ABENHA MEDICAL JOURNAL bmj
Print ISSN 1110-208X
Online ISSN 2357-0016

Original article

Aminophylline versus Ketamine in Prophylaxis Against Post-dural Puncture Headache in Pregnant Females Undergoing Cesarean Section: A Comparative Study

Marianne M. Youssef, Amr Y. Baz, Ahmed S. Khedr

Department of Anesthesia, Intensive Care and Pain Management, Cairo university , Egypt.

Corresponding to: Marianne M. Youssef, Department of Anesthesia, Intensive Care and Pain Management, Cairo university , Egypt.

Email:

mora.magdy.mm@gmail.com

Received: 5 February 2024

Accepted: 30 August 2024

Abstract

Background: Post-dural puncture headache (PDPH) is a leading cause of maternal comorbidity and dissatisfaction following spinal cesarean section (CS). **Objective:** This study aimed to evaluate the efficacy and safety of intravenous administration of aminophylline versus ketamine for the prevention of PDPH in patients scheduled for elective CS with spinal anesthesia. **Methods:** This double-blind, parallel-group, randomized trial recruited American Society of Anesthesiologists I-II adult parturients undergoing elective CS under spinal anesthesia. A total of 100 participants were randomized into two groups (50 participants each). Group A was treated with 1.5 mL/kg of intravenous aminophylline, while Group B was treated with 0.15 mg/kg of intravenous ketamine. The primary outcomes included the incidence and severity of PDPH. Secondary outcomes were the need for paracetamol and the incidence of nausea and vomiting, pruritus, and hypotension episodes. **Results:** Baseline characteristics between the two groups were not significantly different (all $p > 0.05$). Compared to group B, participants in group A had a lower incidence and severity of PDHD both intraoperatively and postoperatively at 2, 6, 12, and 24 hours, but without statistical significance (all $p > 0.05$). However, at 48 hours postoperatively, group A had significantly fewer patients with PDHD and lower pain severity than group B ($p = 0.022$ and 0.022, respectively). The need for paracetamol and the incidence of nausea and vomiting, pruritus, and hypotension were not statistically different between the groups (all $p > 0.05$). **Conclusion:** Administrating intravenous aminophylline or ketamine are effective and safe methods for reducing the incidence and severity of PDPH in women having elective CS under spinal anesthesia.

Keywords: Aminophylline, ketamine, post-dural puncture headache, spinal anesthesia

Introduction

Post-dural puncture headache (PDPH) is a frequently occurring delayed complication of spinal anesthesia. According to the International Classification of Headache Disorders criteria, PDPH is a type of headache that occurs within 5 days after a dural puncture and naturally fades within 1 week or 48 hours following an epidural blood patch. It can be linked to symptoms such as neck stiffness, tinnitus, sensitivity to light, and nausea (1).

The incidence of post-spinal anesthetic headache varies from 0.1% to 36%. The degree of variation depends on several factors, such as the patient's condition, injection technique, and study methodology (2,3). Parturients are highly susceptible to developing PDPH due to factors such as gender, youth, and frequent use of spinal anesthesia. This phenomenon can interfere with the mother's ability to nurture and breastfeed her newborn (3).

The pathophysiology of PDPH is not fully understood. Two interpretations have been proposed for PDPH, neither of which is certain. One theory suggests that PDPH is induced by the depletion of cerebrospinal fluid within the dura, resulting in a reduction in both cerebrospinal fluid volume and pressure. The absence of the cushioning effect typically provided by cerebrospinal fluid leads to tension on the pain-sensitive tissues within the skull, resulting in headache (4). The reduction in CSF volume can directly stimulate adenosine receptors, resulting in dilation of blood vessels in the brain and stretching of pain-related tissues, ultimately leading to PDPH (5). Another theory suggests that cerebral artery dilation occurs due to initial compensation for reduced intrahepatic cholestasis of pregnancy and loss of cerebrospinal fluid (3).

The rational for preventing PDPH is to minimize the loss of cerebrospinal fluid at the lumbar puncture site (6). Treatment for PDPH involves conservative approaches, including pain relievers and medications to reduce nausea and vomiting (7). Currently, theophylline, caffeine, sumatriptan and other methods are used to treat or prevent PDPH. However, none of these approaches have been proven to be effective thus far. Considering the potential challenges related to invasive

procedures, pharmaceutical medication may be a more advantageous alternative (8).

