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ORIGINAL ARTICLE

Intravenous Dexmedetomidine Versus Low Dose Ketamine for Prevention of Shivering in Parturient Undergoing Elective Cesarean Section Under Spinal Anesthesia

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ABSTRACT

Background: Dexmedetomidine and ketamine have been used effectively to prevent shivering following spinal anesthesia (SA). Shivering inhibition occurs via reducing vasoconstriction (VC), lowering the shivering threshold, and inhibiting central thermoregulation. This study compares intravenous (IV) dexmedetomidine (0.3 ug/kg) versus low-dose ketamine (0.25 mg/kg) in preventing shivering during elective cesarean section (CS) under SA. **Methods:** This prospective randomized double-blind controlled trial involved 75 parturients with uncomplicated pregnancy ASA physical status class II, divided into three equal groups (25 each): Control group: parturients received 20 ml normal saline (NS). Dexmedetomidine group: parturients received (0.3 ug/kg) dexmedetomidine diluted in 20 ml NS. Ketamine group: parturient received (0.25 mg/kg) ketamine diluted in 20 ml NS. Over ten minutes, all study medications were administered via IV infusion after clamping the umbilical cord. Shivering occurrences, hemodynamics & core temperature changes, sedation level, total consumed rescue pethidine, and intraoperative complications were evaluated.

Results: Earlier significant onset of shivering was found in the control group (13.23 ± 10.63) minutes, followed by the ketamine group (23.83 ± 3.53) minutes and lastly, the dexmedetomidine group (31.67 ± 1.24) minutes with ($P < 0.05$). Shivering episodes were shorter for those in the dexmedetomidine group, ketamine group, and control group, in that order ($P<0.05$). The incidence and severity of shivering were significantly higher among the control group when compared to the dexmedetomidine group as well as the ketamine group ($P1$ & $P3 < 0.05$). Parturients were more sedated in the dexmedetomidine group and ketamine group when compared to the control group ($P1$ & $P3 < 0.05$).

Conclusions: Intravenous dexmedetomidine and low-dose ketamine are both effective and safe in lowering the occurrence and severity of shivering during cesarean section under spinal anesthesia. Dexmedetomidine, however, is more effective than ketamine.

Keywords: Dexmedetomidine; Ketamine; Cesarean Section; Spinal Anesthesia.

INTRODUCTION

Spinal anesthesia (SA) has become a preferred choice for elective cesarean section (CS); this is based on more maternal morbidity and mortality associated with general anesthesia (GA) and greater incidence of complications such as intubation failure, aspiration, blood loss, and awareness during surgery [1,2]. On the other hand, spinal anesthesia is easy to perform, has minimal depression of the newborn, and permits the mother to be conscious during the birth process so that she can start breastfeeding and ambulation earlier. In addition to reducing the duration spent in the hospital, it also reduces the occurrence of venous thromboembolism, cardiac events, and the requirement for postoperative analgesics. Despite these advantages, the incidence of shivering in CS under SA is still higher than other procedures (up to 55%) [3,4].

Post-anesthetic shivering (PAS) is the uncontrollably occurring, repetitive, oscillating, tremor-like excitation of muscles following general or regional anesthesia and increases metabolic heat production by as much as 600% [5].

Although the precise mechanism of shivering has yet to be determined, it was previously believed that hypothermia induced by sympathetic block in SA led to fast heat loss and the transfer of body heat from the core to the periphery, lowering the threshold for shivering [6,7].

The parturient's experience during childbirth may be negatively impacted by shivering, even while it doesn't pose a threat to her life. It also has a multitude of harmful effects, such as increased heart rate (HR), increased oxygen (O_2) consumption, lactic acidosis, hypertension (HTN), and enhanced morbidity in cardiovascular disease (CVD) patients [8].

Dexmedetomidine is a transmembrane G protein-binding receptor agonist with a high selectivity for alpha$_2$-adrenoceptors. Dexmedetomidine can provide drowsiness, analgesia, amnesia, sympatholytic, anesthetic sparing, and hemodynamic stabilizing effects without impairing respiratory drive, making it ideal for use in the operating room. Dexmedetomidine's fat-soluble properties make it highly retained in the placenta, which may account for the lack of adverse effects when the drug is used during labor and delivery. Dexmedetomidine's anti-shivering mechanism is connected to reducing vasoconstriction (VC) shivering thresholds and blocking central thermoregulation, and numerous studies have shown that its infusion inhibits postoperative shivering without substantial adverse effects [9,10].

Ketamine is involved in thermoregulation in multiple aspects because it acts as a competitive NMDA receptor antagonist. It produces a dissociative anesthetic state and

has characteristics of induction of amnesia, sympathetic system stimulation, bronchial smooth muscle relaxation and analgesia. Research has demonstrated that ketamine when administered to patients under regional anesthesia, can alleviate postoperative shivering without substantially altering blood pressure levels. Ketamine likely regulates shivering through non-shivering thermogenesis, by norepinephrine's beta-adrenergic action or by affecting the hypothalamus [11].

So, we aimed at this study to compare intravenous dexmedetomidine (0.3 ug/kg) versus low-dose ketamine (0.25 mg/kg) for preventing shivering among parturients undergoing elective cesarean section under spinal anesthesia.

METHODS

This prospective randomized, double-blind controlled trial was done on 75 participants with uncomplicated pregnancy ASA physical status class II who were scheduled elective CS under SA at Zagazig University Hospitals from April 2020 to October 2020.

Sample size: Assuming that the percentage of parturient had a shivering score of zero after 10 minutes of spinal anaesthesia, it was 46.6% in the ketamine group versus 80% in the dexmedetomidine group. The estimated sample was 75 cases, 25 cases in each group. The sample size was determined using the open EPI software with a 95% confidence interval and 80% power.

