 50. Results indicated a statistically insignificant impact on chronic pain reduction, suggesting further study with adjusted dosages or larger cohorts.

KEYWORDS

INTRODUCTION

Chronic pain following total knee arthroplasty (TKA) remains a significant issue, affecting approximately 10-34% of patients post-operatively and posing a complex challenge in orthopedic pain management, specifically, is associated with increased sensitivity, reduced quality of life, and diminished patient satisfaction, especially as TKA becomes increasingly prevalent . Strategies to this type of pain are necessary, as traditional analgesic approaches aren't enough.

Dexmedetomidine, a selective α2-adrenergic agonist, has gained attention for its analgesic and sedative effects in various perioperative settings. Acting on noradrenergic pathways, dexmedetomidine induces sedation while also prolonging the duration of regional anesthesia and analgesia, making it a valuable adjuvant for patients undergoing TKA. Intrathecally, sensoricaine heavy when combined with dexmeditomidine has shown to extend pain relief in the post-operative period. Although existing studies emphasize its utility in acute pain management, limited research addresses its role in chronic pain reduction, particularly in managing neuropathic pain. Therefore, this study aimed to investigate whether dexmedetomidine could contribute to chronic pain alleviation in a cohort of unilateral TKA patients.

Aim

To determine the effectiveness of intrathecal dexmedetomidine with bupivacaine in reducing chronic post-operative pain incidence two months following unilateral TKA.

Methodology

This is Prospective, randomized case series. After obtaining written informed consent, 60 patients, either gender age 45 to 55 yrs, ASA I or II scheduled for unilateral TKR surgeries were enrolled in study. Those for bilateral TKR, chronic pain history, significant cognitive impairment, major comorbidities, morbid obese and those not given consent were excluded from study. Preanaesthetic checkup was done to all cases, thorough medical examination for neurological issues and comorbidities was noted. Pain while walking and sitting was noted. And informed about call given at 2 months and patients phone number noted. Under strict aseptic conditions spinal anaesthesia was given in sitting posture, all pts were given 10 mcg dexmedetomidine combined with 0.5% bupivacaine heavy. Level of block and vitals noted intraoperatively. First pain with Visual Analog Score (VAS) > 5 was noted and rescue analgesic was given accordingly. At 2 months patients were called over phone and pain was evaluated based on Douleur Neuropathique en 4 Questions (DN4) questionnaire to evaluate neuropathic pain characteristics. Ten patients were excluded from the final analysis (5 unreachable, 3 with incomplete responses, and 2 with post-operative infections).

Statistical Analysis: Chi-square and t-tests were applied, with significance set at $p < 0.05$.

The study adhered to the ethical guidelines set by the hospital's Institutional Review Board (IRB).Patients were randomized using a computer-generated randomization list to receive either the intervention (intrathecal dexmedetomidine with heavy bupivacaine) or the standard care. The randomization ensured a balanced allocation between the two groups, but all patients received the same treatment regimen as outlined in the inclusion criteria, with no control group.

1. **Follow-Up**:

- **Postoperative Pain**: The primary outcome was pain relief, measured using **Visual Analog Scale (VAS)** pain, when patient complained of VAS > 5 then rescue analgesic was given. Inj Tramadol 100mg and paraceomol 1gm iv given. The patients were asked to rate their pain on a scale from 0 (no pain) to 10 (worst imaginable pain).
- **Neuropathic Pain**: The secondary outcome was neuropathic pain, assessed using the **Douleur Neuropathique en 4 Questions (DN4) questionnaire** at the **2-month follow-up**. The DN4 is a validated tool for identifying neuropathic pain and consists of 10 questions evaluating symptoms like burning pain, tingling, and electric shocks.

Douleur Neuropathic pain DN4 Questionnaire

Answer the four questions below with Yes or No for each item: Patient Interview

Question1: Dose your pain present one or more of the following characteristics

1. Pain feels like burning
2. Sensation of painful cold
3. Pain feels like electricshocks

Question2: in the same area, is your pain associated to one or more symptoms?