Aminophylline is frequently administered during anesthesia to manage bronchospasm. However, recent research suggests that it may also expedite recovery from general anesthesia (9). Prior studies have produced conflicting results regarding the impact of aminophylline on PDPH (10-12).

Ketamine is a noncompetitive inhibitor of N-methyl-D-aspartate receptors, producing analgesic, anti-inflammatory, and antihyperalgesic actions. It has gained a new position in postoperative pain management (13,14). Several placebo-controlled trials have demonstrated the efficacy of aminophylline or ketamine in preventing PDPH (14-17). However, no previous study has compared the efficacy of aminophylline and ketamine as premedication for cesarean section in preventing PDPH. This study aimed to evaluate the efficacy and safety of intravenous administration of aminophylline versus ketamine for the prevention of PDPH in women undergoing elective cesarean delivery with spinal anesthesia.

Patient and Methods

Ethical considerations

The Ethics Committee of the Faculty of Medicine at Cairo University, Egypt, approved this study. Informed consent was obtained in writing from all subjects. The study was submitted, and the trial was registered at Clinical Trials.gov (Trial ID: MS-166-2020). We ensured the confidentiality of all participants' information.

Study design, setting, and date

This double-blinded, parallel-group, randomized, controlled clinical trial was conducted at the Obstetrics and Gynecology Hospital, Cairo University, Egypt between December 2019 and September 2020.

Eligibility criteria

The study enrolled 100 full-term pregnant women undergoing elective cesarean section and classified as American Society of Anesthesiologists (ASA) physical status I or II. Women with a history of migraine headache, gestational hypertension, cardiac morbidity, baseline systolic blood pressure below 100 mm Hg, contraindicated regional anesthesia, or multiple previous attempts were excluded.

Randomization, allocation concealment, and blinding

One hundred parturients were randomized into two groups A and B (50 participants each) via a computer-generated table. The randomization sequence was hidden using sealed opaque envelopes (18). To ensure a double-blinded study, one investigator coded the administered drugs according to the computer-based system, while another investigator observed and collected the data**.**

Interventions

After stabilization of spinal anesthesia at the T4 sensory level and approximately 5 minutes before surgery, participants in group A received 1.5 mg/kg intravenous aminophylline, while those in group B received 0.15 mg/kg intravenous ketamine.

Preoperative preparation

In the operating room, all patients were cannulated using an 18-gauge venous cannula. Prior to administering spinal anesthesia, a preload of Ringer's acetate solution at a rate of 10 mL/kg was given.

A comprehensive monitoring system was installed, involving a non-invasive blood pressure monitor, pulse oximeter, and electrocardiography. The patient received spinal anesthesia in a seated position. A 25- gauge Quincke spinal needle was used to administer the spinal anesthetic, injecting a total volume of 2 mL, consisting of 10mg of bupivacaine and 25 ug of fentanyl. After administering spinal anesthesia, the patient was positioned in the supine posture with the pelvis tilted to the left lateral position.

The efficacy of the block was evaluated through pinprick assessment, and participants who experienced block failure were excluded from the study. This failure referred to the inability to maintain satisfactory surgical conditions, maternal comfort and satisfaction during a cesarean section, regardless of whether it necessitated a conversion to general anesthesia.

Measurement tools

Post-dural puncture headache was evaluated by directly asking patients about the presence of any headache during and after surgery. The patient's evaluation was conducted every 6 hours over a 48-hour period. Patients were instructed to remain seated in bed for 5 minutes and then asked about any headaches. Post-dural

puncture headache was characterized by a dull, pulsating pain in the front and back of the head. The headache typically worsened when sitting or standing and improved when lying down. If the headache did not have a postural component, it was necessary to question the diagnosis. The patient experienced some relief, at least partially, when lying down in the supine posture. Patient assessments were conducted every 6 hours for 48 hours by the Wong-Baker Faces Pain Rating Scale. The initial face corresponds to a pain rating of 0, signifying the absence of any discomfort. The second facial expression corresponds to a pain rating of 2, indicating 'mild discomfort.' The third facial expression corresponds to a pain rating of 4, indicating 'slightly more painful.' The fourth facial expression corresponds to a pain rating of 6, indicating a heightened level of discomfort. The fifth facial expression corresponds to a pain rating of 8, indicating a significant level of discomfort. Conversely, the sixth facial expression corresponds to a pain rating of 10, indicating "hurts worst" (19). Patients with PDPH were treated with intravenous paracetamol (15 mg/kg/dose).