After institutional review board approval of IRB (IRB#6727), All participants were asked to sign an informed consent. Human subjects research adhered to the guidelines set in the Declaration of Helsinki, which is part of the World Medical Association's Code of Ethics.

Inclusion criteria: The study included 75 female patients aged 21–39 years, BMI ≤ 30 kg/m^2, ASA II who were scheduled elective CS under SA, exceeded 37 weeks of gestation and had a parity of fewer than 6.

In this study, 103 parturients were enrolled to undergo elective CS under SA; 28 parturients were excluded as 17 did not meet the inclusion criteria, seven refused to participate, and four parturients for other reasons. Three equal groups were randomly selected from among the 75 parturients who were enrolled in the study (Figure 1).

Exclusion criteria: Parturients who were excluded from the study those who had coagulation disorders, infection at the site of injection and severe spinal deformity, parturients who had any allergy to the study medication, parturient with initial temperature < 36.5 °C or > 37.5 °C, women who are pregnant and have conditions including hypothyroidism, hyperthyroidism, heart disease, Parkinson's, or dysautonomia, Raynaud’s syndrome, preeclampsia, and diabetes mellitus. Also, parturients with a history of convulsions, psychoactive medications, and use of sedatives, hypnotic agents, or vasodilators were excluded from the study.

Complete medical history, physical examinations, and laboratory investigations were performed on all study participants. These investigations included CBC, random blood glucose, kidney function test, liver function test, and coagulation profile. All pregnant women were fasted for the recommended time before surgery (8 hours for fatty meals, 6 hours for light meals, and 2 hours for clear fluids). All mothers received

an IV dose of ranitidine (50 mg) 30 minutes or more before the operation.

Intraoperative

During the perioperative period, the temperature in the operating room was kept between 24°C and 26°C. On arrival at the operative theatre, two IV lines were obtained using 18-gauge cannulas; one for IV fluids and the other for infusion of the study drugs. Routine monitors were applied to record heart rate (HR), mean arterial blood pressure (MAP), and oxygen saturation value (SpO_2) and basal readings were obtained.

The pregnant woman was placed in the sitting position, and then SA was administered at L3/4 or L4/5 interspaces after the back was disinfected with antiseptics. Following SA, the pregnant women received four litres of oxygen per minute through a face mask. A pinprick test was used to evaluate sensory blockade at 0, 5, 10 and 15-minute intervals. A modified Bromage scale was used to evaluate motor block [12]. The fluid deficit was then given. Three milliliters of ringer solution were administered for every millilitre of bleeding. Following the umbilical cord clamping and delivery of the baby, oxytocin was administered intravenously at a concentration of 10 IU/ml.

The seventy-five pregnant females were categorized into three equal groups of the same size (based on the study medicines) using a computer-generated randomization table:

Control group (Group C): Parturients were given 20 ml NS as an IV infusion over 10 minutes by a syringe pump after clamping the umbilical cord.

Dexmedetomidine group (Group D): Parturients were given dexmedetomidine (0.3 ug/kg) diluted with NS to a volume of 20 ml given as IV infusion over 10 minutes by a syringe pump after clamping of the umbilical cord.

Ketamine group (Group K): Parturients were given ketamine (0.25 mg/kg) diluted with NS to a volume of 20 ml given as IV infusion over 10 minutes by a syringe pump after clamping of the umbilical cord.

The mean arterial blood pressure, heart rate, oxygen saturation, and core body temperature were all monitored throughout the entire surgical procedure and recorded every 5 minutes intraoperatively and then every 15 minutes post-operative for 2 hours.

The time interval between study medication administration and the onset of shivering was recorded, if it occurred). The duration of shivering was also recorded (the time taken from the onset to cessation of shivering, if it occurred). The incidence and severity of shivering were recorded at 10-minute intervals intraoperatively and then every 15 minutes postoperatively for 2 hours, if it occurred. Shivering was graded according to a scale validated by Tsai and Chu [13] (G0=no shivering, G1=piloerection or peripheral VC but no visible shivering, G2=muscular activity in only one muscle group, G3=muscular activity in more than one muscle group but not generalized, G4=shivering involving the whole body). Within 15 minutes of administration of the study drug, if the shivering grade was ≥ 3, IV pethidine 25 mg was given as a rescue drug.

The occurrence of adverse events such as hypotension, bradycardia, nausea, and vomiting were noted. Normal saline infusion and, if necessary, 6 mg IV boluses of ephedrine to treat hypotension (a drop in

MAP of more than 20% from baseline value) were used. Treatment for bradycardia (heart rate less than 60 beats per minute) included 0.5 mg of IV atropine.

Intraoperative incidence of N/V was recorded [14]. If vomiting occurred, 10 mg metoclopramide was administered IV over 5 minutes. Sedation level was assessed every 10 minutes after administration of the study drugs till 2 hours postoperative with a four-point scale described by Filos [15] (1:awake and alert, 2:drowsy, responsive to verbal stimuli, 3:drowsy, arousable to physical stimuli, 4:unarousable).

STATISTICAL ANALYSIS

IBM's statistical analysis software, SPSS, version 20.0, was used to process the data. Qualitative data was represented with numerical and percentage-based language. Quantitative information was summarized by means and standard deviations. To test for statistical significance between more than two groups, an ANOVA was performed. The existence of a statistically significant difference between the groups was determined using a student t-test. We used the chi-square test to determine a relationship between two qualitative variables.

RESULTS

All of the age, weight, height, body mass index, pregnancy status, parity, gestational age, duration of surgery, operating room temperature, and American Society of Anesthesiologists risk categories did not differ significantly among the three groups (P> 0.05) (Table 1).

