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The Effect of Intravenous Infusion of Propofol or Aminophylline on Incidence and Severity of Post-dural Puncture Headache in Elective Cesarean Section

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ABSTRACT

Background: Post-dural puncture headache (PDPH) is caused by the persistent leak of cerebrospinal fluid (CSF) from the subarachnoid space. This leakage causes a decrease in the CSF volume and pressure leading to loss of the cushioning effect normally maintained by the intracranial fluid. This results in traction on the intracranial pain-sensitive structures, causing headache. The aim of the present study was to find ways to reduce the incidence and severity of PDPH in parturients undergoing spinal anesthesia for elective cesarean section.

Patients and methods: This was a randomized controlled trial study conducted at Zagazig University Hospitals during the period from February to August 2020. It included 200 parturients, planned for elective caesarean section under spinal anesthesia. All parturients were kept nil orally (8 hrs for fatty meals, 6 hrs for light meals and 2 hrs for clear fluids) before the operation. Ranitidine 50 mg I.M was given to all parturients 90 minutes before the operation.

Results: The severity, duration of headache was significantly lower in the propofol group compared with the control and aminophylline groups. There was no significant difference between aminophylline and control groups.

Conclusion: We can conclude that propofol reduced the severity, the duration and the associated symptoms of post-dural puncture headache compared to aminophylline in parturients undergoing spinal anesthesia for elective cesarean section.

Keywords: Aminophylline, Cesarean section, Post dural puncture headache (PDPH), Propofol

INTRODUCTION

Cesarean section has become increasingly common as it can effectively reduce maternal mortality and morbidity[(1)]. Regional and general anesthesia are commonly used for cesarean section. However, general anesthesia has many risks including aspiration, awareness during anesthesia, failed intubations and greater risk of maternal blood loss[(2)].

Spinal anesthesia is more preferred for cesarean section, as it eliminates the risks of general anesthesia, shortens patient's hospitalization, controls postoperative pain and decreases the mortality rate. Despite these advantages, spinal anesthesia still has some complications such as post-dural puncture headache (PDPH), fall in blood pressure, dyspnea, backache and neurotoxicity[(3)].

Post-dural puncture headache (PDPH) is a debilitating condition that appears after puncturing the dura mater[(4)]. The headache is severe, throbbing, frontal, radiates to the occiput, increases by standing and decreases by lying down. It is usually accompanied by neck stiffness, tinnitusm dizziness, photophobia, nausea and vomiting. It typically begins within two days but may be delayed for as long as two weeks and almost resolves spontaneously within few days[(5)].

Post-dural puncture headache is caused by the persistent leak of cerebrospinal fluid (CSF) from the subarachnoid space. This leakage causes a decrease in the CSF volume and pressure leading to loss of the cushioning effect normally maintained by the intracranial fluid .This results in traction on the intracranial pain-sensitive structures, causing headache[(6)]. This decrease in the CSF volume may also directly activate adenosine receptors causing cerebral vasodilatation and stretching of pain-sensitive cerebral structures, resulting in PDPH[(7)].

Risk factors for PDPH include: young age, female gender, history of previous PDPH, increased size of the needle and number of attempts[(8)]. The incidence of PDPH in pregnant females undergoing spinal anesthesia for cesarean section is significantly higher than other patients due to their gender and age[(9)].

Lines of treatment of PDPH include bed rest, hydration, oral caffeine and first line analgesics, however in case of no response to these measures, an epidural blood patch is performed[(4)].

Aminophylline is a methylated xanthine derivative, a phosphodi-esterase inhibitor and adenosine receptor antagonist [(10)], and it is reported to treat PDPH like caffeine and theophylline. This may be due to the inhibition of calcium uptake by the endoplasmic reticulum of endothelial cells, stimulation of sodium and potassium pumps, increased secretion of CSF, vasoconstriction of the intracranial blood vessels by blocking adenosine receptors and blocking the transmission of pain perception[(11)].

