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THE EFFICACY OF DEXMEDETOMIDINE FOR THE PREVENTION OF SHIVERING DURING SPINAL ANESTHESIA: A RANDOMIZED CONTROLLED TRIAL

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Abstract
This study aimed to assess the effectiveness of dexmedetomidine in preventing shivering during spinal anesthesia. A total of 377 patients aged 18 to 50 were registered for elective minor surgical procedures under bupivacaine spinal anesthesia. The study divided the patients into two groups: those receiving intravenous dexmedetomidine (DEX) and those receiving saline (Placebo). The Bromage Scale was used to evaluate motor block, and an observer blinded to the situation evaluated if shivering occurred following a subarachnoid medication injection loaded with cerebrospinal fluid.

The results showed that shivering occurred in 14% of the DEX group and 28% in the placebo group. The DEX group experienced less severe shivering than the Placebo group. The duration between the initiation of shivering in the DEX group and the placebo group was 30 and 82 minutes, respectively. Additionally, 78% of the DEX group and 3% of the placebo group experienced sedation at level 2.

In conclusion, dexmedetomidine infusion significantly reduced shivering during the perioperative period due to its quick start of action, higher cessation rates, and decreased recurrence. These findings highlight the safety and effectiveness of adding dexmedetomidine to anesthesia protocols to improve patient outcomes and offer insights for anesthesiologists and other healthcare professionals.

Keywords: *Intravenous Dexmedetomidine, Intrathecal Spinal Anesthesia, Incidence of shivering, Sedation level*

Introduction

Spinal anesthesia, also known as intrathecal block, is a localized neuraxial anesthesia that allows patients to remain conscious during surgical procedures. However, post-administration shivering is a common and troublesome complication following intrathecal block, with a mean reported frequency of 55%. Shivering is characterized by pain, intraoperative heat loss, or systemic release of pyrogens, and it can lead to hypothermia and shivering. Risk factors for hypothermia and subsequent shivering include the level of the applied block, the operating room temperature, and the patient's age. Shivering is a multifaceted concern in the context of spinal anesthesia, as it compromises patient comfort, increases oxygen consumption, increases intra-abdominal pressure, and surgical difficulties. It may cause pain, and anxiety, and upset the delicate thermoregulation balance, leading to hypothermia, coagulation problems, surgical site infections, and other complications. Muscle

contractions caused by shivering can also impair surgical accuracy, especially in operations requiring exact surgical methods.

Minimizing shivering during spinal anesthesia is critical for improving patient comfort and satisfaction, maximizing clinical results, and healthcare resource use. One promising approach to mitigating perioperative shivering is the utilization of dexmedetomidine, a highly selective α2-adrenergic receptor (α2-AR) agonist. This study aims to rigorously assess the effectiveness of dexmedetomidine in stopping shivering during spinal anesthesia, providing valuable insights into whether it can serve as a reliable intervention to reduce shivering during intrathecal block, ultimately improving the patient's perioperative experience and potentially enhancing outcomes in this clinical setting.

Spinal anesthesia, also known as intrathecal block, is a crucial aspect of anesthetic practice due to its effectiveness, affordability, and minimal side effects. It involves injecting local anesthetics or opioids into the subarachnoid space, allowing patients to remain awake and aware during surgical procedures. However, postoperative shivering remains a common and vexing complication, with a mean incidence of shivering following intrathecal block at a substantial 55%. Shivering is characterized by involuntary rhythmic contractions of skeletal muscles and is a complex phenomenon stemming from multiple factors, including intraoperative heat loss and systemic release of pyrogens.

Dexmedetomidine, a highly selective α2-adrenergic receptor (α2-AR) agonist, is gaining prominence as an adjunct to other anesthetics for short-term sedation. It is particularly useful when combined with spinal anesthesia for surgical procedures lasting 2-4 hours, such as lower limb surgeries and urological interventions. The efficiency of dexmedetomidine in reducing the incidence of shivering has been studied and established in various clinical settings, making it a viable candidate for improving patient comfort during spinal anesthesia.

Since numerous studies have studied the effects of intrathecal dexmedetomidine, there is a pressing need to bridge this research gap and provide empirical evidence on the utility of dexmedetomidine in the context of spinal anesthesia. By addressing this gap, the study aims to offer valuable insights that may contribute to the development of more effective and evidence-based strategies for managing shivering during intrathecal block, ultimately improving patient care in this clinical setting.

