OPEN ACCESS

ORIGINAL ARTICLE

Comparison of Effect of Prophylactic Aminophylline, Dexamethasone and Placebo in Prevention of Post Dural Puncture Headache

Sehrish Mehmood[1], Yasmeen Afridi[2], Farah Naz[3], Rana Imran Sikandar[4], Suresh Kumar[5], Naheed Fatima[6]

[1]Resident, Department of Anesthesia, Pakistan institute of medical Sciences, Islamabad
[2] Associate Professor, Department of Anesthesia, Pakistan Institute of Medical Sciences, Islamabad
[3] Associate Professor, Department of Anesthesia, Pakistan Institute of Medical Sciences, Islamabad
[4]Professor of Anaethesia, Department of Anaesthesia and Critical Care, Pakistan Institute of Medical Sciences, Islamabad
[5]Associate Professor, Department of Anaesthesia and Critical Care, Pakistan Institute of Medical Sciences, Islamabad
[6]Professor, Department of Anesthesia, Pakistan Institute of Medical Sciences, Islamabad

Correspondence:

Dr. Sehrish Mehmood
sehrish51@outlook.com

Abstract

Objective: To compare the preventive effect of prophylactic aminophylline, dexamethasone and placebo in the prevention for postdural puncture headache in adult patients undergoing below umbilicus surgery.

Material and Methods: This randomized clinical trial was done at department of anesthesia and Critical care at PIMS hospital, Islamabad from January 2018 to June 2018. Adult cases of 18 -45 years of both genders undergoing below umbilicus surgery were included. All the patients were divided in 3 groups. Group A (Aminophylline) patients received 1.5 mg/kg of IV Aminophylline over 10 minutes, group B (Dexamethasone) patients received 0.1 mg/kg of IV Dexamethasone whereas group C (Placebo) patients received IV saline, 15 minutes before the end of the surgery. The frequency of post dural puncture headache along with complications of therapy was noted at 24 hours and 48 hours of surgery and compared in all three groups. Chi-square test was employed to compare the occurrence of PDPH in all three groups and P-value ≤0.05 was considered as significant.

Results: At 24 hours headache was present in 2% of patients in group A, 2% in group D and 10.8% of patients in group P. The frequency of headache was similar in group A and D, but was significantly lesser than placebo group (P = 0.003) at 2 hours. At 48 hours no patient in group A reported headache while headache was present in 7.8% (n=8) of patients in group B and 12.7% (n=13) of patients in group C. The frequency of headache was significantly lesser in group A as compared to group B and C (P = 0.001).

Conclusions: Post-dural puncture headache observed to the significantly lesser in patients treated with Aminophylline and Dexamethasone compared to placebo group at 24 hours, while headache was significantly lesser in patients treated with Aminophylline as compared to Dexamethasone and Placebo group.

Keywords: Aminophylline, Dexamethasone, Post-dural puncture headache

Cite this article: Mehmood S, Afridi Y, Naz F, Sikandar RI, Kumar S, Fatima N. Comparison of Effect of Prophylactic Aminophylline, Dexamethasone and Placebo in Prevention of Post Dural Puncture Headache. BMC J Med Sci. 2023. 4(1): 7-11

Introduction

Postdural puncture headache is the most common side effect that occurs in obstetric patients after receiving a spinal or epidural anaesthesia.[1] The prevalent rate of postdural puncture headache has been reported between 2.8% and 8.7% among patients who received spinal anesthesia, and as high as 59% in those receiving epidural treatments for analgesia that resulted in an unplanned dural puncture.[2] A patient complaint usually starts within two days and headache is debilitating and severe, leading to limitation of routine work.[3] Different mechanisms are responsible for causing PDPH but etiology of PDPH is not well known. The CSF leakage through the puncture of dura mater after the intervention

Authorship Contribution: [1,5]Substantial contributions to the conception or design of the work; or the acquisition, Data analysis, Literature review, [2,3]Drafting the work or revising it critically for important intellectual content, [4,6]Final approval of the version to be published & Supervision