Regarding MAP, it was significantly lower in the dexmedetomidine group from 15 minutes to 25 minutes after administration of the study drugs compared to the control group and ketamine group (P1 & P2 < 0.05). Regarding HR, it was significantly lower in the dexmedetomidine group from 5 minutes to 20 minutes after administration of the study drugs compared to the control group and ketamine group (P1 & P2 < 0.05). In all groups, there was a drop in the tympanic temperature after SA till the end of surgery concerning the corresponding baseline values. It rose gradually postoperatively till it reached the baseline values. The Ketamine group had a smaller temperature decrease compared to the dexmedetomidine and control groups (Figure 2).

There was a statistically significant difference between the groups in the time it took for the shivering to begin after receiving the study medicines (P<0.05). Women in the control group started shivering sooner than in the dexmedetomidine and ketamine groups (P1 and P3<0.05). Furthermore, statistically significant evidence suggests that parturients in the ketamine group experienced the onset of shivering earlier than those in the dexmedetomidine group (P2<0.05). There was a statistically significant difference in the length of time it took for shivering to stop between the groups (P<0.05). Shivering in the control group lasted substantially longer than in the dexmedetomidine and ketamine groups (P1 and P3<0.05). (Table 2). Dexmedetomidine and ketamine groups had significantly reduced incidence and severity of intraoperative shivering as compared to the control group (P1 and P3 <0.05, respectively); significantly more participants in the control group experienced grade 3 shivering (Table 3).

The percentage of those in the control group who used pethidine was significantly higher

than those in the dexmedetomidine group (P1<0.05). Pethidine consumption also varied significantly across control and ketamine groups (P3<0.05) (Table 4).

When comparing control and ketamine groups for the incidence of nausea, the ketamine group had a significantly lower incidence (P3 <0.05). The frequency of vomiting was reduced in dexmedetomidine, and ketamine groups compared to the control group (P1 and P3<0.05). Bradycardia and hypotension occurred more frequently in the dexmedetomidine group compared to the control and ketamine groups (P1, P2<0.05) (Table 5).

Sedation levels were measured on a four-point scale, and there was a statistically significant difference between the three groups (P<0.05) in how sedated they were. Dexmedetomidine and ketamine groups reported higher levels of sedation compared to the control group (P1 and P3<0.05) (Figure 2)

Table (1): Patient characteristics and operative data among the studied groups:

			Group C n=25	Group D n=25	Group K n=25	F/X^2	P
Age (years)			**28.92±4.59**	**28.48±4.87**	**29.08±4.64**	**0.109**	**0.893**
Weight (kg)			**83.16±6.67**	**85.92±8.41**	**83.16±6.67**	**1.561**	**0.217**
Height (cm)			**161.75±6.23**	**160.92±7.04**	**161.40±4.87**	**0.021**	**0.979**
BMI (Kg/m^2)			**32.26±4.85**	**33.18±4.42**	**31.76±3.78**	**2.907**	**0.079**
Gravidity; median (IQR)			**3 (2.5-4.5)**	**3 (3-4)**	**3 (2.5-4)**	**0.363**	**0.834**
Parity; median (IQR)			**2 (1.5-3)**	**2 (2-3)**	**2 (1-3)**	**0.412**	**0.814**
Gestational age (weeks)			**39.44± 1.04**	**39.48± 1.12**	**39.36± 1.11**	**0.078**	**0.925**
Operation duration (minutes)			**42.72±6.85**	**44.2±8.5**	**43.0±7.21**	**0.271**	**0.764**
OR temperature (°C)			**24.96± 0.84**	**25.08± 0.91**	**25.0± 0.87**	**0.123**	**0.885**
ASA	**II**	**n (%)**	**25 (100.0%)**	**25 (100.0%)**	**25 (100.0%)**	**0.0**	**1.0**

Group C = Control group ,Group D = Dexmedetomidine group , Group K = Ketamine group, F =ANOVA X^2 = Chi square P value < 0.05: significant , IQR= Interquartile range ,n = Number ,Data presented as mean ± SD, median, number and percentage , % = percentage

Table (2): Onset and duration of shivering among the studied groups:

	Group				
Variable	**Group C n=25**	**Group D n=25**	**Group K n=25**	**F**	**P**
Onset of shivering after drug administration (minutes)	**13.23 ± 10.63**	**31.67 ± 1.24**	**23.83 ± 3.53**	**50.579**	**<0.001****
	P_1 < 0.001**	**P_2 < 0.001****	**P_3 < 0.001****		
Duration (minutes)	**5.99 ± 1.89**	**2.0 ± 1.0**	**3.50±1.03**	**10.663**	**0.001****
	P_1 0.003*	**P_2 0.066**	**P_3 0.004***		

Group C = Control group, Group D = Dexmedetomidine group; Group K = Ketamine group F =ANOVA ,P value <0.05: Significant , Data presented as mean ± SD ,difference between group C and group D ,P_2: difference between group D and group K , n = Number , P_3: difference between group K and group C

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Table (3): Incidence and severity of intraoperative and postoperative shivering among the studied groups:

Variable			**Groups**			**X^2**	**P**
			Group C n=25	**Group D n=25**	**Group K n=25**		
Intraoperative shivering:							
Incidence	**No**	**n (%)**	**13 (52.0%)**	**24 (96.0%)**	**22 (88.0%)**	**16.37**	**<0.001****
	Yes	**n (%)**	**12 (48.0%)**	**1 (4.0%)**	**3 (12.0%)**		
			P_1 0.001**	**P_2 0.609**	**P_3 0.012***		
Severity	**G0**	**n (%)**	**13 (52.0%)**	**24 (96.0%)**	**22 (88.0%)**	**17.7**	**0.007***
	G1	**n (%)**	**2 (8.0%)**	**0 (0.0%)**	**1 (4.0%)**		
	G2	**n (%)**	**3 (12.0%)**	**0 (0.0%)**	**0 (0.0%)**		
	G3	**n (%)**	**7 (28.0%)**	**1 (4.0%)**	**2 (8.0%)**		
	G4	**n (%)**	**0 (0.0%)**	**0 (0.0%)**	**0 (0.0%)**		
			P_1 0.005*	**P_2 0.459**	**P_3 0.04***		
Postoperative shivering:							