Objectives of Research

To assess the effectiveness of dexmedetomidine in preventing shivering during spinal anesthesia.To determine the incidence of shivering in patients receiving dexmedetomidine during spinal anesthesia. To evaluate the impact of dexmedetomidine on the intensity of shivering experienced by patients undergoing spinal anesthesia as compared to placebo.To monitor perioperative hemodynamic responses including blood pressure, heart rate, oxygen saturation, and body temperature with dexmedetomidine.To assess the degree of sedation in patients receiving dexmedetomidine as part of their anesthesia.

Methodology

The study aims to evaluate the efficacy of intravenous dexmedetomidine in preventing shivering during spinal anesthesia. The research design and protocol involve a randomized controlled trial (RCT) study, with patients grouped into two groups to assess the impact of dexmedetomidine (with intrathecal bupivacaine) compared to another placebo group (saline with intrathecal bupivacaine). The allocation to these groups will be randomized to ensure unbiased results.

A unique approach will be used to maintain blinding between participants and the research team. An independent researcher, unaware of the study's objectives, will prepare syringes containing either IV dexmedetomidine or saline, minimizing potential biases. This rigorous approach ensures the validity

and reliability of the results through randomization, blinding, standardized procedures, and comprehensive monitoring.

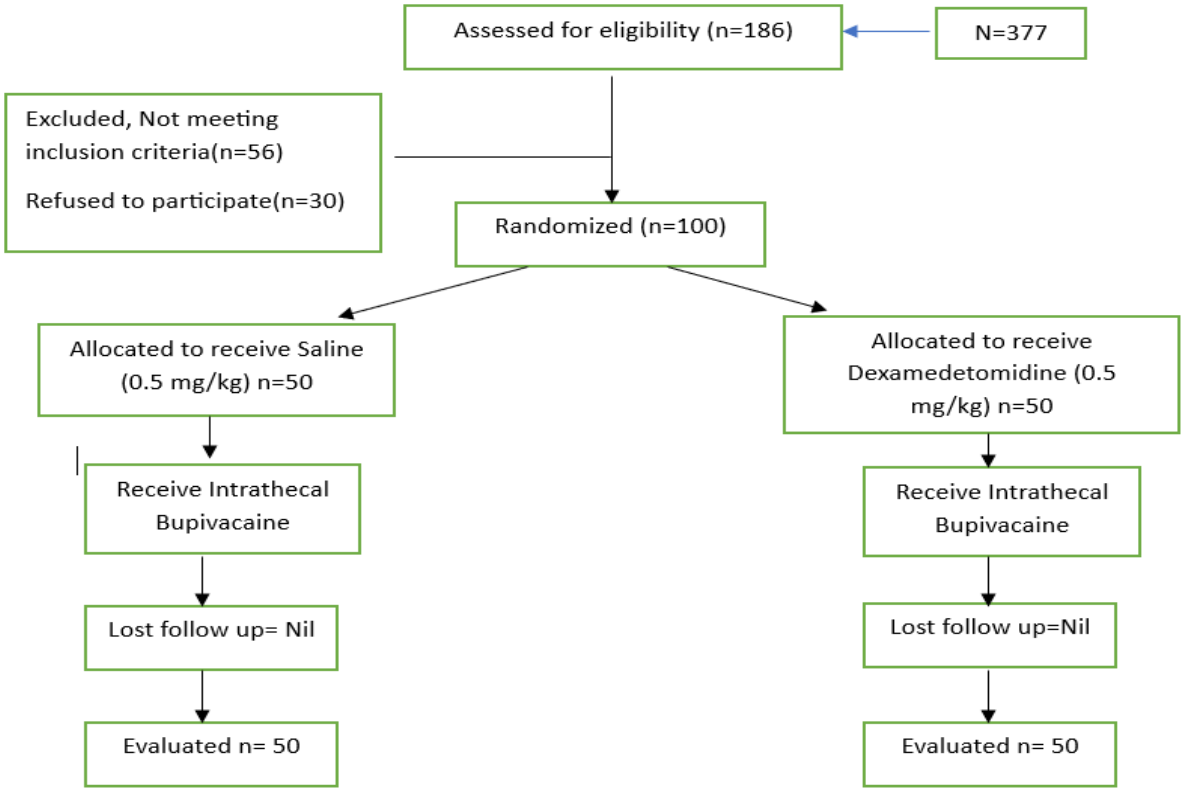
The spinal anesthesia will be administered to all patients at either the L3-4 or L4-5 intervertebral spaces, ensuring uniformity in the anesthesia protocol. Dexmedetomidine will be administered intravenously, diluted to a volume of 50 ml with a concentration of 4 µg/ml bupivacaine and coded by an experienced anesthesiologist to maintain blinding. Group A (intrathecal bupivacaine with IV saline) will receive an intravenous bolus of 1 µg/kg dexmedetomidine via syringe pump over the 10-minute duration, followed by a continuous infusion of 0.5 µg/kg throughout surgery. Group B (intrathecal bupivacaine with IV DEX) will receive an equivalent amount of saline.

