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COMPARISON OF EFFECT OF DEXMEDETOMIDINE INTRATHECAL INJECTION AND INTRAVENOUS INFUSION ON SUBARACHNOID BLOCKADE DURING KNEE ARTHROSCOPY PROCEDURE -A DOUBLE BLINDED RANDOMIZED CONTROLLED TRIAL

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Abstract:
Aim: This study aimed to compare the efficacy and safety of dexmedetomidine administered via intrathecal injection versus intravenous infusion in augmenting subarachnoid blockade during knee arthroscopy procedures.
Materials And Method: A double-blind randomized controlled trial compared dexmedetomidine administered intrathecally versus intravenously during knee arthroscopy. Sixty-four participants per group aged 18-60 years, ASA grade I and II, were recruited. Onset time, duration, and quality of blockade, along with hemodynamic stability and adverse events, were evaluated. Descriptive statistics, independent sample t test and repeated measures ANOVA were used for Statistical analysis. P-value <0.05 is considered to be statistically significance.
Results: Both groups showed similar age, BMI, and surgery duration distributions, with meniscusplasty being the most common procedure. No significant differences were found in analgesia duration, onset time, or sensory-motor blockade quality. However, the intravenous group exhibited higher sedation scores postoperatively.
Conclusion: Both intrathecal and intravenous dexmedetomidine effectively prolonged analgesia during knee arthroscopy, with comparable outcomes in key parameters. While intravenous infusion resulted in higher sedation scores, both routes demonstrated similar safety profiles. These findings contribute to optimizing perioperative pain management strategies, emphasizing the potential of dexmedetomidine as an adjunctive agent in knee arthroscopy procedures.

Keywords: Knee arthroscopy, dexmedetomidine, intrathecal injection, intravenous infusion, analgesia, sedation, perioperative pain management

INTRODUCTION

Osteoarthritis of the knee and degenerative meniscus are prevalent conditions, particularly among the aging population, often leading to significant pain and functional impairment (1). Knee arthroscopy serves as a primary therapeutic approach for addressing meniscal, ligament, and cartilage injuries, particularly in sports medicine (2). Effective analgesia is essential during knee arthroscopy procedures (3).
Subarachnoid blockade, commonly employed in knee arthroscopy procedures, provides effective anesthesia and analgesia. However, the duration and quality of blockade can vary, impacting patient outcomes and procedural success. Dexmedetomidine, a highly selective alpha-2 adrenergic agonist, has gained attention for its potential to enhance the characteristics of regional anesthesia. Subarachnoid block has emerged as a preferred anesthetic technique for lower extremity surgeries like knee arthroscopy due to its efficacy and patient comfort. However, the short duration of knee arthroscopy and concerns associated with epidural catheter insertion, such as catheter-related complications and inadvertent vascular or subarachnoid space entry, have prompted exploration of various strategies to prolong anesthesia (4,5). Among these strategies, intravenous drug administration and the use of local anesthetic adjuvants have garnered attention. Clinical investigations have increasingly focused on the efficacy of

dexmedetomidine, an α2-adrenergic receptor agonist renowned for its sedative and analgesic properties, as an adjuvant to local anesthetics.

Previous meta-analyses have indicated that intrathecal dexmedetomidine can hasten the onset of sensory-motor blockade and prolong its duration with minimal hemodynamic effects, showcasing its potential as an adjunctive agent (5,6). Moreover, intraoperative intravenous dexmedetomidine infusion has been suggested to reduce postoperative opioid requirements and mitigate postoperative stress and adverse events. However, the comparative advantages and drawbacks of these administration routes remain debatable. While intrathecal dexmedetomidine has demonstrated promising results in prolonging the duration and improving the quality of spinal anesthesia, its comparative efficacy with intravenous infusion remains an area of investigation. Understanding the comparative effects of these administration routes is crucial for optimizing anesthesia strategies in knee arthroscopy (7,8,9).