Variable			Groups			X^2	P
			Group C n=25	Group D n=25	Group K n=25		
Incidence	No	n (%)	20 (80.0%)	23 (92.0%)	22 (88.0%)	1.615	0.446
	Yes	n (%)	5 (20.0%)	2 (8.0%)	3 (12.0%)		
Severity	G0	n (%)	20 (80.0%)	23 (92.0%)	22 (88.0%)		
	G1	n (%)	0 (0.0%)	1 (4.0%)	1 (4.0%)	7.615	0.473
	G2	n (%)	2 (8.0%)	1 (4.0%)	2 (8.0%)		
	G3	n (%)	2 (8.0%)	0 (0.0%)	0 (0.0%)		
	G4	n (%)	1 (4.0%)	0 (0.0%)	0 (0.0%)		

Group C = Control group , Group D = Dexmedetomidine group , Group K = Ketamine group , X^2 = Chi-square

P value <0.05: significant , n = Number ,% = percentag, G0= No shivering , G1=Piloerection or peripheral VC G2=Shivering in one muscle group , G3=Shivering in more than one muscle group G4=Shivering involving the whole body , P_1: the difference between group C and group D ,P_2: difference between group D and group K Data presented as number and percentage, P_3: difference between group K and group C

Table (4): The amount of rescue pethidine (mg) among the studied groups:

	Groups			F	P
	Group C n=25	Group D n=25	Group K n=25		
Amount of rescue pethidine (mg)	47.5 ± 7.91	25 ± 0.0	25 ± 0.001	10.38	0.004*
	P_1 0.02*	P_2 1.0	P_3 0.003*		

Group C = Control group , Group D = Dexmedetomidine group,Group K = Ketamine group
F = ANOVA ,n = Number ,P value < 0.05: significant ,Data presented as mean ± SD
P_1: difference between group C and group D , P_2: difference between group D and group K
P_3: difference between group K and group

Table (5): Nausea, vomiting, bradycardia and hypotension among the studied groups:

			Group			X^2	P		
			Group C n=25	Group D n=25	Group K n=25				
Nausea	No	n (%)	16 (64.0%)	21 (84.0%)	23 (92.0%)	6.5	0 .038*		
	Yes	n (%)	9 (36.0%)	4 (16.0%)	2 (8.0%)				
			P_1 0.107	P_2 0.667	P_3 0.037*				
Vomiting	No	n (%)	17 (68.0%)	23 (92.0%)	23 (92.0%)	7.143	0.028**		
	Yes	n (%)	8 (32.0%)	2 (8.0%)	2 (8.0%)				
			P_1 0.034*	P_2 > 0.999	P_3 0.034*				
Total		n (%)	25 (100.0%)	25 (100.0%)	25 (100.0%)				
Bradycardia	No	n (%)	23 (92.0%)		17 (68.0%)	25 (100.0%)	10.51	0 .007*	
	Yes	n (%)	2 (8.0%)		8 (32.0%)	0 (0.0%)			
			P_1 0.033*		P_2 0.004*	P_3 0.49			
Hypotension	No	n (%)	23 (92.0%)		17 (68.0%)	23 (92.0%)	7.14	0.02*	
	Yes	n (%)	2 (8.0%)		8 (32.0%)	2 (8.0%)			
			P_1 0.033*		P_2 0.033*	P_3 > 0.999			
Total		n (%)	25 (100.0%)		25 (100.0%)	25 (100.0%)			

Group C = Control group , Group D = Dexmedetomidine group, Group K = Ketamine group , X^2 = Chi-square ,n = Number, P value <0.05: significant ,P_1: difference between group C and group D, P_2: difference between group D and group K ,% = percentage , P_3: difference between group K and group C , Data presented as number and percentage