Patients were scored on a three-point scale for presence of postoperative nausea/vomiting: 0 indicated the absence of nausea or vomiting, 1 indicated the presence of nausea only, and 2 indicated the presence of both nausea and vomiting.

To evaluate intraoperative hypotension, defined as a reduction in systolic blood pressure of 20% or less than 100 mmHg from the time of spinal anesthesia to delivery of the fetus, a single intravenous bolus of 15 mg ephedrine was administered. Intraoperative bradycardia, defined as a heart rate less than 55 beats/minute, was treated with intravenous atropine at a dose of 0.5 mg. The study recorded the frequency and severity of hypotensive episodes. After delivery, patients received a single intravenous dosage of 5 IU of oxytocin, then a continuous infusion of 10 IU over 15 minutes.

Study outcomes

The primary outcomes included the incidence and severity of PDPH. Secondary outcomes involved paracetamol need, incidence of nausea

and vomiting, pruritus, and hypotension episodes.

Sample size

The sample size was determined using MedCalc software version 14 (MedCalc software bvba, Ostend, Belgium) and was 45 pregnant women in each group. This sample size was large enough to detect a 27% difference in the risk of PDPH after cesarean section as estimated by Naghibi et al. (20), with a 95% confidence level and 80% power. This number was increased by 10% to account for possible dropouts, and the final calculated sample size per group was 50 pregnant women (total sample size = 100).

Statistical analysis

Statistical analysis was conducted via the statistical package for the social sciences software program, IBM SPSS Statistics for Windows, version 27 (IBM Corp., Armonk, N.Y., USA). Categorical data was presented as frequencies (%). Continuous data was presented as mean ± SD or median and range. Unpaired t-test, Mann-Whitney test, Chi-square test, and Fisher's Exact test were utilized as appropriate. Repeated measures ANOVA test was applied to examine the changes over time within each group. The significance level was determined at $p < 0.05$.

Results

One hundred and six patients were assessed for eligibility and six were declined due to difficulties with spinal anesthesia and conversion to general anesthesia. The remaining 100 parturients were randomized into two groups (50 participants each). Group A received aminophylline, while Group B received ketamine (Figure 1).

Baseline characteristics including age, weight, height, volume of local anesthetic used, and ASA physical status did not differ significantly between groups ($p = 0.802$, 0.445, 0.969, 1.000, and 0.678, respectively; Table 1).

Compared to group B, participants in group A had a lower incidence of PDHD both intraoperatively and postoperatively at 2, 6, 12, and 24 hours, but without statistical significance ($p = 0.218$, 0.790, 0.444, 0.183, and 0.766, respectively). However, at 48 hours postoperatively, group A had significantly fewer patients with PDHD compared to group B ($p = 0.022$). The incidence of

PDPH was 22% in group A and 26% in group B, without statistical difference (p=0.640) (Table 2).

Table 3 displays the intraoperative and postoperative evaluation of PDPH severity via the Wong Baker Faces Pain Rating Scale. Both groups had comparable headache severity both intraoperatively and at 2, 6, 12, and 24 hours after delivery, with no statistical differences (all $p > 0.05$). However, at 48 hours postoperatively, group A patients experienced less severe headaches than group B patients ($p = 0.022$).

Over the 48 postoperative hours, the severity scores significantly decreased in groups A and B ($p = 0.020$ and < 0.001, respectively). The median number of headache episodes in 48 hours was similar in the two groups ($p = 1$).

Table 4 shows comparable need for paracetamol, incidence of nausea and vomiting, postoperative pruritus, and hypotension episodes between the study groups ($p = 0.749$, 0.631, 0.779, and 0.677; respectively).