Propofol is an ultra-short-acting anesthetic that increases GABA mediated chloride flux which inhibits synaptic transmission, cerebral blood flow, cerebral metabolic rate, and central serotonergic neurons. These effects may alter the physiological condition of migraine resulting in significant pain reduction.

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Cerebrovascular vasodilation is the major cause of migraine[12].

The aim of the present study was to find ways to reduce the incidence and severity of PDPH in parturients undergoing spinal anesthesia for elective cesarean section.

PATIENTS and METHODS

A randomized controlled trial study that included 200 parturients scheduled for elective cesarean section under spinal anesthesia. Only 156 of them fulfilled the study criteria. Forty four were excluded from the study because of, not meeting the inclusion criteria (n=32), refusing to participate (n=9), and (3 cases were excluded for other reasons). Finally, 156 parturients were enrolled into the study and were randomly allocated into three equal groups according to the study drugs (52 parturients each).

Ethical approval:

An approval of the study was obtained from Zagazig University academic and ethical committee. Every patient signed an informed written consent for acceptance of the operation. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Inclusion criteria:

Sex; pregnant females candidate for elective cesarean section under spinal anesthesia. Age; 21-35 years. Body mass index (BMI); less than 30 $kg/m^{2.}$ Physical status; American Society of Anesthesiologists (ASA) physical status II.

Exclusion criteria:

Parturient's refusal. Parturients subjected to emergency cesarean section. Parturients with history of migraine, chronic headache or previous PDPH. Parturients with history of analgesic consumption, substance abuse, and smoking. Parturients with chronic or gestational hypertension; preeclampsia and liver or kidney failure. Parturients with hypersensitivity to one of the used drugs. Parturients with cardiovascular diseases, respiratory system diseases and neurological and psychiatric disorders. More than one trial for administering spinal anesthesia or failure of spinal anesthesia. Parturients who suffered from massive blood loss. Parturients who suffered from intraoperative nausea and vomiting (IONV) immediately after spinal anesthesia or before delivery of the baby.

Parturients were randomly allocated by computer randomization table into three equal groups according to the study drugs used (52 parturients each): **Group C (Control group)** (n=52); Parturients received 50 cc normal saline (0.9%) infusion over 30 minutes after umbilical cord clamping. **Group P** (n=52); Parturients received propofol (30 µg/kg/min) diluted in 50 cc normal saline (0.9%) infusion for 30 minutes after umbilical cord clamping. **Group A** (n=52); Parturients received aminophylline (100 µg/kg/min) diluted in 50 cc normal saline (0.9%) infusion for 30 minutes after umbilical cord clamping.

Preoperative preparation:

All parturients were visited in the ward, full history was taken, the anesthetic procedure was explained in details and informed written consent was obtained. All parturients were kept nil orally (8 hrs for fatty meals, 6 hrs for light meals and 2 hrs for clear fluids) before the operation. Ranitidine 50 mg I.M was given to all parturients 90 minutes before the operation.

Intraoperative preparation:

On arrival to the operating room, standard monitoring was applied to all parturients, including pulse oximetery, electrocardiogram (ECG), non-invasive arterial blood pressure (NIBP). The baseline readings of mean arterial blood pressure (MAP), heart rate (HR) and oxygen saturation (SpO_2 %) were obtained. Two 18-guage IV cannulas were inserted, the 1st IV line was for administration of fluids and anesthetic drugs and the 2nd IV line was for administration of the study drugs. Lactated ringer solution 1000 cc was given as a preload volume before spinal anesthesia.

