Bull. Pharm. Sci., Assiut University, Vol. 47, Issue 2, 2024, pp. 1105-1117.

Bulletin of Pharmaceutical Sciences
Assiut University
Website: http://bpsa.journals.ekb.eg/

COMPARATIVE EFFICACY OF INTRAVENOUS MIDAZOLAM, MIDAZOLAM-KETAMINE, AND KETAMINE IN REDUCING THE PREVALENCE OF POST-SPINAL SHIVERING: A DOUBLE-BLIND CLINICAL TRIAL

Nasim Alipour[1], Nahid Manouchehrian[2], Maryam Aligholizadeh[3], Siavash Sangi[*3]

[1]*Department of Anesthesiology , School of Paramedicine ,Hamadan University of Medical Sciences,Hamadan ,Iran*
[2]*Department of Anesthesiology, School of Medicine, Hamadan University of Medical Sciences, Hamadan, Iran*
[3]*MSc of Anesthesia Education, Department of Anesthesia Technology, School of Allied Medical Sciences, Iran University of Medical Sciences, Tehran, Iran*

Background: *Post-spinal shivering poses a common challenge following regional anesthesia, presenting patients with an undesirable and distressing experience, and potentially leading to various complications. This study aimed to investigate the efficacy of intravenous midazolam, midazolam-ketamine, and ketamine in reducing the incidence of post-spinal shivering.* ***Methods and Materials:*** *A double-blind clinical trial was conducted on 124 patients aged 18-40 undergoing cesarean section with spinal anesthesia at Fatemieh Hospital, Hamadan. Spinal anesthesia was induced with 0.5% bupivacaine (10 mg) plus 2.5 µg sufentanil. Patients were randomly assigned to four groups: Midazolam 0.075 mg/kg (Group A), Ketamine 0.5 mg/kg (Group B), Ketamine 25.0 mg/kg plus Midazolam 37.5 µg/kg (Group C), and Normal saline 0.9% (Group D). Shivering severity, hemodynamic effects, nausea and vomiting, arterial oxygen saturation, hallucinations, sedation, and pethidine consumption were recorded during surgery and recovery.* ***Results:*** *The study encompassed 124 participants across four groups, ensuring comprehensive analysis without sample omission. Systolic blood pressure significantly reduced post-anesthesia in all groups ($p \leq 0.05$), notably pronounced in the midazolam-ketamine group. Similar reductions were observed in diastolic and mean arterial blood pressure ($p \leq 0.05$), with the most substantial decrease in the midazolam-ketamine group. Heart rate elevation post-anesthesia was significant only in the midazolam-ketamine group ($p \leq 0.05$). Oxygen saturation reduction was significant solely in the midazolam-ketamine group ($p \leq 0.05$). Sedation score elevation post-anesthesia was significant across all groups ($p \leq 0.05$), with the highest increase in the midazolam-ketamine group. Shivering intensity showed no significant inter-group differences. Hallucination incidence was similar across groups, while ketamine exhibited the highest nausea-vomiting incidence. Pethidine consumption did not differ significantly among groups.****Conclusion:*** *The midazolam-ketamine combination effectively reduced blood pressure, increased sedation scores, and lowered oxygen saturation levels, without significantly impacting shivering intensity or pethidine consumption during Cesarean sections under spinal anesthesia*

Keywords: *Shivering, Ketamine, Midazolam, Spinal Anesthesia*

INTRODUCTION

Approximately 18.5 million cesarean deliveries are conducted globally on an annual basis. While nerve anesthesia stands as the predominant technique employed for this surgical procedure, the prevalence of intraoperative shivering remains notably high in cesarean sections conducted under spinal anesthesia[1]. Post-anesthesia shivering (PAS)