This study aimed to compare the efficacy and safety of dexmedetomidine administered via intrathecal injection versus intravenous infusion in augmenting subarachnoid blockade during knee arthroscopy procedures. By evaluating parameters such as onset time, duration, and quality of blockade, along with hemodynamic stability and adverse event profiles, we seek to provide valuable insights into the optimal use of dexmedetomidine in this clinical setting. The findings of this study have the potential to inform clinical practice guidelines, aiding anesthesiologists and surgeons in selecting the most effective and safest anesthesia regimen for knee arthroscopy, ultimately improving patient outcomes and satisfaction.

MATERIAL AND METHODS

A Double-blind randomized control trial design was conducted from March 2023 to March 2024 in the Department of Anaesthesiologists at Saveetha Medical College and Hospital, Chennai. All the study participants gave written informed consent before the interview. Patients aged between 18 to 60 years, categorized as ASA I-II, who underwent knee arthroscopy were included in this study. Exclusion criteria encompassed obesity (defined as a body mass index [BMI] exceeding 30 kg/m2), contraindications to subarachnoid block, a history of allergy to local anesthetics or dexmedetomidine, prolonged use of analgesic or sedative medications, bradycardia, failure of a block, or refusal to undergo subarachnoid block. Utilizing G*Power software, with an effect size d of 0.5, a sample size of 64 per group was projected to yield an 80% efficacy ($\alpha \leq 0.05$) in detecting differences in the duration of analgesia across the two groups.

Patients were subjected to an overnight fast of at least 8 hours before surgery, with no additional medications administered. Upon admission to the operating room, all patients were equipped with open peripheral venous access and received lactated Ringer's solution at a rate of 10 ml/kg/hr. Basic monitoring devices, including pulse oximetry, ECG, and non-invasive blood pressure (NIBP) cuffs, were attached. Oxygen was administered through a mask at a rate of 4 L/min. Patients were randomly assigned into intrathecal and intravenous groups using computer-generated random numbers, with neither the anesthesiologist nor the patients aware of the group assignments or drug regimens. A researcher not involved in subsequent anesthesia or data collection prepared the experimental solutions according to group assignments.

In the intrathecal group, 2.0 ml (1%, 10 mg/ml) of ropivacaine plus 1.0 ml (5 μg/ml) of dexmedetomidine were added to the local anesthetic solution and injected into the subarachnoid space. Simultaneously, an equal volume of saline, infused intravenously at the same rate as dexmedetomidine, was administered. In the intravenous group, 2.0 ml (1%, 10 mg/ml) of ropivacaine plus 1.0 ml of 0.9% saline were added to the local anesthetic solution, while dexmedetomidine was infused intravenously at a rate of 0.5 μg/kg/h. Subarachnoid block was performed in the lateral position under aseptic precautions, using a 25G Quincke needle via a median approach at the L3-L4 interspace. After clear cerebrospinal fluid was observed, 3 ml of the configured local anesthetic solution was injected into the subarachnoid space at a rate of 0.1 ml/s. Subsequent to the block, sensory and motor blocks were evaluated using standardized techniques until predetermined levels were achieved. Blood pressure, heart rate, and oxygen saturation were recorded at regular intervals throughout the procedure. Ramsay sedation scores were documented hourly postoperatively. Postoperative pain was assessed using a Visual Analogue Scale at designated intervals, and all patients received intravenous patient-controlled analgesia (PCA) for pain management.

STATISTICAL ANALYSIS

To analyse the data SPSS (IBM SPSS Statistics for Windows, Version 26.0, Armonk, NY: IBM Corp. Released 2019) is used. The Normality tests, Kolmogorov-Smirnov and Shapiro-Wilks tests results revealed that the data follows normal distribution. Therefore, to analyse the data, parametric test was applied. Descriptive statistics determined the frequency, percentage, mean and SD (standard deviation) for the variables. Independent sample t test was used to analyze the duration of surgery, ASA grades and types of surgery difference between intrathecal and intravenous group. Repeated measures ANOVA was used to assess the intragroup changes of ramasay

sedation score and visual analogue scale within intrathecal and intravenous group. Significance level is fixed as 5% (α = 0.05). P-value <0.05 is considered to be statistically significance.