Table 1. Participants' characteristics

		Group A (n = 50)	Group B (n = 50)	P value
Age, year, Mean±SD		27.9±4.4	28.2±4.4	0.802
Weight, kg, Mean±SD		80.2±12.7	78.2±13.1	0.445
Height, cm, Mean±SD		161.5±4.4	161.4±5.8	0.969
Volume of local anesthetic, mL, Mean±SD		2.6±0.1	2.6±0.1	1.000
ASA physical status, n (%)	**I**	48 (96%)	46 (92%)	0.678
	II	2 (4%)	4 (8%)	

SD: standard deviation; n: numbers; ASA: American Society of Anesthesiologists

Table 2. Post-dural puncture headache

PDPH, n (%)		Group A (n=50)		Group B (n=50)		p value
		n	**%**	**n**	**%**	
Intra-operative	**No**	46	92.0	42	84.0	0.218
	Yes	4	8.0	8	16.0	
After 2 hours	**No**	42	84.0	41	82.0	0.790
	Yes	8	16.0	9	18.0	
After 6 hours	**No**	42	84.0	39	78.0	0.444
	Yes	8	16.0	11	22.0	
After 12 hours	**No**	44	88.0	39	78.0	0.183
	Yes	6	12.0	11	22.0	
After 24 hours	**No**	44	88.0	43	86.0	0.766
	Yes	6	12.0	7	14.0	
After 48 hours	**No**	50	100.0	45	90.0	0.022*
	Yes	0	0.0	5	10.0	
Total number of patients with PDPH	**No**	39	78.0	37	74.0	0.640
	Yes	11	22.0	13	26.0	

PDPH: post-dural puncture headache; SD: standard deviation; n: numbers; *: Significant at $p < 0.05$

Table 3. Severity of pain according to Wong Baker Faces Pain Rating Scale

Severity of pain, median (Min-Max)	Group A (n = 50)	Group B (n = 50)	p value
Intra-operative	0 (0-6)	0 (0-10)	0.224
After 2 hours	0 (0-5)	0 (0-8)	0.650
After 6 hours	0 (0-5)	0 (0-8)	0.386
After 12 hours	0 (0-5)	0 (0-7)	0.159
After 24 hours	0 (0-2)	0 (0-5)	0.680
After 48 hours	0 (0-0)	0 (0-4)	0.022*
p value	0.020*	<0.001*	
Number of episodes of headache in 48 hours	2 (1-4)	2 (1-4)	1

Min: minimum; Max: maximum; n: numbers *: Significant at $p < 0.05$

Table 4. Paracetamol need and intra-operative and postoperative complications

		Group A (n = 50)		Group B (n = 50)		p value
		n	**%**	**n**	**%**	
Paracetamol need, n (%)	**No**	44	88.0	45	90.0	0.749
	Yes	6	12.0	5	10.0	
Nausea and vomiting, n (%)	**0**	38	76.0	34	68.0	0.631
	1	3	6.0	5	10.0	
	2	9	18.0	11	22.0	
Pruritus, n (%)	**No**	43	86.0	42	84.0	0.779
	Yes	7	14.0	8	16.0	
Hypotension episode, n (%)	**No**	33	66.0	31	62.0	0.677
	Yes	17	34.0	19	38.0	
	Once	12	24.0	14	28.0	
	Twice or more	5	10.0	5	10.0	