Funding Source: none
Conflict of Interest: none

Received: Oct 22, 2022
Accepted: Feb 30 , 2023

is held responsible of it, which often leads to distention of intracranial vessels and increase in brain blood flow causes PDPH.[4] Many factors are responsible for increased PDPH incidence including female gender, younger age, nonsmoking, greater puncture frequency, pregnancy, larger size needle, lower body mass index (BMI), taller height, history of headache due to migraine, using catheter for continuous spinal anesthesia and needle level not parallel with neuraxial longitudinal axis.[5]

Lots of pharmacological, interventional and conservative measures have been taken to decrease the incidence of PDPH for example modification in needle size and tip has markedly decreased the incidence of PDPH. Blood patch has high cure rate.[6] Many preventive measures are present for PDPH with varying efficacy and safety. A study by Doroudian et al witnessed occurrence of PDPH in 10/178 (5.6%) cases treated with dexamethasone.[7]

Similarly, a study by Sadeghi et al witnessed 3/14 of a total of 120 patients (5% vs. 23.3%) patients suffering from PDPH after aminophylline intervention as preventive measure as compared to the control group which is significant statistically.[8] An international study reported that there was significantly higher incidence of PDPH in dexamethasone group and aminophylline group compared to aminophylline plus dexamethasone group.[3]

On the other hand Another study by Sirit I et al witnessed that aminophylline did not differ with control in preventing PDPH incidence.[9] The previous scientific evidence on aminophylline and dexamethasone regarding the prevention of PDPH is controversial and not clearly mention the superiority of one drug over another. Locally, in our healthcare setting, the issue of PDPH has not been studied in terms of preventive measures. The situation demands quantification of the current status of PDPH and to find out ways to prevent it. The present study aims to compare the prophylactic effect of aminophylline and dexamethasone compared with placebo (normal saline) in prevention of Post dural puncture headache and to improve post-operative quality of life of these patients.

Material and Method

This randomized control trial (3 arm study), was done at department of anesthesia and critical care at PIMS hospital, Islamabad from January 2018 to June 2018 after taking ethical clearance from the institutional review board (IRB). All the adult cases of 18 -45 years of both genders undergoing below umbilicus surgery were included. Patients who failed spinal anesthesia and required general anesthesia, patients who had any allergic effects of aminophylline or dexamethasone, history of any kind of headache, patients who often consumed analgesic or who had a medication history like aminophylline and those who underwent combined spinal-epidural anesthesia were excluded. Non-probability-consecutive sampling was used. All patients presenting in the operation theater for lower surgeries were asked for participation in the study after explaining the purpose and benefits of the trial. A written informed consent was administered and those agreeing were selected. Patients were randomly (using lottery method) assigned to receive either prophylactic aminophylline, dexamethasone or placebo. The purpose of random sampling was to reduce the chances selection or confounding bias in the study.

The standardized procedure of spinal anesthesia was followed, where patients were infused anesthetic agent in the lumbar sacral region. In group A (Aminophylline) patients received 1.5 mg/kg of IV aminophylline over 10 minutes. In group D (dexamethasone) the patients received 0.1 mg/kg of IV dexamethasone whereas in group P (placebo) patients received IV saline, 15 minutes before the end of the surgery. All the study related procedures and data collection was conducted by the researcher herself to reduce selection bias and to maintain data quality and continuity. The patients were closely followed for 48 hours after surgery. The frequency of post dural puncture headache was noted at 24 hours and finally after 48 hours of surgery. All the information was recorded on a specifically designed structured proforma, including demographic characteristics, BMI, type of surgery, and headache. Data was entered and analyzed in SPSS software version 26.0.