RESULTS

Patient Flowchart

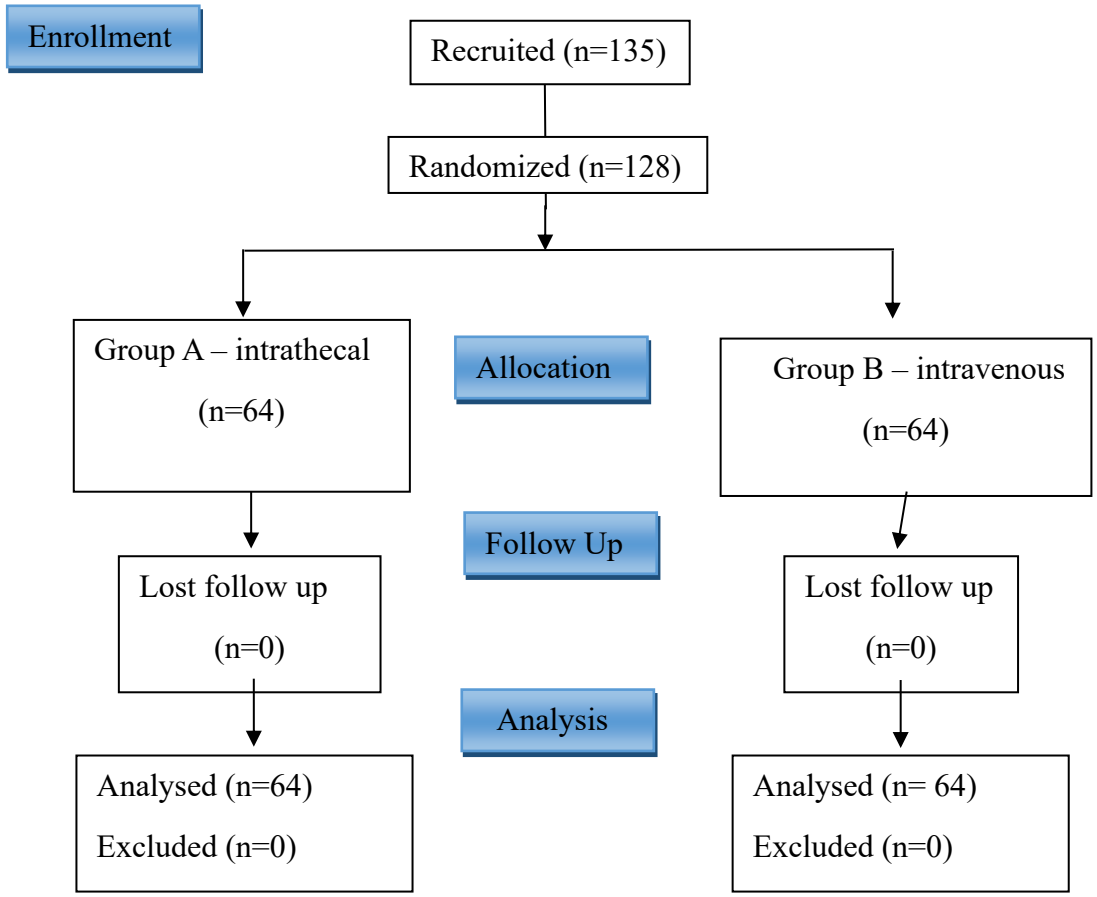

Figure 1 shows the patient flowchart

TABLE 1: AGE-WISE DISTRIBUTION AMONG THE STUDY PARTICIPANTS

AGE GROUP	INTRATHECAL GROUP		INTRAVENOUS GROUP	
	FREQUENCY	PERCENTAGE	FREQUENCY	PERCENTAGE
18-30 years	6	9.4	9	14.1
31-40 years	27	42.2	21	32.8
41-50 years	23	35.9	20	31.3
51-60 years	8	12.5	14	21.9