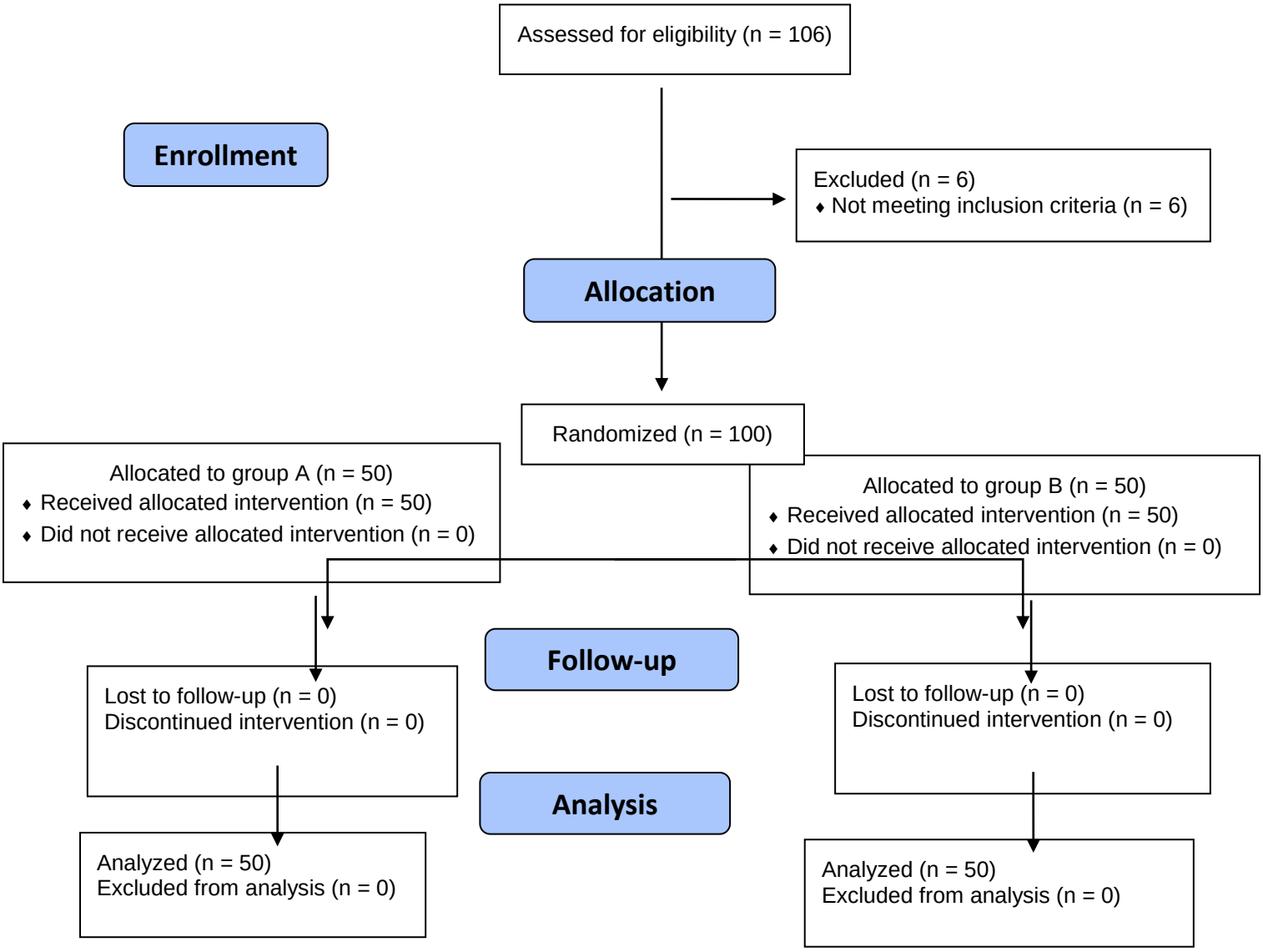

Figure 1. The CONSORT flow diagram of the trial

Discussion

Post-dural puncture headache is a widespread distressing delayed sequela that can occur after spinal anesthesia. It is one of the main causes of maternal comorbidity resulting from medical procedures and can contribute to maternal dissatisfaction. This research aimed to assess the efficacy and safety of intravenous administration of aminophylline or ketamine for the prevention of PDPH in parturient having elective cesarean delivery with spinal anesthesia. The study's main findings indicated that intravenous administration of aminophylline or ketamine effectively reduced pain incidence and severity without significant adverse effects.

Several studies have investigated the use of aminophylline or ketamine to prevent and treat PDPH. In a study by Ghanei et al. (21) on females who underwent spinal anesthesia during cesarean section, intravenous aminophylline was found to be a more effective method for reducing headache compared to placebo. Yang et al. (16) reported similar results following cesarean delivery using combined spinal-epidural anesthesia, without any adverse effects. Sadeghi et al. (22) administered 1 mg/kg aminophylline immediately after infant birth and umbilical cord clamping. The researchers found that aminophylline reduced the incidence of headache within 24 to 48 hours. In their study of lower extremity surgery with spinal anesthesia, Naghibi and Hamidi (20) found that combining aminophylline and dexamethasone effectively reduced the occurrence of PDPH. The incidence of PDPH significantly decreased from 42.5% to a range of 5-20% within 6-48 hours after surgery.