The post-anesthesia care unit and operating room will be maintained at a temperature between 71.6 to 78.8°F (22°C to 26°C), with one layer of surgical drapes covering the patient's entire body. Key vital signs such as heart rate, oxygen saturation, blood pressure, and body temperature will be continuously monitored throughout the procedure and postoperatively. Adverse effects, including bradycardia, nausea, hypotension, vomiting, headache, and allergy, will be recorded and treated.

Sample Size

This study uses a statistical approach to determine the sample size necessary for detecting the effects of spinal anesthesia. The population size was estimated using the Krejcie & Morgan table, with 186 patients selected for the study. Key parameters include a 94% confidence level, a margin of error of 4%, a baseline incidence of 56%, a statistical power of 90%, and a significance level of 0.04. 100 patients were characterized based on these parameters, with 86 excluded due to exclusion criteria. The study aims to detect a 20% reduction in shivering incidence, and a minimum of 50 patients in each group is required to achieve the desired power and significance level. A total of 100 patients were included, with 50 patients in each group meeting the inclusion criteria, to meet the required sample size for robust statistical analysis. This ensures the study has sufficient statistical power to detect meaningful differences in shivering incidence between the two groups.

Figure 3.1: *Flow chart of patient selection*



Data Analysis

The analysis will be performed using the Statistical Package for the Social Sciences (SPSS) version 20.0, a widely used and trusted statistical analysis software tool.

For quantitative variables, such as numerical measurements and continuous data, the t-test will be employed to determine the significance of differences. The t-test is a statistical test that helps compare the means of two groups and assess whether the observed differences are statistically significant. It is particularly useful when analyzing variables like temperature, heart rate, and time-related measurements. The results of these analyses will be presented as mean values accompanied by the standard deviation (±SD). The mean represents the average value of the variable, and the standard deviation indicates the dispersion or variability of the data points around the mean.

Demographic Analysis

These interpretations offer a fundamental comprehension of the demographic characteristics and patterns of facility usage within the provided dataset in Table 4.1. The data indicates that a larger proportion of individuals within the sample are female (52%) in comparison to males (48%). The significance of this information may vary depending on its intended application, such as healthcare planning or marketing strategies.

A substantial segment of the population is comprised of individuals aged between 18 and 40 years, accounting for 73% of the total. The age cohort ranging from 41 to 50 constitutes 14% of the sample, whereas the age group spanning from 51 to 60 represents 13% of the sample. This observation suggests the presence of a comparatively youthful demographic, potentially leading to ramifications in terms of healthcare provisions and preferences for medical interventions.

According to the data, the Gynae OT (Gynecology Operating Theatre) emerges as the predominant facility, accounting for 57% of the sample. The Orthopedic Operating Theatre, commonly referred to as Ortho OT, is the second most frequently utilized operating theatre, accounting for 30% of the sample. Following closely behind is the General Operating Theatre, known as General OT, which is employed by 13% of the participants. The provided information holds significant value in the context of healthcare facility management and the decision-making process related to resource allocation.

Table 4.1 Demographic Analysis

Characteristic	Options	Percentage%
Gender	Male	48%
	Female	52%
Age	18-40	70%
	41-50	14%
	51-60	8%
	61-above	8%
Operation Theater	Gynae OT	57%
	Ortho OT	30%
	General OT	13%
Total n= 100		100%

The pie chart in Figure 1 illustrates a notable discrepancy in the utilisation of spinalanesthesiabased on gender. The study findings indicate that a majority of patients (52.1%) who underwent spinal anesthesia were identified as female, while the remaining proportion (47.9%) consisted of male patients. The data presented in the chart indicates that a significant percentage of female patients are choosing or necessitating the use of spinal anesthesia within the specific context in which this information was gathered.