Table 1 depicts the frequency and percentage distribution of age groups ranging from 18 to 60 years according to both groups. There were 6 patients in the age group of 18- 30 years (9.4%). There were 27 patients in the age group of 31- 40 years (42.2%). There were 23 patients in the age group of 41- 50 years (35.9%). There were 8 patients in the age group of 51- 60 years (12.5%) according to the intrathecal group. In the intravenous group, there were 9 patients in the age group of 18- 30 years (14.1%). There were 21 patients in the age group of 31- 40 years (32.8%). There were 20 patients in the age group of 41- 50 years (31.3%). There were 14 patients in the age group of 51- 60 years (21.9%) in this present study.

TABLE 2: GENDER DISTRIBUTION AMONG STUDY PARTICIPANTS

GENDER	INTRATHECAL GROUP		INTRAVENOUS GROUP		P VALUE
	FREQUENCY	PERCENTAGE	FREQUENCY	PERCENTAGE	

MALE	55	85.9	51	79.7	0.64
FEMALE	9	14.1	13	20.3	

Table 2 depicts the gender distribution of Study subjects. The percentage distribution of male and female subjects is 85.9% and 14.1% in the intrathecal group and in the intravenous group 79.7% and 20.3% in this present study. There was no statistically significant difference found between gender for both group (P=0.64).

TABLE 3: MEAN AND STANDARD DEVIATION FOR AGE, BODY MASS INDEX (BMI), AND DURATION OF SURGERY AMONG STUDY PARTICIPANTS IN INTRATHECAL GROUP

VARIABLES	MEAN	STANDARD DEVIATION	MINIMUM	MAXIMUM
AGE	40.31	11.959	18	60
BMI	24.150	3.9465	18.5	30.0
DURATION OF SURGERY	79.08	16.180	46	106

Table 3 depicts the mean and Standard deviation of age in years, BMI, and duration of surgery according to intrathecal group. In the present study, the mean age of subjects was 40.3 ± 11.959 years, the BMI was 24.1 ± 3.946 kgs and the duration of surgery was 79.0 ± 16.180 hours in this present study.

TABLE 4: MEAN AND STANDARD DEVIATION FOR AGE, BODY MASS INDEX (BMI), AND DURATION OF SURGERY AMONG STUDY PARTICIPANTS IN INTRAVENOUS GROUP

VARIABLES	MEAN	STANDARD DEVIATION	MINIMUM	MAXIMUM
AGE	39.25	10.349	18	60
BMI	24.431	3.6888	18.5	30.0
DURATION OF SURGERY	80.22	14.831	45	105

Table 4 depicts the mean and Standard deviation of age in years, BMI, and duration of surgery according to intravenous group. In the present study, the mean age of subjects was 39.2 ± 10.349 years, the BMI was 24.4 ± 3.688 kgs and the duration of surgery was 80.2 ± 14.831 hours in this present study.

TABLE 5: STANDARD ERROR MEAN FOR BODY MASS INDEX AMONG STUDY PARTICIPANTS

GROUPS	STANDARD ERROR MEAN	F	P VALUE
INTRATHECAL GROUP	0.4933	0.453	0.502
INTRAVENOUS GROUP	0.4611		

Table 5 depicts the Standard error mean for BMI according to both groups. In the present study, the standard error mean of subjects was 0.4933 in the intrathecal group and the intravenous group was 0.4611. There was no statistically significant difference found between BMI for both groups (P=0.502).

TABLE 6: STANDARD ERROR MEAN FOR DURATION OF SURGERY AMONG STUDY PARTICIPANTS

GROUPS	STANDARD ERROR MEAN	F	P VALUE
INTRATHECAL GROUP	2.022	0.495	0.483
INTRAVENOUS GROUP	1.854		

Table 6 depicts the Standard error mean for the duration of surgery according to both groups. In the present study, the standard error mean of subjects was 2.022 in the intrathecal group, and in the intravenous group was 1.854. There was no statistically significant difference found between the duration of surgery for both groups (P=0.483).