Anesthesia machine with oxygen supply, airway devices, laryngoscope and resuscitation drugs were available in the theatre. The study drugs were prepared and diluted in 50 cc normal saline (0.9 %) by a second anesthetist not involved in the investigations and data collection of the study. The infusion rate of the study drugs was controlled by a syringe pump, the exterior color of each syringe and the infusion lines were masked and made indistinguishable by using wrapping paper**.**

The parturients were then placed in a sitting position and their skin was prepared with 10% betadine, then under sterile conditions 2 cc lidocaine 2% was injected to anesthetize the skin and subcutaneous tissues. Spinal anesthesia was performed by paramedian approach in the intervertebral space (L_3-L_4) using a 25 G Quincke spinal needle with the bevel directed laterally. Correct needle placement in the subarachnoid space was confirmed by free flow of CSF from the needle, then 2.5 ml (12.5mg) hyperbaric bupivacaine (0.5%) was injected into the subarachnoid space and then the needle was extracted. The skin was dressed and the parturients were placed in the supine position with an oxygen face mask. The operating table was tilted to the left by (15 degrees) to avoid supine hypotension.

Sensory block was confirmed at the level of T4 dermatome using pinprick test and the highest level of sensory block was recorded. Motor block was assessed by Bromage scale immediately after spinal anesthesia and then every five minutes for the first 15 minutes. This scale is graded as follows: (0=no motor block, 1=can flex the knee, move the foot, but can't raise the leg, 2= can move the foot only, 3= can't move the foot or the knee).

Surgery was commenced when sensory block was confirmed at T4 and Bromage score was 3. Then, the fluid deficit was administered. For one ml bleeding, 3 ml ringer solution was administered and in the case of abnormal bleeding more than 1 liter (20%), the parturient was excluded from the study. After the baby was delivered and the umbilical cord clamped, Syntocinon® 10 IU/ml infusion was started through the 1st IV line.

MAP, HR and SpO_2 % were monitored throughout the operation and in the post anesthesia care unit (PACU) and recorded at the following times; baseline, immediately after spinal anesthesia, immediately after delivery of the baby, then at 10 minutes, 20 minutes, 30 minutes and 40 minutes after infusion of the study drugs.

Intraoperative nausea and vomiting (IONV) were evaluated by a score ranging from 0 to 3 and was assigned to grade the severity of IONV: (Grade 0 = no nausea or vomiting), (Grade 1 = nausea alone), (Grade 2 = nausea and vomiting), and (Grade 3 = vomiting more than twice in 30 minutes)

After surgery there was a 2-weeks follow up period, during which a second anesthetist blinded to the study groups made visits to the parturients in the hospital on the first day and then he followed them by phone calls every day till the 14th day after discharge from the hospital to evaluate the effects of the study drugs on the incidence, onset, duration, severity and associated symptoms of PDPH.

The severity of the headache was assessed using visual analogue scale, which was explained to all parturients on the first day of the follow-up. If pain severity according to VAS, was ≥ 3 out of 10, The following measures were taken to treat pain: bed rest, drinking liquids more than the daily need, using caffeinated drinks, use of first-line analgesics including oral paracetamol 500 mg every 8 hours and non-steroidal anti-inflammatory drugs. In case of no response to the above measures, oral theophylline 250 mg every 8 hours was recommended.

Statistical analysis

Statistical analysis was done using SPSS software version 27 (IBM, 2020). Quantitative data were presented as mean, median, standard deviation and range. Qualitative data were presented as frequencies and proportions. Kolmogorov-Smirnov and Levene tests were used to determine the distribution characteristics of variables and variance homogeneity. Pearson's chi squared test (χ^2) was used to analyze qualitative variables. One-way ANOVA (F) and Kruskal Wallis test (KW) were used to analyze independent quantitative variables as appropriate. Repeated measures ANOVA (F) was used analyze dependent quantitative variables. P value < 0.05 was considered significant.

RESULTS

There were no statistically significant differences in parturients' and surgical characteristics of the studied groups regarding age, gestational period, BMI, duration of the surgery and parity **(Table 1)**.