Received : 8/3/2024 & Accepted : 23/6/2024

*Corresponding author: Siavash Sangi, E-mail: siavashsangi3@chmail.ir

represents a prevalent complication following both general and regional anesthesia, with reported incidences ranging from 5-65% and 60-40%, respectively. The severity of shivering varies from mild manifestations, such as piloerection, to more pronounced effects, including sustained contraction of skeletal muscles[2,3]. Characterized by rhythmic shaking movements in the upper, lower, neck, and jaw regions, shivering is an involuntary, repetitive muscular activity with spontaneous onset. Notably, shivering is frequently encountered during and after spinal anesthesia (SA) due to vasodilation, an effect of regional anesthesia that facilitates heat redistribution from the core to the periphery, consequently inducing hypothermia and lowering the shivering threshold[4,5]. Factors such as blood transfusion, pain, and surgical procedures also contribute to hypothermia[6]. Acknowledging shivering as a physiological response aimed at combatting hypothermia[7,8], it is crucial to recognize its potential implications on perioperative complications. The heightened risk of myocardial ischemia resulting from increased oxygen consumption (100% - 600%) underscores the clinical significance of managing PAS. Moreover, shivering may impede electrocardiography (ECG) and blood pressure monitoring, elevate intracranial and intraocular pressures, increase carbon dioxide and catecholamine production, contribute to patient discomfort, intensify pain at surgical incision sites, enhance minute ventilation and basal metabolic rate, and introduce delays in mother-baby communication. Cesarean section, a common surgical procedure for women, exhibits a notable prevalence of shivering ranging from 45% to 85%[9]. Consequently, preventive measures for shivering in this patient cohort are of paramount importance. While non-pharmacological interventions, including heating blankets and fluid warming, have been employed postoperatively, studies highlight the efficacy of certain pharmacological agents such as Meperidine, clonidine, ketamine, ondansetron, midazolam, sufentanil, tramadol, and physostigmine in mitigating postoperative shivering[5,10,11], with Meperidine being the most commonly utilize[2,12,13].

However, the utilization of Meperidine is not without complications, as it is associated with adverse effects such as respiratory weakness, nausea, vomiting, somnolence, prolonged recovery time, confusion (especially in the elderly), urinary- retention, itching, and constipation[14]. In light of these considerations, exploring alternative pharmacological options becomes imperative[15]. Ketamine, an anesthetic drug, and non-competitive N-Methyl-D-aspartate (NMDA) antagonist has emerged as a potential candidate for preventing PAS due to its ability to suppress pain and regulate temperature at sub-anesthetic doses. Research indicates that combining ketamine with midazolam is more effective compared to using ketamine alone. However, concerns regarding hallucinations, nausea, and vomiting have restricted the widespread use of ketamine as the primary pharmacological treatment for shivering[16]. However, recent studies suggest that ketamine, at doses of 0.75 mg/kg or less, may effectively prevent PAS while avoiding the side effects observed at higher doses, including cardiovascular stimulation. Minimize delusions, and other psychotic effects[11,17,18]. Midazolam, a short-acting benzodiazepine with anxiolytic and sedative properties, has demonstrated safety and efficacy as a sedative and anxiolytic at a recommended dose of 0.02 mg/kg. Studies have shown minimal impact on the cardiorespiratory system and oxygen saturation (SpO2) at this dosage[19-21]. Additionally, a study demonstrated that the utilization of benzodiazepines, specifically midazolam, for sedation and shivering management is correlated with a notable elevation in the incidence of delirium[22]. Given the potential adverse effects associated with meperidine and the imperative for alternative options, particularly in scenarios where meperidine may be unavailable or contraindicated, and recognizing the dearth of sufficient investigations regarding the efficacy of administering ketamine, midazolam, and their combination for shivering control, the current investigation was undertaken to compare the efficacy of intravenous administration of midazolam, ketamine, and a combination of midazolam-ketamine in mitigating the incidence of shivering after spinal anesthesia during cesarean section. This study aims to furnish valuable insights into the selection of pharmacological agents for mitigating maternal shivering while upholding

maternal and fetal welfare as primary considerations.

MATERIALS AND METHODS

This study is a double-blind randomized clinical trial with the trial registration code in the center: IRCT 21016043012251N3 and the ethics code IR.UMSHA.REC.1395.2, which was conducted on 124 pregnant women aged 18 to 40 years who underwent cesarean section with spinal anesthesia in Fatemieh Hospital, Hamadan. Inclusion criteria included: American Society of Anesthesiologists (ASA) physical status classification 1 or 2, term pregnancies (36-40 weeks of gestation), and cesarean delivery of singletons. Before anesthesia initiation, comprehensive explanations detailing the study methodology and anesthesia techniques were provided, and written informed consent was obtained from each participant. Exclusion criteria comprised high-risk pregnancies, pre-eclampsia, cardiovascular and pulmonary diseases, mental illnesses, thyroid disorders, type 1 and 2 diabetes mellitus, the necessity for blood product administration, fever exceeding 38 degrees Celsius, surgery duration exceeding one hour, history of nausea and vomiting post-surgery, pre-existing body temperature reduction or shivering due to fear or other causes. Additionally, patients exhibiting such conditions were disqualified from spinal anesthesia. Preoperatively, no pre-medication was administered, and all patients received Ringer's serum infusion at a rate of 5-10 ml/kg before spinal anesthesia commencement, continuing at 15 ml/kg during the procedure. Cardio-respiratory monitoring was implemented throughout. Standard spinal anesthesia, using a 25 Quincke-type needle in the L3-4 or L4-5 intervertebral space, involved injecting 10 mg of 0.5% bupivacaine with 2.5 micrograms of sufentanyl (total volume: 2.5 ml) into the subarachnoid space.