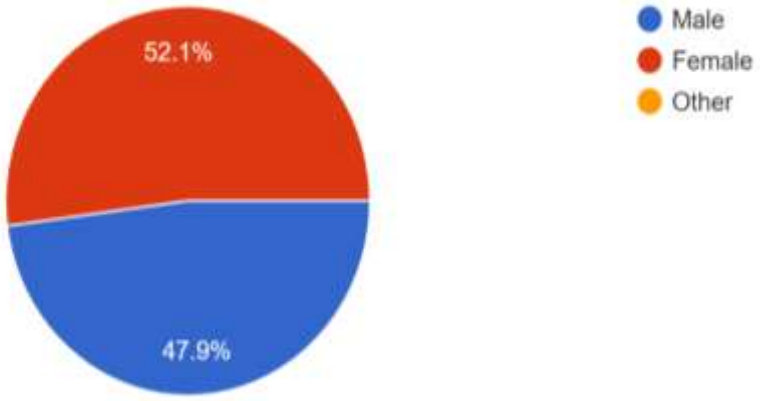


Figure 4.1: Pie chart of Gender

The majority of patients, comprising 73% of the total, fall within the age range of 18 to 40 years, as indicated by the age distribution depicted in Figure 2. The data indicates that the research sample is predominantly composed of individuals in younger age groups. The age distribution of participants in the study is as follows: 41 to 50 years old constitute 14% of the sample, while those aged 51 and above 16% of the sample

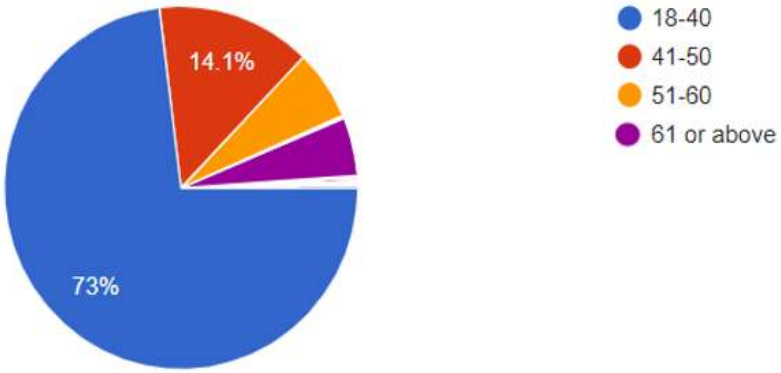


Figure 4.2: Pie chart of age

Descriptive analysis

In table 4.2 that is provided, data are compared between two groups, one of which received "Intrathecal Bupivacaine + IV saline" was group A and the other group B " Intrathecal Bupivacaine + IV DEX " across several parameters. Here is how the table can be understood:

The table displays the mean age of participants as 31.2 years with a standard deviation (SD) of 4.91 for group A and 33.04 years with an SD of 5.1 for group B. The p-value for age (0.75) indicates that there is no statistically significant age difference between the two groups of participants. This indicates that the ages of the two groups are similar.

Participants in the " Intrathecal Bupivacaine + IV saline" group A had a mean weight of 77.05 kg with an SD of 8.12, while those in the " Intrathecal Bupivacaine + IV DEX " group B had a mean weight of 74.6 kg with an SD of 7.2. There is no statistically significant difference in the weights of the participants between the two groups, according to the p-value for weight (0.92). This implies that the weights of the two groups are comparable.

The average surgery time in the " Intrathecal Bupivacaine + IV saline" group was 50.84 minutes, with a standard deviation of 18.4, and in the " Intrathecal Bupivacaine +IV DEX" group, it was 53 minutes, with a standard deviation of 19. The p-value for the surgery's duration (0.27) indicates that there is

not a statistically significant distinction between the two groups' surgical times. Consequently, both groups have similar duration.

Spinal anesthesia lasts for an average of 112.6 minutes with a 16.2 standard deviation in the " Intrathecal Bupivacaine + IV saline" group A and 116 minutes with a 20.1 standard deviation in the " Intrathecal Bupivacaine + IV DEX" group B. There is no statistically significant difference between the two groups in the length of spinal anesthesia, according to the p-value of the duration (0.25). This indicates that the lengths of spinal anesthesia in both groups are comparable.

Table 4.2 Descriptive analysis

Parameters	**GROUP A**		**GROUP B**		**P-value**
	Mean	SD	Mean	SD	
Age (years)	31.2Â	4.91	33.04Â	5.1	0.75
Weight (kg)	77.05Â	8.12	74.6Â	7.2	0.92
Duration of surgery	50.84Â	18.4	53Â	19	0.27
Duration of Spinal anesthesia(min)	112.6 Â	16.2	116 Â	20.1	0.25

Intrathecal Bupivacaine + IV saline (Group A), Intrathecal Bupivacaine + IV dexmedetomidine (Group B; SD -standard deviation; n -Number of patients. Test done was T-test.