In a recent systematic review, Barati-Boldaji et al. (23) found that theophylline and aminophylline have therapeutic but not preventive effects after the onset of PDPH. In another meta-analysis, Hung et al. (24) found no preventive benefit of aminophylline against PDPH in full term pregnant who underwent cesarean delivery under spinal anesthesia. However, no subgroup analysis was performed to evaluate the influence of various criteria, such as study quality, on the results. In a retrospective study, Sirit et al. (12) found that the administration of intravenous aminophylline during spinal anesthesia did not impact the occurrence of PDPH in cesarean delivery. The researchers explained that this is due to the temporary

pharmacological effect in preventing PDPH, and therefore cannot influence its development. Furthermore, Dehghanpisheh et al. (25) reported that aminophylline did not decrease the incidence or intensity of PDPH when compared to ondansetron.

The mechanism underlying the potential benefits of aminophylline is still a topic of debate. It is believed that aminophylline can alleviate pain associated with PDPH by causing vasoconstriction inhibiting endothelial sarcoplasmic reticulum calcium uptake. Aminophylline also counteracts the function of adenosine, causing the contraction of blood vessels within the skull (22). It also stimulates the secretion of cerebrospinal fluid by activating sodium and potassium pumps and hinders the transmission of pain signals (15).

Ketamine is a derivative of phencyclidine with a rapid onset of action (26). It is the only intravenous anesthetic medication with analgesic properties. Ketamine exerts its analgesic action by inhibiting N-methyl-D aspartate receptors at low doses (0.1 - 0.8 mg/kg). This inhibition prevents the transmission of pain signals in the central nervous system, which may be beneficial in preventing headaches caused by dura perforation (27). Ketamine has been suggested as a potential countermeasure to reduce the intracranial pressure associated with PDPH. This is achieved by slightly increasing the pressure inside the skull (28).

Zangouei et al. (14) demonstrated that administering ketamine as a premedication during cesarean section can reduce the intensity of postoperative headache. Similarly, Sen et al. (29) reported that ketamine reduced the discomfort and suffering in the first days after spinal anesthesia following surgery. Moradi Farsani et al. (30) discovered that in deep vitrectomy surgery, the use of ketamine or paracetamol effectively reduced pain intensity compared to aminophylline and placebo, without causing significant adverse hemodynamic changes.

The current study reported no adverse reactions to aminophylline or ketamine. Likewise, Yang et al. (16) proposed a dose of 250 mg of aminophylline with minimal adverse effects. Aminophylline can be given to women who have recently given birth

without interfering with breastfeeding. Zangouei et al. (14) showed that ketamine effectively reduced the incidence of pruritus from 50% to 18.5% immediately after surgery, with a slight decrease in the incidence of nausea. In a systematic review, Bell et al. (31) found that ketamine had a positive effect on reducing postoperative nausea and vomiting. Behdad et al. (26) demonstrated that the use of ketamine did not result in significant harmful effects and was well tolerated by patients. Though, Song et al. (32) declared that the administration of ketamine to patients not only failed to decrease the occurrence of nausea and vomiting but also resulted in an increase in both the rate and intensity of these symptoms. Nausea and vomiting can cause stress for patients, surgeons, and anesthesiologists, leading to distress, repulsion, heightened anxiety, and reduced efficiency. If persistent, the use of this medication can even lead to hypotension and bradycardia (33,34). Therefore, it was critical to monitor for these adverse effects.

This study is the initial randomized study to evaluate the effects of aminophylline versus ketamine in parturients scheduled for elective cesarean delivery. The results of this study could benefit a wide range of obstetric populations by improving post-delivery activity and preventing unplanned expenses.

Limitation

The study is limited by the lack of measurement of confounding variables, such as maternal parity, serum hemoglobin and hematocrit levels, and neonatal Apgar scores. In addition, this was a single-center, tertiary hospital study that involved only elective cesarean sections. In addition, the optimal timing of drug administration was not clearly defined. Several anesthesiologists performed spinal anesthesia. However, we attempted to standardize the inclusion criteria by excluding cases of multiple punctures and needle redirection.

Conclusion

In elective cesarean section with spinal anesthesia, the intravenous administration of aminophylline or ketamine effectively and safely reduces the incidence and severity of PDPH.

References

1. Kuczkowski KM. Post-dural puncture headache in the obstetric patient: an old problem. New solutions. Minerva Anestesiol. 2004;70:823-30.

2. Olesen J. The international classification of headache disorders. 2nd edition (ICHD-II). Rev Neurol (Paris). 2005;161:689-91.