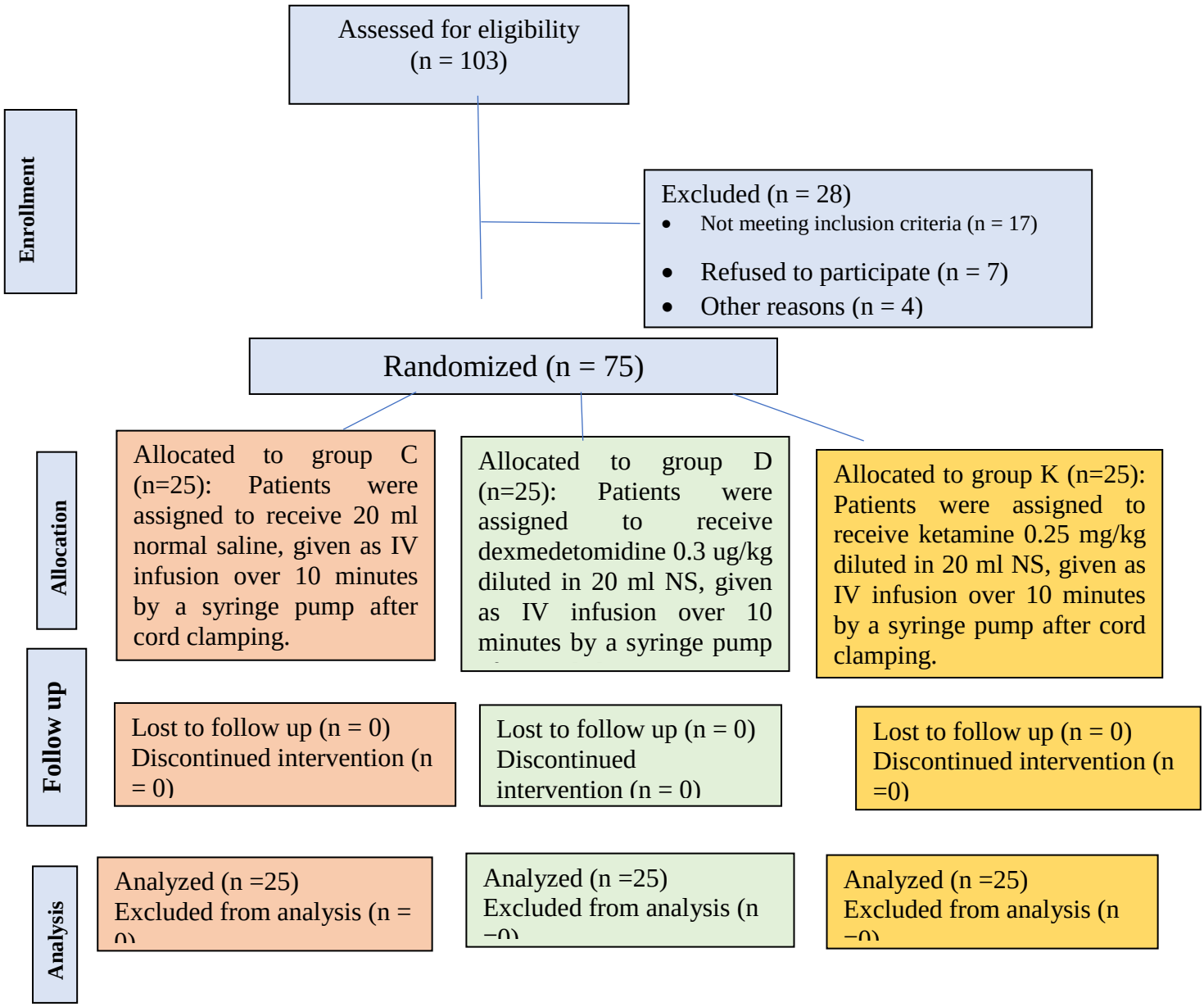

Figure 1: Consort flow diagram

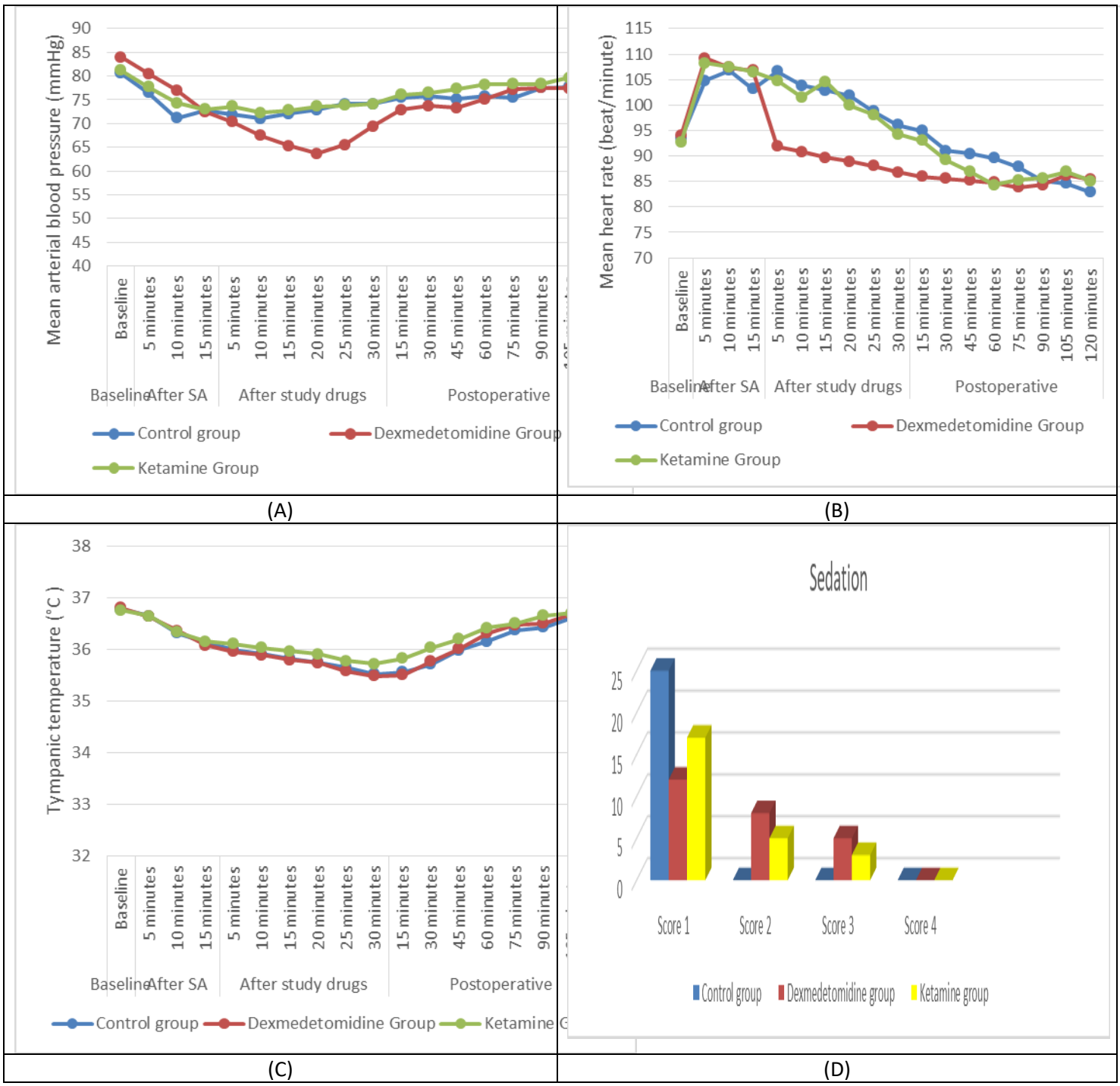

Figure 2: (A): MAP among the studied groups at different times, (B): HR among the studied groups at different times, (C): Tympanic temperature among the studied groups at different times (D): Sedation scores among the studied groups

DISCUSSION

Shivering may help regulate body temperature but also puts the body under extra stress. The body responds to this stress by increasing oxygen demand, carbon dioxide production, and heart effort. Treatment of shivering is less effective than its prevention [16].