TABLE 7: ASA GRADE DISTRIBUTION AMONG STUDY PARTICIPANTS

ASA GRADE	INTRATHECAL GROUP		INTRAVENOUS GROUP	
	FREQUENCY	PERCENTAGE	FREQUENCY	PERCENTAGE
GRADE I	49	76.6	43	67.2
GRADE II	15	23.4	21	32.8

Table 7 depicts the ASA grade distribution of Study subjects. The percentage distribution of grade I and grade II subjects is 76.6% and 23.4% in the intrathecal group and in the intravenous group 67.2% and 32.8% in this present study.

TABLE 8: MEAN AND STANDARD DEVIATION OF ASA GRADE DISTRIBUTION AMONG STUDY PARTICIPANTS

GROUPS	MEAN	STANDARD DEVIATION	STANDARD ERROR MEAN	F	P VALUE
INTRATHECAL GROUP	1.23	0.427	0.427	5.528	0.02*
INTRAVENOUS GROUP	1.33	0.473	0.473		

Table 8 depicts the mean and Standard deviation of age in the ASA distribution of Study subjects for both groups. In the present study, the mean ASA grade of subjects was 1.23 in the intrathecal group, and in the intravenous group was 1.33. There was a statistically significant difference found between ASA grades for both groups (P=0.02*).

TABLE 9: TYPES OF DISTRIBUTION AMONG STUDY PARTICIPANTS

TYPES	INTRATHECAL GROUP		INTRAVENOUS GROUP		P VALUE
	FREQUENCY	PERCENTAGE	FREQUENCY	PERCENTAGE	
MENISCUS PLASTY	47	73.4	47	73.4	0.639
CYST REMOVAL	6	9.4	4	6.3	
ACL RECONSTRUCTION	7	10.9	9	14.1	
SYNOVECTOMY	4	6.3	4	6.3	

Table 9 depicts the types of surgery distribution of study subjects according to both groups. Based on that most of the patients had done meniscusplasty (73.4%), followed by ACL reconstruction (10.9%), cyst removal (9.4%), and synovectomy (6.3%) according to the intrathecal group. In the intravenous group, most of the patients had done meniscusplasty (73.4%), followed by ACL reconstruction (14.1%), cyst removal, and synovectomy (6.3%) in this present study. There was no statistically significant difference found between types of surgery for both groups (P=0.063).

TABLE 10: RAMSAY SEDATION SCORE DISTRIBUTION AMONG STUDY PARTICIPANTS

RAMSAY SEDATION SCORE	INTRATHECAL GROUP FOR RAMSAY SEDATION SCALE	INTRAVENOUS GROUP FOR RAMSAY SEDATION SCALE	P VALUE
1 hr after anesthesia	2	3	0.06

2 hr after anesthesia	2	2.25	0.56
1 hr after surgery	2	2	0.56

Table 10 depicts the Ramsay sedation score distribution of study subjects according to the time interval for both groups. There was no statistically significant difference found between Ramsay's sedation score for both groups.

TABLE 11: VISUAL ANALOGUE SCALE DISTRIBUTION AMONG STUDY PARTICIPANTS

VISUAL ANALOGUE SCALE	INTRATHECAL GROUP FOR VISUAL ANALOGUE SCALE	INTRAVENOUS GROUP FOR VISUAL ANALOGUE SCALE SCALE	P VALUE
1 hr after anesthesia	0	0	0.56
2 hr after anesthesia	1	2.25	0.07
1 hr after surgery	2	2	0.56

Table 11 depicts the Visual analogue scale distribution of study subjects according to the time interval for both groups. There was no statistically significant difference found between Visual analogue scale for both groups.