Results

A total of 306 adult patients were enrolled in the study. In group A there were 50.0% males and 50.0% females, in group D 41.2% were males and 58.8% were females and in group P, males were 47.1% and 52.9% were females (P=0.475). 78(76.5%) patients were overweight in group A, 70(68.6%) patients were overweight in group D and 73(71.6%) patients were overweight in group P (p=0.450). In all the three groups, 49% (n=50) underwent gynecological surgeries, 25.5 % (n=26) underwent general surgeries, 9.8% (n=10) underwent orthopedic surgeries and 15.7% (n=16) underwent urological surgeries (P=1.0). Table I

The treatment with aminophylline and dexamethasone was well tolerated, and there were no significant side effects reported in group A and D as compared to placebo group. Nausea and vomiting were the most frequent side effect reported in all groups (4.9% in group A, 9.8% in group D and 7.8.4% in group P, (P=0.621). Overall efficacy of treatment was measured in terms frequency of post dural puncture headache at 24 hours and 48 hours after surgery. At 24 hours headache was significantly lower in group A (2%) and in group D (2%) compared to group P (10.8%) (P= 0.003). At 48 hours no patient in group A reported headache while headache was present in present in 7.8% (n=8) of patients in group D, 12.7% (n=13) of patients in group P. The frequency of headache was significantly lesser in group A as compared to group D and P (P = 0.001). Table. II

Discussion

Post-dural puncture headache (PDPH) is the most frequently encountered complication of spinal anaesthesia.[10,11] Many preventive measures are present for PDPH with varying efficacy and safety. The present study was designed to compare two different types of treatments (aminophylline and dexamethasone in comparison with placebo) for prevention of PDPH in our population. The frequency of post-dural puncture headache was recorded and compared in all three groups at 24 and 48 hours after surgery. At 24 hours the frequency of headache was similar in group A and D, however, it was significantly lesser than in placebo group (P = 0.003). At 48 hours the frequency of headache was significantly lesser in group A as compared to group D and P (P = 0.001). The treatment with aminophylline and dexamethasone was well tolerable and there were no significant side effects reported in group A and D as compared to placebo group. There are not many studies found in the literature evaluating and comparing the efficacy of aminophylline and dexamethasone in a head-to-head fashion. In a quite similar study, Naghibi K et al[2], evaluated the effects of combining administration of I/V aminophylline and dexamethasone on PDPH in patients

Table I: Demographic profile of the study population (n=306)

Variables		Study groups			P-value
		Aminophylline	Dexamethasone	Placebo	
Age groups	18-30 years	42(41.2%)	41(40.2%)	44(43.1%)	0.910
	> 30 years	60(58.8%)	61(59.8%)	58(56.9%)	
	Total	102(100.0%)	102(100.0%)	102(100.0%)	
Gender	Males	51 (50.0%)	42(41.2%)	48(47.1%)	0.475
	Females	51(50.0%)	60(58.8%)	54(52.9%)	
	Total	102(100.0%)	102(100.0%)	102(100.0%)	
BMI Kg/m^2	<30 Kg/m^2	24(23.5%)	32(31.4%)	29(28.4%)	0.450
	≥30 Kg/m^2	78(76.5%)	70(68.6%)	73(71.6%)	
	Total	102(100.0%)	102(100.0%)	102(100.0%)	
Types of surgeries	Gynae/OBS	50(49.0%)	50(49.0%)	50(49.0%)	1.00
	General surgery	26(25.5%)	26(25.5%)	26(25.5%)	
	Ortho	10(9.8%)	10(9.8%)	10(9.8%)	
	Urology	16(15.7%)	16(15.7%)	16(15.7%)	
	Total	102(100.0%)	102(100.0%)	102(100.0%)	

Table II: Comparison of headache at 24 hours and at 48 hours in all groups (n=306)

Variables		Study groups			P-value
		Aminophylline	Dexamethasone	Placebo	
Headache at 24 hours	Present	2(2.0%)	2(2.0%)	11(10.8%)	0.003
	Absent	100(98.0%)	100(98.0%)	91(89.2%)	
	Total	102(100.0%)	102(100.0%)	102(100.0%)	
Headache at 48 hours	Present	--	8(7.8%)	13(12.7%)	0.001
	Absent	102(100.0%)	94(92.2%)	89(87.3%)	
	Total	102(100.0%)	102(100.0%)	102(100.0%)	

who were undergoing lower extremity surgery and compared using either drug alone and also with placebo.