Throughout the operation, 6 liters of oxygen per minute were administered via a face mask. Sensory and motor assessments were conducted 5 minutes post-spinal anesthesia initiation. The operating room temperature was maintained at 23 degrees Celsius. Subsequently, patients meeting inclusion criteria were randomized into four groups (In each group, 31 participants were included in the study): Group A received midazolam (75 µg/kg), Group B received ketamine (0.5 mg/kg), Group C received a combination of ketamine (0.5 mg/kg) and midazolam (37.5 µg/kg), and Group D (control) received 0.9% normal saline. Intravenous drug administration occurred within 10-15 seconds post-umbilical cord clamping, ensuring homogeneity in drug presentation. The study implemented a double-blind approach, where neither the patients nor the sample collector was aware of the drug administered. The method of completing the questionnaire was taught to a group of recovery department personnel who were blinded to the assignment of the intervention group .Evaluated parameters included systolic and diastolic blood pressures, mean arterial pressure, heart rate, arterial blood oxygen saturation percentage, and temperature. Data were recorded before anesthesia, every 1-5 minutes within the first 5 minutes post-anesthesia, every 5 minutes up to 15 minutes, and subsequently every 10 minutes until procedure completion. The questionnaire also captured the level of sedation, hallucinations, nausea and vomiting, shivering intensity, and pethidine consumption. Sedation levels were assessed using the modified Ramsey scoring system while shivering severity was classified based on Crosley Mahajan scoring. Grading of sedation based on Ramsey scoring includes: fully awake and anxious = 1, quiet and calm with sufficient cooperation = 2, asleep and wakes up with a verbal command = 3, asleep and wakes up with mild stimulation, but with painful stimulation Strong reaction = 4, slow reaction to painful stimuli = 5 and no reaction to painful stimuli = 6, and, grading of shivering based on Crosley Mahajan's scoring includes 0 = no shivering, 1 = presence of one or more of these symptoms: hair spikes, peripheral vasoconstriction, peripheral cyanosis with or without cause, but without muscle activity, 2 = visible muscle activity limited to one muscle group, 3 = visible muscle activity in more than one muscle, 4 = intense muscle activity that involves the whole body[23,24]. These two criteria are valid and reliable[25-27.]

In the case of shivering score 2, intravenous pethidine (0.25-0.5 mg/kg) was administered, and if necessary, up to 50 mg was administered every 4 hours. Metoclopramide (10 mg intravenously) was

used to treat postoperative nausea and vomiting. Patients were taken to the recovery room, covered with a blanket, and maintained at a constant temperature of approximately 23 degrees Celsius. No additional heating devices were used, and continuous cardio-respiratory monitoring was applied. Questionnaire information was collected upon arrival and at 10-20- and 30 minutes post-recovery.

RESULT AND DISCUSSION

Result

The study enrolled a total of 124 participants distributed across four groups, and it is noteworthy that no samples were omitted from the final analysis. To assess the impact of intravenous administration of midazolam, midazolam-ketamine, and ketamine on mitigating the incidence of shivering induced by spinal anesthesia during Cesarean section surgery, a rigorous analytical approach was adopted. Specifically, a within-group t-analysis employing dependent methods was utilized in the current investigation. This methodological choice ensures a comprehensive and nuanced examination of the interventional effects, allowing for a robust evaluation of the efficacy of the administered agents in the context of spinal anesthesia-induced tremors during Cesarean section surgery.

As delineated in **Table 1**, an examination of the mean systolic blood pressure post-anesthesia across all four groups, namely midazolam, ketamine, midazolam-ketamine, and the control, reveals a noteworthy reduction compared to pre-anesthesia levels. This reduction was found to be statistically significant ($p \leq 0.05$) within each group. Remarkably, the group administered midazolam-ketamine exhibited the most pronounced reduction in systolic blood pressure.