3. Kwak KH. Postdural puncture headache. Korean J Anesthesiol. 2017;70:136-43.

4. Morewood GH. A rational approach to the cause, prevention and treatment of postdural puncture headache. Cmaj. 1993;149:1087-93.

5. Grant R, Condon B, Hart I, Teasdale GM. Changes in intracranial CSF volume after lumbar puncture and their relationship to post-LP headache. J Neurol Neurosurg Psychiatry. 1991;54:440-2.

6. Ahmed SV, Jayawarna C, Jude E. Post lumbar puncture headache: diagnosis and management. Postgrad Med J. 2006;82:713-6.

7. Zajac K, Zajac M, Hładki W, Jach R. [Is there any point in pharmacological prophylaxis of PDPH (post-dural puncture headache) after spinal anaesthesia for Caesaren section?]. Przegl Lek. 2012;69:19-24.

8. Kleine-Brüggeney M, Kranke P, Stamer UM. [Prophylaxis and therapy of postdural puncture headache--a critical evaluation of treatment options]. Anasthesiol Intensivmed Notfallmed Schmerzther. 2011;46:516-24.

9. Hüpfl M, Schmatzer I, Buzath A, Burger H, Hörauf K, Ihra G, et al. The effects of aminophylline on bispectral index during inhalational and total intravenous anaesthesia. Anaesthesia. 2008;63:583-7.

10. Saafan A, Zaki M, Ghaly SI, Youssef AMA. A comparative study between the effect of Aminophylline, Neostigmine and Gabapentin on prevention of post dural puncture headache after cesarean section. QJM. 2021.

11. Saafan AAE, Mahmoud Zaki MS, Ghaly SI, Ahmed Youssef AM. A comparative study between the effect of Aminophylline, Neostigmine and Gabapentin on prevention of post dural puncture headache after cesarean section. QJM: An International Journal of Medicine. 2021;114.

12. Sirit I, Ibrahim O, Dilek Y. Aminophylline does not Prevent Postdural Puncture Headache in Caesarean Section. International Journal of Anesthetics and Anesthesiology. 2015;2:031.

13. Zaman B, Hojjati Ashrafi S, Seyed Siamdoust S, Hassani V, Mohamad Taheri S, Noorizad S. The Effect of Ketamine and Dexamethasone in Combination with Lidocaine on the Onset and Duration of Axillary Block in Hand and Forearm Soft Tissue Surgery. Anesth Pain Med. 2017;7:e15570.

14. Zangouei A, Zahraei SAH, Sabertanha A, Nademi A, Golafshan Z, Zangoue M. Effect of Low-Dose Intravenous Ketamine on Prevention of Headache After Spinal Anesthesia in Patients Undergoing Elective Cesarean Section: A Double-Blind Clinical Trial Study. Anesthesiology and pain medicine [Internet]. 2019 2019/12//; 9(6):[e97249 p.].

15. Wu C, Lian Y, Guan D, Wang L, Miao Y, Xie N, et al. A Multicenter Clinical Study on Treating Post-Dural Puncture Headache with an Intravenous Injection of Aminophylline. Pain Physician. 2016;19:E761-5.

16. Yang CJ, Chen T, Ni X, Yu WY, Wang W. Effect of pre-administration with aminophylline on the occurrence of post-dural puncture headache in women undergoing caesarean section by combined spinal-epidural anaesthesia. J Int Med Res. 2019;47:420-6.

17. Safarpour AR, Mehrabi M, Tarkesh F, Ashrafizadeh H, Keshtkar A, Askari H, et al. Aminophylline for Prevention and/or Treatment of Post-Dural Puncture Headache: A Systematic Review and Meta-Analysis Study Protocol. Anesth Pain Med. 2021;11:e119674.

18. Doig GS, Simpson F, Delaney A. A review of the true methodological quality

of nutritional support trials conducted in the critically ill: time for improvement. Anesth Analg. 2005;100:527-33.

19. Wong D, Baker C. Smiling face as anchor for pain intensity scales. Pain. 2001;89:295-7.

20. Naghibi K, Hamidi M. Prophylactic administration of aminophylline plus dexamethasone reduces post-dural puncture headache better than using either drug alone in patients undergoing lower extremity surgery. Adv Biomed Res. 2014;3:5.