DISCUSSION

In the present study, the age groups of these patients ranged from 18 to 60 years in both groups. There were 6 patients in the age group of 18- 30 years (9.4%). There were 27 patients in the age group of 31- 40 years (42.2%). There were 23 patients in the age group of 41- 50 years (35.9%). There were 8 patients in the age group of 51- 60 years (12.5%) according to the intrathecal group. In the intravenous group, there were 9 patients in the age group of 18- 30 years (14.1%). There were 21 patients in the age group of 31- 40 years (32.8%). There were 20 patients in the age group of 41- 50 years (31.3%). There were 14 patients in the age group of 51- 60 years (21.9%). Notably, the majority of participants in both groups fell within the 31-40 years age range, comprising 42.2% and 32.8% of the intrathecal and intravenous groups, respectively. This age distribution aligns with findings from previous studies, indicating that individuals within this age range may be more susceptible to the conditions or procedures under investigation. Interestingly, while there were minor variations in the distribution across age groups between the two groups, the differences were not statistically significant. For instance, the intrathecal group had slightly higher proportions of participants in the 41-50 years age range compared to the intravenous group (35.9% vs. 31.3%, respectively). Conversely, the intravenous group had a slightly higher proportion of participants aged 18-30 years compared to the intrathecal group (14.1% vs. 9.4%, respectively). However, these differences did not reach statistical significance, as evidenced by the non-significant p-value of 0.64. The mean age was slightly higher in the intrathecal group compared to the intravenous group. The mean age of participants in both intrathecal groups compared to the intravenous group is approximately 40.3 years and 39.2 years, with standard deviations indicating a moderate level of variance around the mean. The study conducted by Liu et al in the year 2024 has contrasting findings showing that the intrathecal group has less mean age than the intravenous group (10). The study conducted by Sharma et al in the year 2020 has similar findings showing that the intrathecal group has more mean age than the intravenous group (11).

In this present study, both groups show a higher prevalence of male participants compared to females, although the difference is more pronounced in the intrathecal group (85.9% male) compared to the intravenous group (79.7% male). The study conducted by Sharma et al in the year 2020 has similar findings showing that the male participants are more prevalently found than females (11). This gender skew aligns with the epidemiological trends observed in similar studies within the medical field. However, despite the numerical differences in gender distribution between the two groups, statistical analysis revealed no significant disparity ($p = 0.64$).

In the present study, the BMI of study subjects was 24.1 ± 3.946 kgs in the intrathecal group and the intravenous group was 24.4 ± 3.688 kgs. The study conducted by Liu et al in the year 2024 and Sharma et al in the year 2020 has similar findings showing that the intrathecal group has slightly less mean BMI than the intravenous group (10,11). The Duration of surgery among study subjects was 79.0 ± 16.180 hours in the intrathecal group and in the intravenous group was 80.2 ± 14.831 hours. The study conducted by Liu et al in the year 2024 has similar findings showing that the intrathecal group has less mean duration of surgery than the intravenous group (10). The study conducted by Sharma et al in the year 2020 has contrasting findings showing that the intrathecal group has less mean duration of surgery than the intravenous group (11).

The percentage distribution of grade I and grade II subjects is 76.6% and 23.4% in the intrathecal group and in the intravenous group 67.2% and 32.8% in this present study. The study conducted by Liu et al in the year 2024 and Sharma et al in the year 2020 has similar findings showing that the higher ASA grade I than ASA grade II in both the intrathecal group and intravenous group (10,11). Based on that most of the patients had done meniscusplasty (73.4%), followed by ACL reconstruction (10.9%), cyst removal (9.4%), and synovectomy (6.3%) according to the intrathecal group. In the intravenous group, most of the patients had done meniscusplasty (73.4%), followed by ACL reconstruction (14.1%), cyst removal, and synovectomy (6.3%) in this present study. There was no statistically significant difference found between types of surgery for both groups (P=0.063). The study conducted by Liu et al in the year 2024 has similar findings showing that the types of surgery has no statistically significant difference found between both groups (10).