They included 140 patients and randomized them into four groups and they found that patients in aminophylline 1.5 mg/kg plus dexamethasone 0.1 mg/kg (AD group) had significantly lower incidence of PDPH ($P < 0.05$) and furthermore, they concluded that combined administration of aminophylline 1.5 mg/kg plus dexamethasone 0.1 mg/kg significantly reduced PDPH better than using either drug alone in patients who underwent lower extremity surgery under spinal anesthesia.[3] The results with aminophylline and dexamethasone when used alone were similar to the present study results. In the comparison of this study, Ona BX et al[12], in their systematic review evaluated the efficacy and safety of different drugs being used in the prevention of PDPH and they demonstrated that use of I/V aminophylline resulted in reduction in the number of patients affected by PDPH of any severity after a lumbar puncture when compared to control group. The results are similar to the present study's result, where we also found that at 48 hours after surgery, the frequency of headache was significantly lesser in patients treated with aminophylline as compared to those treated with dexamethasone and the placebo group. They also demonstrated that dexamethasone increased the risk of PDPH, after spinal anaesthesia for a caesarean section, when compared to placebo. These results are somewhat different to the present study results.

We found aminophylline had better efficacy than dexamethasone and placebo and dexamethasone was better than placebo group. The difference may be attributed to the different demographic characteristics of two studies. Ona BX enrolled majority of women (72%), mostly were in labour and underwent cesarean section, while in the present study women comprised of 53.9% of total enrolled participants in all groups. Furthermore, in the present study we included the patients undergoing different kinds of surgeries (Gynae/obs, orthopedic, urological and other general surgeries). Although the mechanism of action of aminophylline yielding headache controlling effect is not exactly known. It has been hypothesized that aminophylline could be acting through several mechanisms. Firstly, aminophylline by inhibiting phosphodiesterase enzyme reduces the inflammatory process associated with traction on the pain sensitive intracranial structures due to lowering of CSF pressure after lumbar puncture. Secondly, aminophylline by stimulating the Na-K pumps increases CSF production and hence reduces the compensatory vasodilatation caused by loss of the CSF after lumbar puncture.

Aminophylline can also cause cerebral vasoconstriction by blocking the effects of adenosine and increasing the secretion of adrenaline from the adrenal medulla.[13] In the line of this study Sadeghi SE et al evaluated single dose of IV aminophylline (1-1.5-mg/kg) for reducing the incidence of PDPH in women undergoing cesarean section and they demonstrated that the incidence of PDPH was significantly lower in aminophylline group as compared to the control group (5% vs. 23.3%, P <0.001.8 Sadeghi et al[14] demonstrated similar results in their previous study as well. They found IV aminophylline administered after spinal anesthesia was effective for reducing PDPH. Wu C, et al[15] has reported a case of severe PDPH after spinal anesthesia and demonstrated the efficacy of IV aminophylline in that patient. They reported that administration of IV-aminophylline resulted in marked improvement in the intensity of headache in that patient. Inconsistently Zajac et al[16] on the other hand demonstrated contrasting results and reported that aminophylline 250 mg once daily, when administered i.v., was not effective in decreasing the incidence of PDPH in comparison to caffeine or magnesium premedication and Najafi Anaraki A et al[17] also found contrast findings. On the other hand, Fawaz AA et al[18] observed that the treatment of PDPH with aminophylline is simple, does not involve any sort of intrusive procedure, is successful, safe, and has enhanced early-stage efficacy. In support of our findings, Hung KC et al[2] observed that aminophylline could be a viable alternative for the treatment of PDPH. A recent study highlighted the effectiveness of aminophylline as it decreased the frequency of postdural puncture headaches following CS under SA in contrast to gabapentin and neostigmine did, while also requiring less analgesic treatment and having fewer negative side effects.[19] In accordance to several study limitations, especially small sample size, controversies with few recent international studies and being conducted at only one center, therefore larger, placebo-controlled trials are recommended to assess the effects of these drugs more accurately.