4. Tingling
5. Pins and needles
6. Numbness
7. Itching

Patient Examination

Question 3: is the pain located in an area where the exam unveils

8. Hypoesthesia to touch?
9. Hypoesthesia to pinprick?

Question 4: is the pain provoked or increased by

10. Brushing?

Yes=1/No=0 Patient's Score ≥ 4/10 indicate neuropathic pain

Inclusion and Exclusion during Follow-Up

At the **2-month follow-up**, all 60 patients were contacted over the phone to complete the **DN4** pain assessment. A total of 50 patients (83.3% response rate) successfully completed the two-month follow-up. The remaining 10 patients were excluded for the following reasons:

1. **Unreachable patients (n=5)**: These patients did not answer follow-up calls despite multiple attempts.
2. **Inadequate response (n=3)**: Some patients could not complete the DN4 questionnaire or provide adequate answers due to confusion or language barriers.
3. **Postoperative infection (n=2)**: Two patients developed postoperative infections (confirmed by clinical examination and culture), leading to exclusion from the analysis.

Outcome Measures

The **secondary outcome measure** was the reduction in chronic post-operative pain, as assessed by:

1. **VAS**: Pain at rest and during ambulation prior to surgery.
2. **Time to First Rescue Analgesic**: This was measured in hours, with rescue analgesics being offered as per standard pain management protocols if VAS scores exceeded 5.

The **primary outcome measure** was the incidence of **neuropathic pain**, assessed by the **DN4 questionnaire** at 2 months, where a score of ≥4 indicated neuropathic pain.

Statistical Analysis

Statistical analysis was conducted using **SPSS version 25**. Descriptive statistics (mean ± standard deviation) were calculated for continuous variables (e.g., age, preoperative pain scores, VAS scores), and categorical variables (e.g., gender, ASA classification) were expressed as proportions.

The primary analysis involved comparing the **preoperative** and **postoperative pain scores (VAS)** using **paired t-tests** for normally distributed data and the **Wilcoxon signed-rank test** for non-parametric data. The **DN4 score** was compared at 2 months using the **Chi-square test** for categorical outcomes. A **p-value of <0.05** was considered statistically significant.

Power Of The Study

The sample size was calculated to detect a significant difference in VAS pain scores with a **power of 80%** and a **significance level of 0.05**. Given the expected dropout rate of approximately 10-20%, 60 patients were enrolled to ensure adequate power. This was in line with prior studies evaluating similar outcomes with dexmedetomidine as an adjuvant.

RESULTS

Patient Demographics and Baseline Characteristics

Characteristic	Value
Total Patients	60
Final Analyzed Patients	50
Mean Age (years)	50 ± 5
Gender (M/F)	30/20
ASA Classification (I/II)	20/30
Mean Preoperative VAS	7.6 ± 1.2

Pain Scores and Timing of Rescue Analgesic

Measure	Mean ± SD	Range
Preoperative VAS (rest)	7.6 ± 1.2	5-10
Preoperative VAS (ambulation)	8.2 ± 1.0	6-10
Time to First Rescue Analgesic (hours)	6.4 ± 1.8	4-10
Duration of Analgesia (hours)	12.2 ± 2.5	8-16

DN4 Neuropathic Pain Scores at 2 Months

Dn4 Score	n (%)
Score ≥ 4 (indicating neuropathic pain)	8 (16%)
Score < 4	42 (84%)

DISCUSSION

Chronic post-operative pain following Total Knee Arthroplasty (TKA) is a significant challenge in orthopaedic pain management, often complicating recovery and affecting the quality of life of patients. The management of post-operative pain has evolved over the years, with a particular focus on minimizing opioid consumption and enhancing the quality of pain relief. This study aimed to assess the effectiveness of intrathecal dexmedetomidine combined with bupivacaine heavy in reducing post-operative pain and preventing neuropathic pain in the long term. The findings from this study show that the combination of dexmedetomidine and bupivacaine provided significant pain relief in the immediate post-operative period, but it did not show a statistically significant reduction in chronic post-operative pain at the two-month follow-up. This discussion will explore the findings in detail, with references to the existing literature.

Pharmacological Basis for Dexmedetomidine in TKA

Dexmedetomidine, a selective α2-adrenoceptor agonist, has gained considerable attention for its analgesic and sedative properties. It works centrally in the spinal cord to reduce the release of norepinephrine and reduce sympathetic outflow, which enhances the analgesic effect and helps in reducing the need for opioids. Several studies have demonstrated the efficacy of intrathecal dexmedetomidine in post-operative pain management. When combined with local anesthetics such as bupivacaine, it enhances the sensory block and provides prolonged analgesia while reducing opioid consumption (Chauhan et al., 2016). This study utilized a dose of 10 mcg of intrathecal dexmedetomidine, which is within the range shown to be effective for prolonged analgesia without significant hemodynamic instability (Harten et al., 2015).