Applying the paired t-test to assess the dependent variable of diastolic blood pressure before and after spinal anesthesia, the results manifested significant reduction in average diastolic blood pressure post-anesthesia compared to pre-anesthesia levels in all four groups ($p \leq 0.05$). The most substantial decrease in diastolic blood pressure was observed in the midazolam-ketamine group. Furthermore, a comprehensive analysis of mean arterial blood pressure post-anesthesia compared to pre-anesthesia levels across all four groups - midazolam, ketamine, midazolam-ketamine, and control - unveiled a statistically significant reduction ($p \leq 0.05$). Notably, the midazolam-ketamine group showed the most prominent reduction in mean arterial blood pressure, as described in **Table 1**. This statistical evidence underscores the efficacy of the midazolam-ketamine combination in inducing a significant reduction in both systolic and diastolic blood pressure, as well as mean arterial blood pressure, following spinal anesthesia in the context of Cesarean section surgery. Within the ketamine, midazolam-ketamine, and control groups, the post-anesthesia average heart rate experienced an increase relative to pre-anesthesia levels. However, this elevation achieved statistical significance solely within the midazolam-ketamine group ($p \leq 0.05$). Conversely, in the midazolam group, a non-significant decrease in heart rate was observed. This nuanced distinction underscores the differential impact of the administered agents on heart rate modulation following spinal anesthesia during Cesarean section surgery. In the context of arterial blood oxygen saturation, an investigation into the midazolam, midazolam-ketamine, and control groups revealed a significant reduction post-anesthesia compared to pre-anesthesia levels. Notably, this reduction attained statistical significance solely within the midazolam-ketamine group ($p \leq 0.05$), as detailed in **Table 1**. This outcome underscores the distinctive influence of the midazolam-ketamine combination in the context of oxygen saturation alterations post-spinal anesthesia during Cesarean section surgery. Examining the mean sedation score across all four groups - midazolam, ketamine, midazolam-ketamine, and control - a statistically significant increase post-anesthesia relative to pre-anesthesia levels was noted ($p \leq 0.05$). Intriguingly, the midazolam-ketamine group exhibited the highest elevation in sedation score, as elucidated in **Table 2**. This finding reinforces the particular efficacy of the midazolam-ketamine combination in inducing a significant increase in sedation levels, thereby contributing valuable insights into the nuanced sedative effects of these agents in the specified clinical context.

Table 1: Comparison among the groups in terms of systolic, diastolic, mean arterial blood pressure, heart rate, and oxygen saturation of arterial blood before and after anesthesia.

Control Mean (SD)	**Midazolam – Ketamine** Mean (SD)	**Ketamine** Mean (SD)	**Midazolam** Mean (SD)		**Variable**
127/19 (13.51)	124/67 (12.77)	124/24 (13.17)	122/61(24.18)	Before SA	**Systolic blood pressure**
113/73 (11.36)	105/26 (10.24)	117/05 (13.03)	108/74 (6.02)	After SA	
0/001**	0/001**	0/033*	0/002**	P	
83/00(14.67)	77/74 (12.11)	76/46 (12.47)	76/86 (16.10)	Before SA	**Diastolic blood pressure**
63/82 (9.78)	57/32 (10.06)	63/51 (7.84)	59/27 (7.54)	After SA	
0/001**	0/001**	0/001**	0/001**	P	
94/46 (13.56)	93/19 (12.14)	91/51 (13.76)	95/58 (15.63)	Before SA	**Mean arterial pressure**
79/27 (12.76)	72/44 (11.18)	78/80 (8.63)	74/06 (12.56)	After SA	
0/001**	0/001**	0/001**	0/001**	P	
93/56 (13.68)	94/03 (16.81)	95/87 (14.90)	96/77 (22.30)	Before SA	**Heart Rate**
97/86 (17.72)	100/48 (15.22)	100/15 (13.38)	95/01 (15.92)	After SA	
0/085	0/046*	0/112	0/51	P	
97/65 (2.05)	97/77 (1.49)	97/33 (3.14)	94/70 (16.94)	Before SA	**SPO_2**
97/62 (12.87)	96/32 (12.44)	98/8 (13.90)	94/39 (17.79)	After SA	
0/92	0/015*	0/496	0/33	P	

** p≤0.01
* p≤0.05

Table 2: Comparison among the groups in terms of sedation score before and after anesthesia.

Sig	**The mean difference**	**After anesthesia** Mean (SD)	**Before anesthesia** Mean (SD)	
0/001**	-1/21	2/26 (0.85)	1/05 (0.25)	**Midazolam**
0/001**	-0/91	2/09 (0.63)	1/18 (0.39)	**Ketamine**
0/001**	-1/24	2/36 (0.89)	1/12 (0.38)	**Midazolam-Ketamine**
0/001**	-0/74	1/98 (0.4)	1/24 (0.43)	**Placebo**

** p≤0.01
* p≤0.05

The mean intensity of shivering was the highest in the ketamine group (0.56) and the lowest in the control group (0.27), but there was no significant difference between the four groups in terms of the intensity of shivering **(Table 3 and Fig. 1).**

There was no significant difference between the four groups of midazolam, ketamine, midazolam-ketamine, and control in terms of the number of patients who had hallucinations during the operation ($p \leq 0.05$) **(Fig. 2).** There was a significant difference between the four groups of midazolam, ketamine, midazolam-ketamine, and control in terms of the number of patients who had nausea and vomiting during the operation ($p \leq 0.05$). The largest number of patients who had nausea and vomiting during the operation were in the ketamine group **(Fig. 3)**. Regarding the consumption of pethidine, there were no significant differences among the four groups ($p \leq 0.05$) **(Table 4).** but there was no significant difference between the four groups in terms of pethidine consumption **(Fig. 4).**

Table 3: Comparison among the groups in terms of shivering intensity after anesthesia.