21. Ghanei M, Sahraei R, Zabetian H, Radmehr M, Sotoodeh jahromi A, Ghobadifar MA, et al. Intravenous Aminophyline Prevents Post Dural Puncture Headache In Women Undergoing Cesarean Section: A Randomized Placebo-Controlled Trial. Revista Kasmera. 2015;43:305-19.

22. Sadeghi S, Gholamreza A, Narjes Al-sadat N, Mehrabi M, Safarpour A. Effectiveness of Single Dose Intravenous Aminophylline Administration on Prevention of Post Dural Puncture Headache in Patients Who Received Spinal Anesthesia for Elective Cesarean Section. World Journal of Medical Sciences. 2013;7:13-6.

23. Barati-Boldaji R, Shojaei-Zarghani S, Mehrabi M, Amini A, Safarpour AR. Post-dural puncture headache prevention and treatment with aminophylline or theophylline: a systematic review and meta-analysis. Anesth Pain Med (Seoul). 2023;18:177-89.

24. Hung K-C, Ho C-N, Chen IW, Hung IY, Lin M-C, Lin C-M, et al. The impact of aminophylline on incidence and severity of post-dural puncture headache: A meta-analysis of randomised controlled trials. Anaesthesia Critical Care & Pain Medicine. 2021;40:100920.

25. Dehghanpisheh L, Bayani S, Azemati S, Rakhshan M. The effect of intravenous administration of ondansetron compared toaminophylline on incidence and severity of post-dural puncture headache(PDPH) in cesarean section surgeries. Biomedical Research. 2019;30:1-6.

26. Behdad S, Hajiesmaeili MR, Abbasi HR, Ayatollahi V, Khadiv Z, Sedaghat A. Analgesic Effects of Intravenous Ketamine during Spinal Anesthesia in Pregnant Women Undergone Caesarean Section; A Randomized Clinical Trial. Anesth Pain Med. 2013;3:230-3.

27. Han SY, Jin HC, Yang WD, Lee JH, Cho SH, Chae WS, et al. The Effect of Low-dose Ketamine on Post-caesarean Delivery Analgesia after Spinal Anesthesia. Korean J Pain. 2013;26:270-6.

28. Klimek M, Rossaint R, van de Velde M, Heesen M. Combined spinal-epidural vs. spinal anaesthesia for caesarean section: meta-analysis and trial-sequential analysis. Anaesthesia. 2018;73:875-88.

29. Sen S, Ozmert G, Aydin ON, Baran N, Caliskan E. The persisting analgesic effect of low-dose intravenous ketamine after spinal anaesthesia for caesarean section. Eur J Anaesthesiol. 2005;22:518-23.

30. Moradi Farsani D, Nikkhoo I, Rafiee Zadeh A, Nourian N, Montazeri K. Effect of aminophylline, ketamine and paracetamol on pain intensity after deep vitrectomy surgery. Int J Physiol Pathophysiol Pharmacol. 2022;14:289-95.

31. Bell RF, Dahl JB, Moore RA, Kalso E. Perioperative ketamine for acute postoperative pain. Cochrane Database Syst Rev. 2006:Cd004603.

32. Song JW, Shim JK, Song Y, Yang SY, Park SJ, Kwak YL. Effect of ketamine as an adjunct to intravenous patient-controlled analgesia, in patients at high risk of postoperative nausea and vomiting undergoing lumbar spinal surgery. Br J Anaesth. 2013;111:630-5.

33. Pierre S, Whelan R. Nausea and vomiting after surgery. J Continuing Education in Anaesthesia, Critical Care Pain and Therapy. 2013;13:28-32.

34. Bantie AT, Woldeyohannes M, Ferede ZA, Regasa BA. Magnitude and associated factors of nausea and vomiting after ce-sarean section under spinal anesthesia in Gandhi memorial Hospi-tal, Addis Ababa, Ethiopia. A cross-sectional study. Afr J Health Sci Med. 2020;3.

To cite this article: Marianne M. Youssef, Amr Y. Baz, Ahmed S. Khedr. Aminophylline versus Ketamine in Prophylaxis Against Post-dural Puncture Headache in Pregnant Females Undergoing Cesarean Section: A Comparative Study. BMFJ 2024;41(8): 427-441