The current study aimed to compare intravenous dexmedetomidine (0.3 ug/kg) versus low-dose ketamine (0.25 mg/kg) to prevent shivering among parturients undergoing elective cesarean section under spinal anesthesia.

Compared to the control group, patients in the dexmedetomidine and ketamine groups had a

decreased incidence of intraoperative shivering (4.0% and 12.0%, respectively). Several researchers confirmed this result by reporting that the shivering frequency during surgery under spinal anesthesia significantly decreased when dexmedetomidine or ketamine was administered intravenously.

Consistent with the findings of a previous investigation by Abdel-Fattah et al. [17], who studied the effect of IV dexmedetomidine (1 μg/kg), ketamine (0.5 mg/kg) and MgSO4 on prevention of shivering in transurethral resection of the This prostate (TURP) under spinal anesthesia. Shivering was reported by fewer people in the dexmedetomidine group (10%) and ketamine group (15%) compared to the control group (55%).

Also, the impact of IV administration of dexmedetomidine (0.5 μg/kg) on shivering in CS while anesthetized with spinal anesthesia was studied by Nesioonpour et al. [18]. They noted a significant decrease in shivering with IV dexmedetomidine compared to the control group.

Sween et al. [19] study were in harmony with the current findings, as they reported that the IV administration of 10 μg dexmedetomidine significantly reduced shivering in parturient undergoing CS under spinal anesthesia from 19.5% in the control group to 9.3% in dexmedetomidine group.

In accordance with our results, in Hasan et al.'s [20] study, two different dosages of IV ketamine (0.25 mg/kg) and (0.5 mg/kg) were assessed for their ability to prevent cesarean section patients from shivering while sedating. Both doses were shown to be superior to the control group in minimizing the occurrence of shivering.

While against the current study results, Ameta et al. [21] examined the efficacy of preoperative IV administration of ketamine (0.5 mg/kg), dexmedetomidine (0.5 μg/kg), and tramadol (0.5 mg/kg) in preventing shivering during the spinal anesthesia-assisted lower abdomen and lower limb surgery. It is inconsistent with these findings that more participants in the ketamine group (46.0%) experienced shivering than control group participants (42.0%).

Forty-eight percent of people in the control group experienced shivering during the current study. When compared to the 40% in the control group in an investigation done by Kose et al. [22] who compared two doses of IV ketamine (0.25 mg/kg) and (0.5 mg/kg) for prevention of shivering in CS under spinal anesthesia, this incidence was relatively high. Possible explanations for the discrepancy include using warmed fluids and forced air warming in their study.

In the current study, shivering severity was substantially greater in the control group than in the ketamine group. According to the research by Hasan et al. [20], participants in the control group experienced considerably more severe shivering during CS when compared to the ketamine groups.

Regarding hemodynamic parameters, the current study showed that MAP and HR were significantly lower in the dexmedetomidine group than in the ketamine and control groups. This is because dexmedetomidine reduces sympathetic tone by interacting with α_2 adrenergic receptors in the central nervous system. Sedation is induced by this sympatholytic activity, although there is no respiratory depression.

Rehim et al. [23] who compared between IV dexmedetomidine (0.4 μg/kg) and ketamine (0.3 mg/kg) in controlling shivering in elective lower abdominal and lower limb surgery under spinal anesthesia found similar outcomes.

Also, Houssein and Ibrahim [24] compared IV dexmedetomidine (loading dose of 1 μg/kg, followed by a continuous infusion of 0.4 μg/kg/h) and ketamine (0.25 mg/kg) in preventing intraoperative shivering in patients undergoing elective lower abdominal surgery under spinal anesthesia. They reported that patients in the dexmedetomidine group had significantly lower MAP and HR compared to the ketamine group.

In disagreement with this study's results**,** Farouk et al. [25] compared the hemodynamic effects of IV infusion of dexmedetomidine (0.5 μg/kg/h), $MgSO_4$, and placebo in patients undergoing bilateral inguinal hernial surgeries under SA. Their findings showed no statistically significant variations in MAP or HR between dexmedetomidine and control groups. This could be attributed to the slow rate of administration of dexmedetomidine in their study, as dexmedetomidine was administered as continuous IV infusion at a rate of (0.5 μg/kg) over an hour. In the current study, dexmedetomidine was administered as an IV infusion at a rate of (0.3 μg/kg) over 10 minutes.

Tympanic temperatures dropped significantly in all groups following SA compared to pre-SA values. Inhibition of thermoregulation, vasodilation leading to heat loss, and transfer of heat from the core to the periphery all contribute to the hypothermia that occurs during SA.

It appears that ketamine's sympathetic activation and vasoconstrictive action, which reduces the core to peripheral redistribution of heat, prevents the drop in temperature associated with SA, as measured by tympanic temperature. Over time, the patient's temperature in the recovery room after surgery rose above the temperature reported at admission. The patient's increased tympanic temperature during SA weaning may be connected to using a blanket to keep warm in the recovery area [26].

The findings contradicted those of Houssein and Ibrahim [24], as they reported a lower average core temperature in the ketamine group than the dexmedetomidine group. According to Abdel-Fattah et al. [17], participants with the lowest temperature were in the control group, next ketamine, and finally, dexmedetomidine group.