Sig	Mean (SD) of shivering intensity	
0/56**	0/45 (0.98)	**Midazolam**
	0/56 (1.10)	**Ketamine**
	0/53 (1.02)	**Midazolam- Ketamine**
	0/27 (0.63)	**Placebo**

** p≤0.01

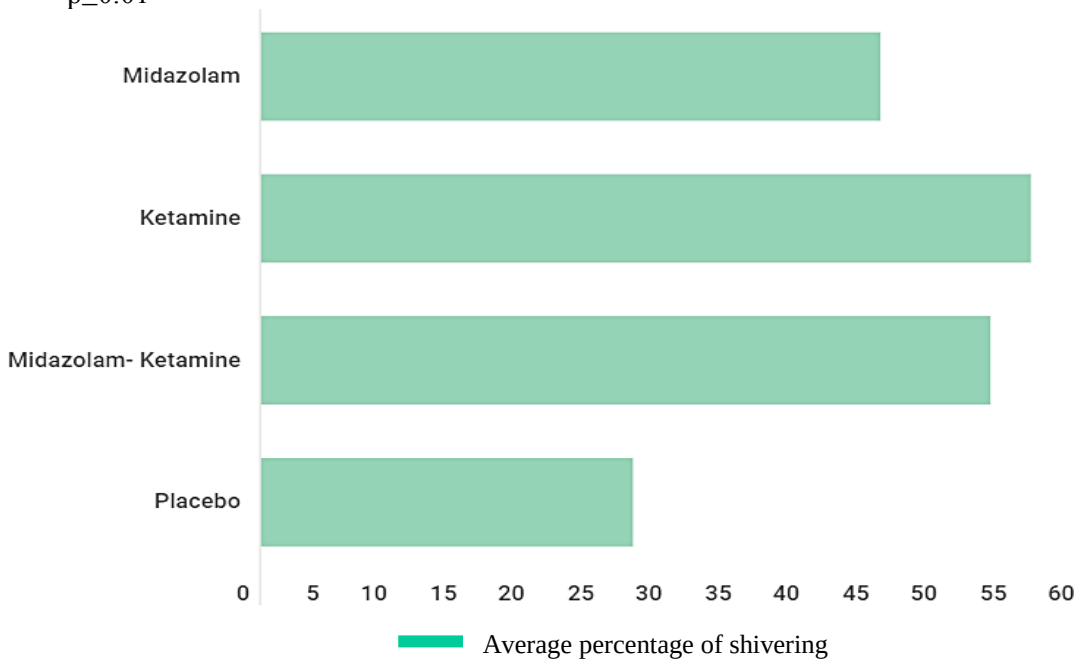

Fig 1: Comparison of groups in terms of Shivering intensity after anesthesia.

Table 4: Comparison among the groups in terms of hallucinations, nausea, and vomiting during surgery and pethidine consumption.

Sig	K score	Placebo	Midazolam-Ketamine	Ketamine	Midazolam	**Hallucination during surgery**
0/264	3/97	8	6	12	8	Yes
		33	25	20	27	No
Sig	K score	Placebo	Midazolam-Ketamine	Ketamine	Midazolam	**Nausea and vomiting during surgery**
0/017*	10/14	1	1	5	0	Yes
		40	30	27	35	No
Sig	K score	Placebo	Midazolam-Ketamine	Ketamine	Midazolam	**Use of pethidine**
0/711	1/37	4	6	5	5	Yes
		37	25	27	30	No

** p≤0.01
* p≤0.05

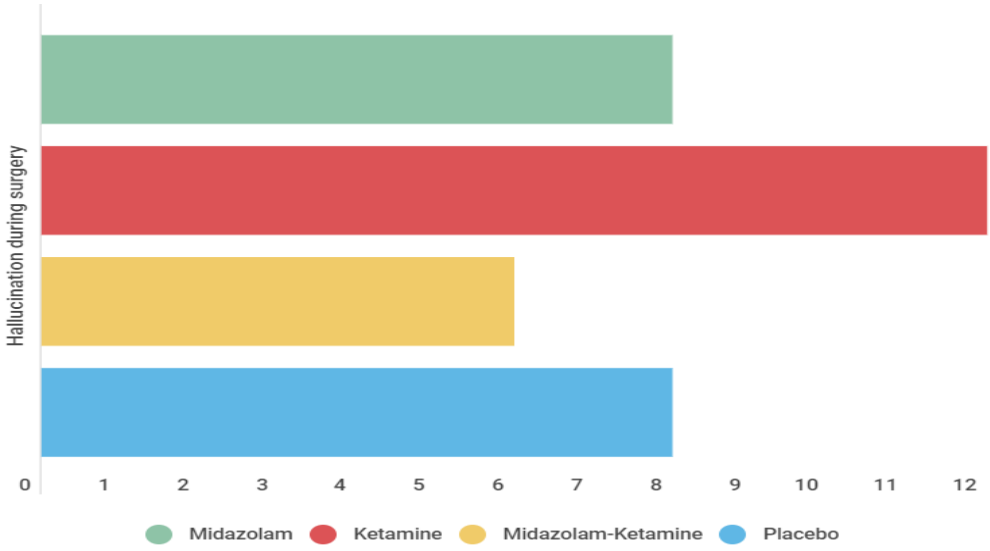

Fig 2: Comparison of the number of patients who had hallucinations during the operation.