Intensity of shivering

The table categorizes the intensity of shivering into different levels (0, 1, 2, 3, and 4). The percentages in each cell represent the proportion of patients in each group who experienced shivering at each respective level of intensity. The results suggests that the amount of shivering that occurs during the procedure is affected by the addition of Intrathecal dexmedetomidine (DEX) to bupivacaine. Compared to the group A (28%), a higher proportion of patients in the group B (76%) did not shiver (level 0). In comparison to the group A, the group B had a lower percentage of patients who shivered at levels 1 and 2. Both groups had few patients at the more severe levels of shivering (levels 3 and 4), with the group A with slightly more at level 3 as shown in figure 3.

Table 4.3 Intensity of shivering, n (%)

Shivering	GROUP A	GROUP B	Total (n=100)
0	13 (28%)	40 (76%)	53
1	8 (35%)	6 (20%)	14
2	3 (11%)	1 (4%)	4
3	1 (4%)	0	1
4	0	0	0

Intrathecal Bupivacaine + IV saline (Group A), Intrathecal Bupivacaine + IV dexmedetomidine (Group B)

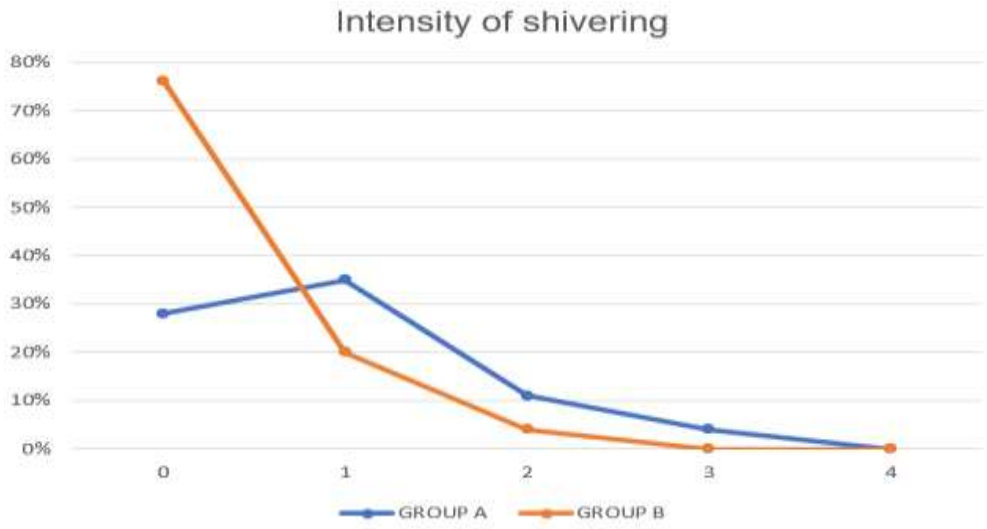


Figure 4.3 Graph of shivering level in both groups

Shivering Incidence

In table 4.4, average shivering intensity in the group A is 0.72, with a standard deviation of 0.83. The mean intensity of shivering in the group is 0.3, with standard deviation of 0.55.

When comparing the group B to the group A, the mean intensity of shivering was lower in the former. This suggests that use of IV dexmedetomidine (DEX) reduces the intensity of shivering.

The duration between blocks and the onset of shivering in the group A is 30 minutes. The group B experiences a longer time interval of 82 minutes. The group B experienced a longer period of time between the administration of blocks and the onset of shivering than the group A, indicating that the use of dexmedetomidine may postpone the onset of shivering.

Shivering was reported by 28% of patients in group A. Of the patients in the group B, 14% experienced shivering. According to the data, there is a decreased incidence of shivering when dexmedetomidine is used. In comparison to the group B, a smaller proportion of patients shivered in the group A.

The statistical significance of the differences between the two groups in terms of shivering incidence (0.03) and the time interval from blocks to shivering occurrence (0.12) is indicated by the p-values.

Table 4.4 Shivering Incidence

	GROUP A	GROUP B	Total (n=100)	P-value
Mean	0.72	0.3	0.6	
SD	0.83	0.55	0.72	
Time interval from blocks to shivering occurrence, minutes	30	82	67	0.12
Shivering incidence, n (%)	36 (28%)	6 (14%)	42	0.03

Intrathecal Bupivacaine + IV saline (Group A), Intrathecal Bupivacaine + IV dexmedetomidine (Group B)

In comparison with the use of bupivacaine with saline alone, the data indicate that IV dose of dexmedetomidine after intrathecal bupivacaine is linked with a decrease in the intensity of shivering, an extension in the onset of shivering, and a decreased frequency of shivering. The incidence and time intervals of shivering are confirmed by statistically significant p-values.