In the present study, there were relatively higher incidences of nausea and vomiting in control group than in the dexmedetomidine and ketamine groups. The antiemetic effect of dexmedetomidine may be mediated through inhibition of catecholamine by parasympathetic tone but may induce its side effects of bradycardia and hypotension [27].

These results align with Modir et al.'s [28] study, who compared the prophylactic effect of IV dexmedetomidine, ketamine and dexamethasone on the occurrence of nausea and vomiting in CS under SA. They showed that nausea and vomiting occurred less frequently in the dexmedetomidine and ketamine groups compared to the control group.

Our findings were in contrast with those of Sween et al. [19] who studied the effect of IV administration of 10 μg dexmedetomidine after cord clamping on the incidence of shivering in parturient undergoing CS under spinal anesthesia. They found no significant difference between dexmedetomidine and control groups in the prevalence of nausea and vomiting (9.3 percent). The current study employed a substantially higher dose of dexmedetomidine than the dose used in their study (10 μg), suggesting that the anti-emetic effect is dose-dependent, which could explain the discrepancy. The symptoms of

hypotension and bradycardia, which might lead to nausea and vomiting, were not triggered at this low dose.

In this study, the dexmedetomidine group had a considerably higher incidence of bradycardia and hypotension than ketamine and control groups.

In agreement with these results, Abdel-Fattah et al. [17] reported that bradycardia was observed in seven out of a total of 20 patients in the dexmedetomidine group (35.0%) compared to three out of a total of 20 patients in the control group (15.0%). In contrast, no cases were reported in ketamine group. They also reported that the incidence of hypotension was higher in patients in the dexmedetomidine group (40.0%) compared to the control group (15.0%) and ketamine group (5.0%).

On the other side, Sween et al. [19] found two patients (4.9%) in the control group to have bradycardia during surgery compared to zero (0%) patients in the dexmedetomidine group. There was a significant difference regarding the incidence of bradycardia between the two groups (P=0.008), which disagreed with our results. This could be because of the relatively small amount of dexmedetomidine (10 μg) utilized in their research.

In the current study, sedation scores in the dexmedetomidine group and ketamine group were significantly higher than in the control group. Moreover, the dexmedetomidine's group sedation scores were higher than the ketamine group, but this difference was insignificant.

Similarly, Kumar and Ammu. [29] who compared the efficacy of IV dexmedetomidine (0.5 μg/kg), ketamine (0.25 mg/kg), and tramadol in the prevention of intraoperative shivering in patients undergoing surgery (lower abdominal, urological, orthopedic) under subarachnoid block. They reported that 93.33% of the dexmedetomidine group developed a sedation score of 3 (drowsy, arousable to physical stimuli), according to a four-point scale described by Filos, compared to 56.67% in the ketamine group at 15 minutes after administration of both drugs.

On the other hand, Rehim et al. [23] reported that more patients were sedated in the ketamine group compared to dexmedetomidine group, as 33.3% of patients in the ketamine group developed a sedation score of 3, compared to 30% of patients in dexmedetomidine group.

Also, Lamontagne et al. [30] evaluated the efficacy of an IV bolus of 30 ug of dexmedetomidine in the treatment of shivering in CS under spinal anesthesia. They reported that no score of 3 or 4 of sedation was observed after dexmedetomidine administration, this doesn't come in line with our results.

Limitations:

The current study had some limitations, including that the room temperature and temperature of IV fluids were not tightly controlled. Standard anti-shivering medicine like meperidine was not used as a control group. Another limitation was that the study drugs were administered after delivery, when the mechanisms that induce shivering may already be underway, so prevention of shivering may not be as effective as drug administration before the SA was placed.

CONCLUSIONS

Intravenous dexmedetomidine and low-dose ketamine are both effective and safe in lowering the occurrence and severity of shivering during elective cesarean section under spinal anesthesia. Dexmedetomidine,

however, is more effective than ketamine at preventing shivering.

Conflict of Interest: Nothing to declare.