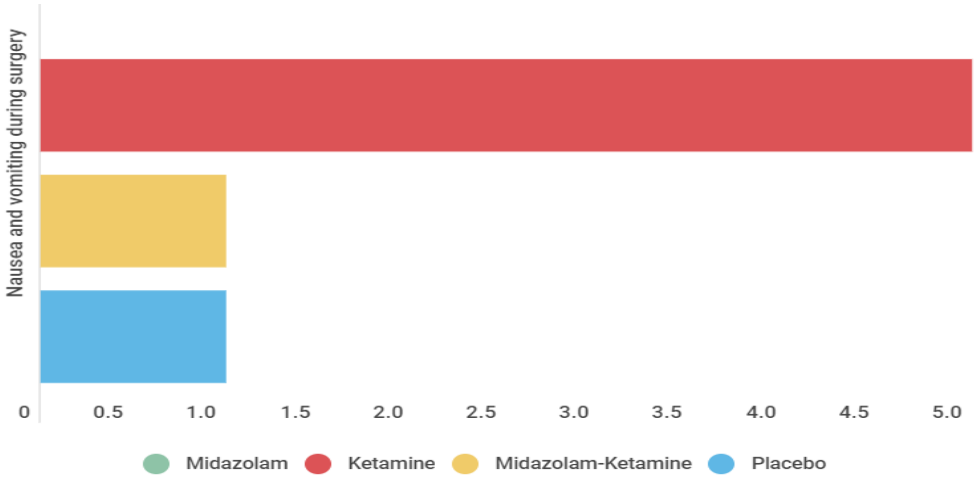

Fig 3: Comparison among the number of patients who had nausea and vomiting during the operation.

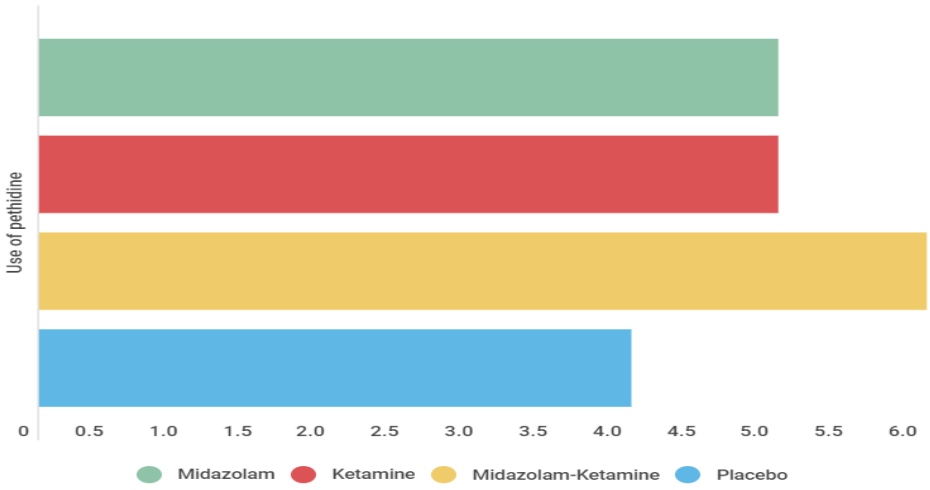

Fig 4: Comparison among the groups in consumption of pethidine after anesthesia.