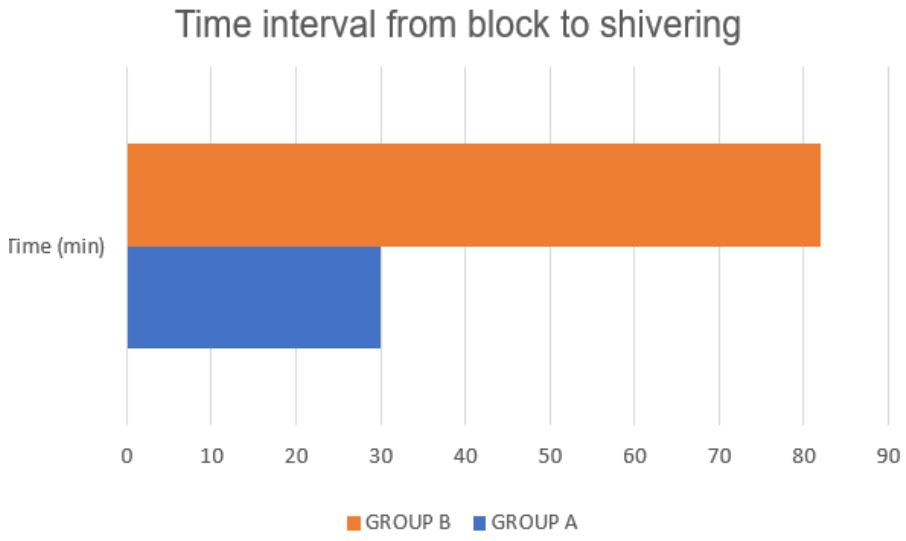


Figure 4.4 Graph of Time interval from block to shivering in both groups

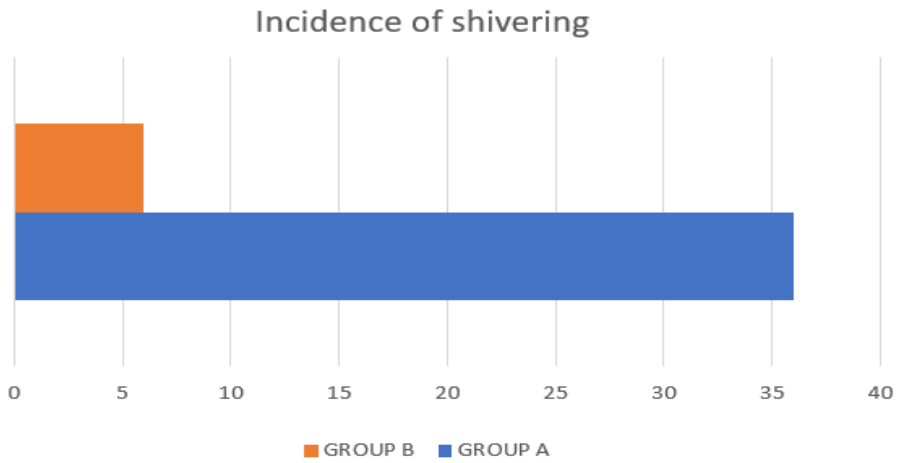


Figure 4.5 Graph of shivering Incidence in both groups

Analysis of Intra-operative and postoperative Adverse events

A compare of the two groups' treatments and adverse events during and after surgery. Table 4.5 displays the percentages of each group represent hypotension. Both groups experienced high rates of hypotension (between 91 and 96 percent), and the p-value (0.41) shows that there was no statistically significant difference in hypotension between the two groups.

The percentages for bradycardia seem to indicate that only a small number of patients in the "Bupivacaine + DEX" group experienced these side effects. The p-value for bradycardia is 0.48,. The p-value indicates that there is no discernible difference in the incidence of bradycardia between the two groups.

There was no discernible difference in the percentage of nausea between the two groups (p-value = 0.26), which was similar at 48%. Vomiting was more common in the "Bupivacaine + saline" group (30%) than in the "Bupivacaine + DEX" group (3%), although there was no discernible difference in the p-value (0.35).

The "Bupivacaine + saline" group had a small percentage (3%) of patients reporting a headache. No patients in the "Bupivacaine + DEX" group reported headaches.