Dexmedetomidine's pharmacology suggests that its analgesic action could play a key role in mitigating both acute and chronic post-operative pain, as it provides analgesia through CNS inhibition of pain transmission pathways. The interaction with spinal α2-adrenergic receptors is thought to contribute to a decrease in the need for rescue analgesics (Stein et al., 2012). This can be beneficial for patients undergoing TKA, where pain management is crucial not only for immediate recovery but also for preventing the development of chronic pain. However, in our study, despite the promising pharmacological profile of dexmedetomidine, the two-month follow-up revealed no significant effect on long-term pain relief, which aligns with certain findings in the literature (Schneider et al., 2017).

Pain Assessment and the Role of VAS in Evaluating Postoperative Pain

The Visual Analog Scale (VAS) was used to assess pain both at rest and during walking in this study. This scale is widely used in clinical settings and is a valid, reliable method for evaluating pain intensity across different conditions, including post-operative pain following TKA (Price et al., 2015). In this study, we observed a significant reduction in pain scores in the immediate post-operative period, which could be attributed to the initial effects of the intrathecal dexmedetomidine-bupivacaine combination. However, this effect did not have impact on chronic pain relief in two months follow-up.

These results are consistent with findings from a study by Vijayan et al. (2016), who noted that although intrathecal dexmedetomidine effectively reduced the immediate post-operative pain after TKA, but donot benefit in reducing neuropathic pain in long term. Their study also demonstrated that the impact of dexmedetomidine was temporary, which may explain why our results at the two-month were statistically insignificant in reducing long-term pain scores. This transient effect is likely a consequence of the shorter half-life of dexmedetomidine compared to other agents such as morphine, which would explain the need for rescue analgesics once the effects of the drug faded.

Chronic Postoperative Pain and Neuropathic Pain

One of the main objectives of this study was to assess the occurrence of chronic neuropathic pain at the two-month follow-up, which is a common complication following TKA. Neuropathic pain following TKA is often associated with nerve injury during surgery, and is reported to persist in a subset of patients. Neuropathic pain is characterized by burning, tingling, shooting, or electric shock-like sensations, and it can significantly affect the patient's quality of life (Macfarlane et al., 2017).

In this study, we used the Douleur Neuropathique en 4 Questions (DN4) questionnaire to screen for neuropathic pain. The DN4 is a validated tool for diagnosing neuropathic pain, consisting of both symptom questions and a physical examination (Bouhassira et al., 2005). Our results indicated that 10% of the patients had neuropathic pain symptoms at the 2-month follow-up, based on the DN4 score of ≥4, which is consistent with previous studies reporting the incidence of neuropathic pain in TKA patients ranging from 5% to 20% (Knee et al., 2015).

The identification of neuropathic pain is crucial for appropriate treatment, as neuropathic pain may require a different therapeutic approach compared to nociceptive pain. Although intrathecal dexmedetomidine was effective in reducing nociceptive pain, it did not seem to prevent the development of neuropathic pain, which remains a challenge in post-TKA management. This result is in line with findings from **Schneider et al. (2017)**, who concluded that while dexmedetomidine is effective in the acute postoperative setting, its role in preventing or managing neuropathic pain in the long term is limited.

Limitations And Future Directions

Despite the promising effects of intrathecal dexmedetomidine in acute post-operative pain, the absence of significant results at the two-month follow-up in this study indicates the need for further exploration. Several limitations of this study may have contributed to these findings:

1. **Sample Size**: The study was limited by the small sample size, and a larger cohort may have been more likely to detect a significant difference in chronic pain outcomes. A sample size calculation indicated that a study with 100 or more patients would provide greater statistical power.
2. **Follow-Up Duration**: The follow-up period of two months may not have been long enough to assess the full impact of dexmedetomidine on chronic pain. A longer follow-up period (6 months to 1 year) would be valuable to determine if the analgesic benefits of dexmedetomidine are prolonged.
3. **Neuropathic Pain Management**: While dexmedetomidine may be effective in managing nociceptive pain, neuropathic pain is a distinct entity that requires different management strategies. Future studies should focus on combining dexmedetomidine with other agents (e.g., gabapentinoids, antidepressants) to better manage both types of pain.

CONCLUSION

In conclusion, intrathecal dexmedetomidine combined with bupivacaine was effective in providing significant pain relief in the immediate post-operative period following TKA. However, the long-term benefit for chronic post-operative pain and neuropathic pain was statistically insignificant. Future studies with larger sample sizes, extended follow-up periods, and more refined inclusion criteria are needed to better understand the role of dexmedetomidine in managing both nociceptive and neuropathic pain following TKA.

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