Discussion

In this investigation, the impact of intravenous administration of midazolam, ketamine, midazolam-ketamine, and a control group in mitigating the prevalence of shivering following spinal anesthesia during cesarean section procedures was systematically studied. The findings revealed a significant reduction in mean systolic blood pressure, diastolic blood pressure, and mean arterial pressure post-regional anesthesia across all four groups. Notably, the most pronounced decrease was observed in the midazolam-ketamine group, indicative of the unique synergistic effect of this combination. Furthermore, an elevation in average heart rate after spinal anesthesia relative to pre-anesthesia levels was noted in the ketamine, midazolam-ketamine, and control groups, with statistical significance achieved solely in the midazolam-ketamine group. Additionally, a decrease in mean arterial blood oxygen saturation post-spinal anesthesia was observed in the ketamine, midazolam-ketamine, and control groups, with statistical significance exclusively in the midazolam-ketamine group. These nuanced cardiovascular and respiratory findings underscore the distinctive impact of the midazolam-ketamine combination on these parameters. The average sedation score exhibited a significant increase in post-regional anesthesia in all groups, with the highest elevation observed in the midazolam-ketamine group. The examination of shivering intensity revealed no significant inter-group differences, although the ketamine group displayed the highest intensity, albeit non-significant. The average consumption of pethidine did not exhibit statistical significance among the four groups; however, the ketamine group demonstrated the highest consumption, while the control group exhibited the lowest. Comparative analyses with previous research provided valuable contextual insights. For instance, findings from the current study align with Gvalani et al.'s research, indicating that the combined use of ketamine and midazolam can be more effective in reducing shivering compared to ketamine alone[7]. Abdul Wahid et al.'s prospective cohort study suggested a lower shivering incidence with ketamine[28], Additionally, following the findings delineated by Lema et al., the prophylactic administration of intravenous ketamine or low-dose intravenous tramadol has been established as efficacious in attenuating both the frequency and intensity of shivering. Noteworthy observations suggest that ketamine yields a more pronounced reduction in shivering manifestations, particularly among female patients undergoing surgical procedures under spinal anesthesia, notably cesarean section[9], while the present study observed an increased intensity of shivering in the ketamine group, though not statistically significant. Honarmand et al.'s study on magnesium sulfate and midazolam-ketamine combination concurs with our findings regarding shivering prevention, although it is important to note differences in the study focus and outcomes. In terms of side effects, the present study demonstrated a significant decrease in blood pressure across all groups, while the midazolam-ketamine group exhibited a significant increase in sedation score. Nausea and vomiting were more prevalent in the ketamine group, aligning with the results obtained by Ramalingaraju et al. in their study on ketamine and pethidine prophylaxis[15,29].

In their study titled "Investigation of the Impact of Intravenous Ketamine on Shivering Severity in Patients Undergoing Spinal Anesthesia," Kayalha et al. demonstrated that ketamine administration via injection proved to be a superior approach in managing intraoperative shivering compared to alternative methods. Notably, their study implemented a pre-spinal anesthesia injection of ketamine using an infusion pump, diverging from our research in terms of administration method, timing, and criteria for assessing shivering intensity[30]. Moreover, findings from the meta-analysis by Yang Zhou and colleagues align with the current study, emphasizing ketamine's efficacy in preventing post-anesthesia shivering without severe side effects[11]. However, variations in the study designs, patient populations, and administration methods necessitate careful interpretation of the results. Honarmand et al.'s study on magnesium sulfate and midazolam-ketamine combination concurs with our findings regarding shivering prevention, although it is important to note differences in the study focus and outcomes. In terms of side effects, the present study demonstrated a significant decrease in blood pressure across all groups,

while the midazolam-ketamine group exhibited a significant increase in sedation score. Nausea and vomiting were more prevalent in the ketamine group, aligning with the results obtained by Ramalingaraju et al. in their study on ketamine and pethidine prophylaxis[15,29]. In conclusion, this comprehensive study contributes nuanced insights into the effects of midazolam, and ketamine, and their combination in preventing shivering after spinal anesthesia during cesarean section. The results provide valuable considerations for clinical practice and further research, highlighting the importance of tailored interventions in mitigating post-anesthesia complications.

Conclusion

The study findings revealed that the midazolam-ketamine combination effectively mitigated blood pressure and induced elevated sedation scores, albeit without significant impact on shivering severity or pethidine consumption compared to other treatment modalities .Notably, ketamine monotherapy exhibited the highest shivering intensity and pethidine utilization, yet these variations did not attain statistical significance. Subsequent investigations may explore optimal midazolam-ketamine dosing strategies to optimize anti-shivering efficacy while mitigating adverse events such as nausea and vomiting associated with ketamine .Additionally, assessing its influence on diverse postoperative outcomes including pain levels, recovery duration, and maternal and fetal welfare would offer a more comprehensive understanding of its clinical implications. Enhanced generalizability necessitates larger sample sizes across diverse demographic cohorts.

limitation

The potential limitation of the study examining the efficacy of intravenous administration of midazolam, midazolam-ketamine, and ketamine in mitigating shivering prevalence following spinal anesthesia in cesarean section procedures pertains to the susceptibility to confounding variables. Variables such as maternal age, body mass index, gestational age, and underlying medical conditions may exert influence on shivering occurrence independent of the administered medications. Inadequate control of these variables could potentially obscure the true impact of the interventions and impede the generalization of the findings. Thus, future investigations must consider comprehensive adjustments for pertinent confounders to bolster the validity and robustness of the study outcomes.