Conclusion

As per the study conclusion, post-dural puncture headache observed to the significantly lesser in patients treated with Aminophylline and Dexamethasone

compared to placebo group at 24 hours, while headache was significantly lesser in patients treated with Aminophylline as compared to the Dexamethasone and Placebo group.

References

1. Guglielminotti J, Landau R, Li G. Major neurologic complications associated with postdural puncture headache in obstetrics: a retrospective cohort study. Anesthesia & Analgesia. 2019;129(5):1328-36.
2. Hung KC, Ho CN, Chen IW, Hung IY, Lin MC, Lin CM, Wang LK, 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(4):100920.
3. 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;3:5-7
4. Masoudifar M, Aghadavoudi O, Adib S. Effect of venous dexamethasone, oral caffeine and acetaminophen on relative frequency and intensity of postdural puncture headache after spinal anesthesia. Adv Biomed Res. 2016;5:66-9
5. Golfam P, Yari M, Rezaei M. The effect of intravenous propofol on the incidence of post-dural puncture headache following spinal anesthesia in cesarean section. J Kermanshah Univ Med Sci. 2016;20(2):51-5
6. Deo G. Post Dural Puncture Headache. J Chitwan Med Coll. 2013;3(1):5-10
7. Doroudian MR, Norouzi M, Esmailie M, Tanhaeivash R. Dexamethasone in preventing post-dural puncture headache:a randomized, double-blind, placebo-controlled trial. Acta Neurologica Belgica. 2011;62:143–6
8. Sadeghi SE, Abdollahifard G, Nasabi NA, Mehrabi M, Safarpour AR. 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 J Med Sci. 2012;7(1):13–6
9. Sırıt I, Ozturk I, Yazıcıoglu D. Aminophylline does not Prevent Postdural Puncture Headache in Caesarean Section. Int J Anesthetic Anesthesiol. 2015;2:31-4
10. Peralta F, Higgins N, Lange E, Wong CA, McCarthy RJ. The Relationship of Body Mass Index with the Incidence of Postdural Puncture Headache in Parturients. Anesth Analg. 2015; 121(2):451-6.
11. Heesen M, Klöhr S, Rossaint R, Van De Velde M, Straube S. Can the incidence of accidental dural puncture in laboring women be reduced? A systematic review and meta-analysis. Minerva Anestesiol. 2013; 79(10):1187-97.
12. Ona BX, Tuma USM, García ML, Solà I, Cosp BX. Drug therapy for preventing post-dural puncture headache. Cochrane Database Syst Rev. 2013 ;(2):CD001792
13. Anderson M. The properties of aminophylline. Emerg Nurse. 2007;15:24–7
14. Sadeghi SE, Rahimian MN, Razmi R, Abdollahfard GH. Effect of intravenous single dose of aminophylline on prevention of post-dural puncture headache in patients who underwent spinal anesthesia. J Gorgan Uni Med Sci. 2010;12:24–8
15. Wu C, Lian Y, Xie N. Aminophylline Injection Alleviates Pain in Postdural Puncture Headache. Pain Medicine. 2015; 16:2038–40
16. Zajac K, Zajac M, Hl/adki W, Jach R. Is there any point in pharmacological prophylaxis of PDPH (post-dural puncture headache) after spinal anaesthesia for Caesarean section? Przegl Lek. 2012;69:19–24
17. Najafi Anaraki A, Mirzaei K. Comparing the Prophylactic Effect of Pregabalin with that of Aminophylline Plus Dexamethasone on Postdural Puncture Headache after Spinal Anesthesia in Cesarean Section: A Double-Blind Controlled Randomized Clinical Trial. ISMJ. 2019;22(5):307-16.
18. Fawaz AA, El-Gendy HA, Saleh AN, Fath-Allah ME. Aminophylline versus Acetaminophen in the treatment of post-dural puncture headache. Ain Shams Medical Journal. 2021 Mar 1;72(1):49-58.
19. Saafan AA, 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 Oct;114(Supplement_1):hcab086-018.s

.