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REFERENCES

1. **Zhou C, Zhu Y, Bao Z, Wang X, Liu Q**. Efficacy of ondansetron for spinal anesthesia during cesarean section: a meta-analysis of randomized trials. J Int Med Res. 2018;46(2):654-62.
2. **Mcglennan A and Mustafa A.** General anesthesia for Caesarean section. CEACCP. 2009; 9(5): 148-51.
3. **Dharmalingam TK, Ahmad Zainuddin NA**. Survey on maternal satisfaction in receiving spinal anesthesia for cesarean section. Malays J Med Sci. 2013;20(3):51-4.
4. **Hong JY and Lee IH.** Comparison of the effects of intrathecal morphine and pethidine on shivering after Caesarean delivery under combined-spinal epidural anesthesia. Anesthesia. 2005;60 (12) : 1168-72.
5. **Ozaki M, Kurz A, Sessler DI, Lenhardt R, Schroeder M, Moayeri A, et al.** Thermoregulatory thresholds during epidural and spinal anesthesia. Anesthesiology. 1994;81 (2):282-8.
6. **Kranke P, Eberhart LH, Roewer N, Tramèr MR.** Pharmacological treatment of postoperative shivering: a quantitative systematic review of randomized controlled trials. Anesth Analg. 2002;94(2).
7. **Abdelrahman RS**. Prevention of shivering during regional anesthesia: Comparison of Midazolam, Midazolam plus ketamine, Tramadol, and Tramadol plus Ketamine. Life Sci. 2012; 9(2): 132-39.
8. **Wódarski B, Chutkowski R, Banasiewicz J, Moorthi K, Wójtowicz S, Malec-Milewska M, et al.** Risk factors for shivering during cesarean section under spinal anesthesia. A prospective observational study. Acta Anaesthesiol Scand. 2020;64(1):112-6.
9. **Liu ZX, Xu FY, Liang X, Zhou M, Wu L, Wu JR, et al.** Efficacy of dexmedetomidine on postoperative shivering: a meta-analysis of clinical trials. Can J Anaesth. 2015;62(7):816-29.
10. **Talke P, Tayefeh F, Sessler DI, Jeffrey R, Noursalehi M, Richardson C**. Dexmedetomidine does not alter the sweating threshold, but comparably and linearly decreases the vasoconstriction and shivering thresholds. Anesthesiology. 1997;87(4):835-41.
11. **Sharma DR and Thakur JR.** Ketamine and shivering. Anesthesia. 1990;45(3):252-3.
12. **Bromage PR.** A comparison of the hydrochloride and carbon dioxide salts of lidocaine and prilocaine in epidural analgesia. Acta Anaesthesiol Scand Suppl. 1965;9(16):55-69.
13. **Tsai YC and Chu KS**. A comparison of tramadol, amitriptyline, and meperidine for post-epidural anesthetic shivering in parturients. Anesth Analg. 2001; 93(5): 1288-92.
14. **Lema GF, Gebremedhn EG, Gebregzi AH, Desta YT, Kassa AA**. Efficacy of intravenous tramadol and low-dose ketamine in the prevention of post-spinal anesthesia shivering following cesarean section: a double-blinded, randomized control trial. Int J Womens Health. 2017;9:681-8.
15. **Filos KS, Goudas LC, Patroni O, Polyzou V**. Hemodynamic and Analgesic Profile after Intrathecal Clonidine in HumansA Dose-Response Study. Anesthesiology. 1994; 81(3): 591-601.
16. **Hoshijima H, Takeuchi R, Kuratani N, Nishizawa S, Denawa Y, Shiga T,et al.** Incidence of postoperative shivering comparing remifentanil with other opioids: a meta-analysis. J Clin Anesth. 2016;32:300-12.
17. **Abdel-Fattah AM, Hamzawy HA, Noor El-Din T**. Preventive Effect of Intraoperative Dexmedetomidine, Ketamine, Magnesium Sulfate on Perioperative Shivering Related to Transurethral Resection of the Prostate [TURB]; A

randomized Controlled Study. IJMA. 2022; 4(2): 2164-70.

18. **Nesioonpour S, Bayat S, Ghomeishi A, Behaeen K, Savaie M, Ahmadzadeh A**. Effect of Intravenous Dexmedetomidine on Shivering in Cesarean Section under Intrathecal Anesthesia: Randomized Clinical Trial. Anesth Pain Med. 2022;12(3):e122735.
19. **Sween LK, Xu S, Li C, O'Donoghue MA, Ciampa EJ, Kowalczyk JJ, et al**. Low-dose intravenous dexmedetomidine reduces shivering following cesarean delivery: a randomized controlled trial. Int J Obstet Anesth. 2021;45:49-55.
20. **Hasan OM, Mahdi ES, Ebraheem EY**. Different doses of ketamine in preventing chills in pregnant lady with cesarean section under spinal anesthesia. CAJMS. 2023;4(2): 373-80.
21. **Ameta N, Jacob M, Hasnain S, Ramesh G.** Comparison of prophylactic use of ketamine, tramadol, and dexmedetomidine for prevention of shivering after spinal anesthesia. J Anaesthesiol Clin Pharmacol. 2018;34(3):352-
22. **Kose EA, Honca M, Dal D, Akinci SB, Aypar U.** Prophylactic ketamine to prevent shivering in parturients undergoing Cesarean delivery during spinal anesthesia. J Clin Anesth. 2013;25(4):275-80.
23. **Rehim SS, Aboalfadl GM, Abdelatif AM**. Comparison between dexmedetomidine, ketamine, or dexmedetomidine–ketamine combination for control of shivering during spinal anesthesia. Curr. Med. Res. Pract. 2019; 4(3): 277.
24. **Houssein MM and Ibrahim IM**. Intravenous low-dose ketamine injection versus dexmedetomidine infusion for prevention of intraoperative shivering during spinal anesthesia. Ain Shams J. Anesthesiol. 2016; 9(4): 524.
25. **Farouk I, Hassan MM, Fetouh AM, Elgayed AEA**, Eldin MH, Abdelhamid BM. Analgesic and hemodynamic effects of intravenous infusion of magnesium sulphate versus dexmedetomidine in patients undergoing bilateral inguinal hernial surgeries under spinal anesthesia: a randomized controlled study. Braz J Anesthesiol. 2021;71(5):489-97.
26. **Seyam SH**. Prevention of post-spinal anesthesia shivering: Low dose ketamine vs tramadol. AIMJ. 2020; 1(4): 108-15.
27. **Jin S, Liang DD, Chen C, Zhang M, Wang J.** Dexmedetomidine prevent postoperative nausea and vomiting on patients during general anesthesia: A PRISMA-compliant meta analysis of randomized controlled trials. Medicine (Baltimore). 2017;96(1):e5770.
28. **Modir H, Moshiri E, Kamali A, Shokrpour M, Shams N.** Prophylatic efficacy of dexamethasone, ketamine and dexmedetomidine against intra-and postoperative nausea and vomiting under spinal anesthesia. Formos. J. Surg. 2019; 52(1): 17-23.
29. **Kumar RA and Ammu S**. Comparing the efficacy of tramadol, ketamine and dexmedetomidine in the prevention of intraoperative shivering in patients undergoing surgery under subarachnoid blockade. IJCA. 2021; 8: 446-51.
30. **Lamontagne C, Lesage S, Villeneuve E, Lidzborski E, Derstenfeld A, Crochetière C.** Intravenous dexmedetomidine for the treatment of shivering during Cesarean delivery under neuraxial anesthesia: a randomized-controlled trial. Can J Anesth. 2019; 66(7): 762-71.

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