Acknowledgment

We wish to express our heartfelt gratitude to our esteemed colleagues and authorities at Fatemieh Hospital, located in Hamadan City, Iran. Their invaluable insights and profound guidance have significantly contributed to the advancement of our research efforts. Their eloquent discourse and meticulous attention to detail have not only enriched scholarly discourse but also provided us with a steadfast direction throughout the execution and completion of our research project.

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Bull. Pharm. Sci., Assiut University, Vol. 47, Issue 2, 2024, pp. 1105-1117.

نشرة العلوم الصيدليـــة
جامعة أسيوط

BULL. PHARM. SCI. Assiut Univ.

مقارنة فاعلية اعطاء الميدازولام ،الميدازولام-كيتامين، والكيتامين عن طريق الوريد في تقليل انتشارالرعشة بعدالتخديرالشوكي: تجربة سريرية مزدوجة التعمية

نسيم عليبور[١] – ناهد منوشهريان[٢] – مريم عليقلي زاده[٣] – سيافاش سانجي[٣*]

[١] طالبة دكتوراه في التمريض، مركز أبحاث الطلاب، كلية التمريض والتوليد، جامعة كرمانشاه للعلوم الطبية، كرمانشاه، إيران

[٢] قسم التخدير، كلية الطب، جامعة همدان للعلوم الطبية، همدان، إيران

[٣] طالبة ماجستير في تعليم التخدير، قسم تكنولوجيا التخدير، كلية العلوم الطبية المتحالفة، جامعة إيران للعلوم الطبية، طهران، إيران

الخلفية : تشكل الرعشة بعد النخاع الشوكي تحديًا شائعًا بعد التخدير الشوكى ، مما يعرض المرضى لتجربة غير مرغوب فيها ومؤلمة، وقد تؤدي إلى مضاعفات مختلفة. هدفت هذه الدراسة إلى التحقق من فعالية الميدازولام والميدازولام-كيتامين والكيتامين عن طريق الوريد في الحد من حدوث الرعشة الشوكية.

الطرق والمواد: أجريت تجربة سريرية مزدوجة التعمية على ١٢٤ مريضة تتراوح أعمارهن بين ١٨ و٤٠ عامًا يخضعن لعملية قيصرية مع التخدير الشوكي في مستشفى فاطمية، همدان. تم إحداث التخدير الشوكي باستخدام ٠.٥٪ بوبيفاكائين (١٠ مجم) بالإضافة إلى ٢.٥ ميكروجرام سوفينتانيل. تم توزيع المرضى عشوائيًا على أربع مجموعات: ميدازولام ٠.٠٧٥ مجم / كجم (المجموعة أ)، كيتامين ٠.٥ مجم / كجم (المجموعة ب)، كيتامين ٠.٢٥ مجم / كجم بالإضافة إلى ميدازولام ٣٧.٥ ميكروجرام / كجم (المجموعة ج)، ومحلول ملحي عادي ٠.٩٪ (المجموعة د). تم تسجيل شدة الارتعاش والتأثيرات الديناميكية الدموية والغثيان والقيء وتشبع الأكسجين الشرياني والهلوسة والتخدير واستهلاك البيثيدين أثناء الجراحة والتعافي.

النتائج: شملت الدراسة ١٢٤ مشاركا في أربع مجموعات، مما يضمن التحليل الشامل دون حذف العينة. انخفض ضغط الدم الانقباضي بشكل ملحوظ بعد التخدير في جميع المجموعات($p \leq 0.05$) ، وكان ذلك واضحًا بشكل خاص في مجموعة الميدازولام-كيتامين. لوحظت انخفاضات مماثلة في ضغط الدم الانبساطي ومتوسط ضغط الدم الشرياني($p \leq 0.05$) ، مع أكبر انخفاض في مجموعة الميدازولام-كيتامين. كان ارتفاع معدل ضربات القلب بعد التخدير مهمًا فقط في مجموعة الميدازولام-كيتامين ($p \leq 0.05$). كان انخفاض تشبع الأكسجين مهمًا فقط في مجموعة الميدازولام-كيتامين ($p \leq 0.05$). كان ارتفاع درجة التخدير بعد التخدير مهمًا في جميع المجموعات($p \leq 0.05$) ، مع أعلى زيادة في مجموعة الميدازولام والكيتامين. لم تظهر شدة الارتعاش أي اختلافات كبيرة بين المجموعات. كان معدل حدوث

الهلوسة متشابهًا عبر المجموعات، بينما أظهر الكيتامين أعلى معدل حدوث للغثيان والقيء. لم يختلف استهلاك البيثيدين بشكل كبير بين المجموعات.

الخلاصة: قلل مزيج الميدازولام والكيتامين بشكل فعال من ضغط الدم، وزاد من درجات التخدير، وخفض مستويات تشبع الأكسجين، دون التأثير بشكل كبير على شدة الارتعاش أو استهلاك البيثيدين أثناء العمليات القيصرية تحت التخدير الشوكي.