In this trial, we aimed to ascertain the most effective dexmedetomidine application for prolonging analgesia during knee arthroscopy, to minimize complications from epidural catheter insertion and reduce physiological and psychological impacts on patients while enhancing satisfaction. We established two groups to compare intrathecal versus intravenous infusion, revealing differences in analgesia duration, sensory-motor block duration. The meta-analysis study conducted by Abdallah et al in the year 2013 comprising 7 trials and 364 patients assessed the impact of intravenous dexmedetomidine on spinal anesthesia. This meta-analysis indicated a prolongation of sensory blockade and delayed need for analgesia. However, our study found no statistical disparity in analgesia duration between both groups of dexmedetomidine (12).

Regarding the onset of sensory-motor blockade, the intrathecal group exhibited a significantly shorter duration compared to the intravenous group, which contrasts with findings from certain studies. Notably, the difference between the intravenous group and the intrathecal group was not statistically significant, which can be attributed to the delayed onset of action associated with intravenously administered dexmedetomidine. Typically, dexmedetomidine is administered intravenously at a loading dose of 1.0 μg/kg over a 10-minute period in most experimental studies. This study refrained from utilizing a loading dose, instead opting for a maintenance dose of 0.5 μg/kg/h during the administration of local anesthetic solution intravenously. However, this deviation from the loading dose protocol may introduce bias in the onset time of sensory-motor block in the study results (13,14).

The findings of this study revealed significantly higher sedation scores at all three time points in the intravenous group compared to the intrathecal group. Interestingly, the intrathecal group did not demonstrate superior sedation scores to the intravenous group during the postoperative period, suggesting a potential disparity in sedation pathways between the two administration routes. Previous studies have suggested that dexmedetomidine's sedative effect may result from inhibiting norepinephrine release from the brain's hypothalamus, ultimately leading to reduced histamine release and a sedative-hypnotic effect (15). The mechanisms of analgesia between intravenous and intrathecal administration of dexmedetomidine appear to be different. While intravenous dexmedetomidine is thought to inhibit norepinephrine release through α2-adrenergic receptor activation, reducing sympathetic activity and inducing analgesia, intrathecal injection may produce analgesia by reducing ERK1/2 activation in the spinal cord via dilutional effects (16). Despite concerns about potential neurotoxicity, numerous animal and human studies have indicated that intrathecal dexmedetomidine is not associated with neurological dysfunction. Intrathecal dexmedetomidine could serve as an effective adjunct to multimodal analgesic regimens for patients undergoing knee arthroscopy with subarachnoid blocks. However, many of these investigations are still in their early phases, and further clinical trials are needed to determine the optimal intrathecal dose of dexmedetomidine and its long-term effects on neurological function.

LIMITATION OF THE STUDY

This present study may be limited by its relatively small sample size, which could affect the generalizability of the findings. A larger sample size would provide more robust statistical power and enhance the reliability of the results. Conducting the study at a single center may limit the generalizability of the findings to broader populations. Multi-center studies involving diverse patient populations and settings would provide more representative data. This study's design may have selection bias, as only patients meeting specific criteria were included. This could potentially skew the results and limit their applicability to broader patient populations. This study may be susceptible to confounding variables that were not accounted for, such as concomitant medications or comorbidities, which could influence the outcomes of interest.

CONCLUSION

In conclusion, this study compared the efficacy and safety of intrathecal versus intravenous administration of dexmedetomidine for prolonging analgesia during knee arthroscopy. Despite certain limitations, including the small sample size and potential biases, the findings provide valuable insights into the clinical utility of dexmedetomidine in perioperative pain management. The results suggest that both intrathecal and intravenous

routes of dexmedetomidine administration demonstrate comparable efficacy in prolonging analgesia duration, with differences observed in the onset of sensory-motor blockade and sedation scores. These findings contribute to the growing body of literature on dexmedetomidine's role in multimodal analgesia regimens and highlight the need for further research to optimize dosing strategies and elucidate its mechanisms of action. Ultimately, dexmedetomidine holds promise as an adjunctive agent for enhancing perioperative pain control and improving patient outcomes in knee arthroscopy procedures.

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