Table 4.5 Intra-operative and postoperative Adverse events

Adverse events	GROUP A(n=50)	GROUP B (n=50)	Total, n=100	P-value
Hypotension, n (%)	22 (96.03)	21 (91)	43	0.41
Bradycardia, n (%)	2 (8.33)	1 (4)	3	0.48
Tachycardia, n (%)	1(3)	-	-	-
Nausea, n (%)	10 (48)	12 (48)	22 (48)	0.26
Vomiting, n (%)	3(30)	1(3)	-	0.35
Headache, n (%)	1(3)	-	-	-

Intrathecal Bupivacaine + IV saline (Group A), Intrathecal Bupivacaine + IV dexmedetomidine (Group B .Data are presented as number and frequency. Significant difference between groups at P value < 0.05).

Table 4.6 Sedation level

Sedation, n (%)	GROUP A (n=50)	GROUP B (n=50)	Total, n=100	P-value
				0.004
1	0	1 (3)	1	
2	4 (3)	36 (78)	40	
3	0	2 (8)	2	
4	0	6 (10)	6	

The table 4.6 displays the percentages of each group for the various sedation levels, which are denoted by the numbers 1, 2, 3, and 4. There is no patient in the "Bupivacaine + saline" group were sedated at level 1, compared to 3% in the "Bupivacaine + DEX" group. Level 2 sedation was experienced by

68% of patients in the "Bupivacaine + DEX" group, and level 3 sedation was experienced by 8% of patients, while 10% in level 4.

In contrast to "Bupivacaine + DEX," which had higher sedation levels (level 2), the use of "Bupivacaine + saline" produced lower level of sedation (level 2) as shown in graph figure 6. The p-value indicates that there was a significant difference in the two groups' levels of sedation.

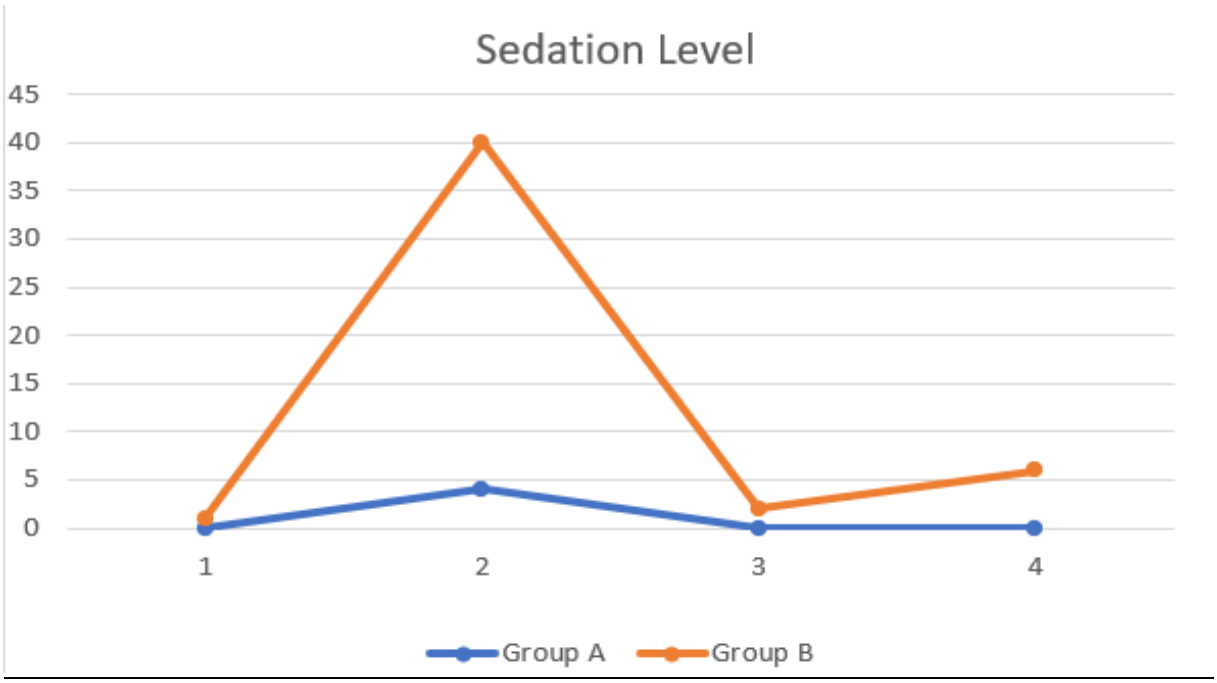


Figure 4.6 Sedation level in both groups

Discussion

This study looked into the effects of treating shivering caused by spinal anesthesia with intravenous dexmedetomidine. Excessive shivering brought on by spinal anesthetic was efficiently controlled in all studied groups by dexmedetomidine, which also produced mild hypotension and drowsiness. Shivering is caused by complex neurotransmitter pathways that include opioids, α-2 adrenergic, serotonergic, as well as anti-cholinergic receptors [27]. Numerous studies have examined the anti-shivering effects of dexmedetomidine and have demonstrated its superior capacity to lessen shivering following intrathecal bupivacaine delivery. The shivering thresholds decreased with intravenous dexmedetomidine infusion, but the sweating threshold remained same. These results support research by Talke et al. (1997), who discovered that dexmedetomidine's anti-shivering effects maintained a linear pattern. Consequently, dexmedetomidine improved patient comfort by preventing shivering reactions [86].

The study findings indicate that dexmedetomidine, at a dose of 0.5 µg/kg, is more effective than saline in treating shivering. The reasons for this include the drug's quick onset of action, faster rate of shivering cessation, and decreased recurrence of shivering. Dexmedetomidine can modulate the positive and negative effects of hypothermic shivering, including elevated catecholamine levels, increased oxygen consumption, elevated blood pressure, and hypertension. This result was corroborated by researchers who [30][301][38] discovered that in the brain and spinal cord, dexmedetomidine causes selective and specific α-2 adrenoceptor agonism. When these receptors are activated, sympathetic activity is decreased, which lessens the hemodynamic and neuroendocrine reactions that occur during anesthesia and surgery [24].

As a result, the sedation levels of patients receive 0.5 µg/kg of dexmedetomidine changed significantly, whereas the group receiving saline showed the least amount of sedation changes. The study found that 0.5 µg/kg of dexmedetomidine efficiently controlled shivering, although it also caused tolerable hemodynamic instability and drowsiness [59]. When given dexmedetomidine

intravenously at a dose of 0.5 μg/kg, more individuals experienced drowsiness than those in the other group (P 0.004). There were differences in the level and length of sedation between the saline and dexmedetomidine groups. The sedative effect of DEX is distinguished from other clinically accessible sedatives by its short-term and easily reversible nature (arousable sedation). Patients in DEX groups who experienced sedation were easily woken, and the sedation lasted for a shorter period. According to a European phase III experiment, main dexmedetomidine medication can accomplish even the most difficult tasks, like pen-and-paper communication [93]. According to another study, dexmedetomidine administered intravenously first causes bradycardia, hypotension, and sedation before producing a central sympathomimetic effect and mild drops in heart rate and mean arterial pressure [49][33] .

Differences in related risk variables and intravenous fluid consumption may be the cause of the reduced incidence of shivering (14%) seen in this study. According to Crowley and Buggy (2008), the median incidence of shivering associated with intrathecal anesthesia has been observed to reach 55% (interquartile range: 40–64%) [15]. The kind and length of anesthesia, the surgical technique, the degree of sensory blocking, the patient's age, the operating room's temperature, and the infusion fluids' temperature are all variables linked to shivering [45]. In this study, these factors were specifically examined. Furthermore, the study indicates that throughout the procedure, none of our patients developed respiratory depression. This result is consistent with earlier studies that found little to no respiratory depression when using α2-adrenergic agonists [1][16].

Conclusion

In this comprehensive analysis, we have drawn meaningful conclusions from a range of data and interpretations across various aspects, data comparing two treatment groups, "Intrathecal Bupivacaine + IV saline" and " Intrathecal Bupivacaine + IV DEX," yielded vital information. A significant difference in sedation levels between the two groups indicates that IV of dexmedetomidine (Dex) after intrathecal bupivacaine can result in modest sedation levels. This has important implications for clinical practice, as patient comfort and sedation levels play a critical role in various medical procedures. Furthermore, the data indicated that the introduction of dexmedetomidine is associated with a reduction in the intensity of shivering, a delay in the onset of shivering, and a lower incidence of shivering. These findings have the potential to improve patient comfort and overall outcomes in procedures involving spinal anesthesia. This analysis of intra-operative and postoperative adverse events and treatments provided insights into the impact of our interventions. The reduction in the incidence of shivering in the "Bupivacaine + DEX" group B suggests the potential benefits of this intervention. These findings are particularly important for anesthesiologists and healthcare practitioners as they highlight the safety and efficacy of incorporating dexmedetomidine into anesthesia protocols.

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