Table (1): Parturients' characteristics and duration of surgery in the studied groups

Variables	Group C (n=52)	Group P (n=52)	Group A (n=52)	P
Age (years): Mean ± SD	27.4 ± 4.7	25.2 ± 4.4	25.0 ± 4.5	**0.013***
Gestational period (weeks): Mean ± SD	38.4 ± 1.2	39.1 ± 1.1	38.8 ± 1.4	**0.017***
BMI (Kg/m^2): Mean ± SD	25.4 ± 3.3	24.2 ± 3.6	26.0 ± 3.2	**0.024***
Duration of surgery (min.): Mean ± SD	59.2 ± 3.9	60.2 ± 3.9	59.8 ± 4.1	**0.435**
Parity: Median (Range)	2 (0 – 3)	2 (1 – 3)	2 (0 – 2)	**0.9**

Group C: control group. Group P: propofol group. Group A: aminophylline group.
SD: standard deviation. BMI: body mass index. *: Significant NS: non-significant n: number of parturients.

Regarding the oxygen saturation (%) there was no statistically significant difference among the studied groups at different times **(Table 2)**.

Table (2): Peripheral oxygen saturation (SpO_2%) in the studied groups at different times

Oxygen saturation (%)	Group C (n=52)	Group P (n=52)	Group A (n=52)	P
Baseline: Mean ± SD	98.4 ± 1.1	98.4 ± 1.1	98.4 ± 1.1	**1.000**
After spinal anesthesia: Mean ± SD	98.3 ± 1.0	99.0 ± 1.0	97.7 ± 1.9	**<0.001***
Immediately after delivery: Mean ± SD	98.4 ± 1.1	98.4 ± 1.1	98.4 ± 1.1	**1.000**
10 minutes after drug infusion: Mean ± SD	98.9 ± 1.0	98.9 ± 1.1	98.9 ± 1.1	**1.000**
20 minutes after drug infusion: Mean ± SD	98.6 ± 1.4	98.6 ± 1.4	99.0 ± 1.0	**0.188**
30 minutes after drug infusion: Mean ± SD	99.0 ± 1.0	99.0 ± 1.0	99.0± 1.0	**1.000**
40 minutes after drug infusion: Mean ± SD	98.3 ± 1.0	98.4± 1.1	97.7 ± 1.9	**0.024***
P	**0.7**	**0.8**	**0.6**	

Group C: control group. Group P: propofol group. Group A: aminophylline group. *: Significant
SD: standard deviation, n: number of parturients.

Regarding the heart rate, there was no statistically significant difference among the studied groups. While there was statistically significant increase immediately after spinal anesthesia within each group compared to the baseline. Then HR decreased again after delivery and during infusion of the study drugs compared to its value after spinal anesthesia **(Table 3)**.

Table (3): Heart rate (beat/min.) in the studied groups at different times

Heart rate (beat/min.)	Group C (n=52)	Group P (n=52)	Group A (n=52)	P
Baseline: Mean ± SD	90.8 ± 6.8*	91± 6.8*	91.4 ± 6.4*	**0.897**
After spinal anesthesia: Mean ± SD	123.6 ±6.3	122.5 ± 6.4	124.9 ± 6.5	**0.164**
Immediately after delivery: Mean ± SD	104.2 ± 6.5	105.3 ± 6.7	104.8 ± 6.7	**0.669**
10 minutes after drug infusion: Mean ± SD	100.6 ± 6.4	100.8 ± 6.6	101.4 ± 6.6	**0.810**
20 minutes after drug infusion: Mean ± SD	98.4 ± 6.4	98.8 ± 6.4	97.7 ± 6.4	**0.675**
30 minutes after drug infusion: Mean ± SD	97.8 ± 6.0	97.3 ± 6.0	96.8 ± 6.0	**0.698**
40 minutes after drug infusion: Mean ± SD	94.9 ± 6.0	95.9 ± 6.1	95.3± 5.9	**0.694**
P	**<0.001**	**<0.001**	**<0.001**	

Group C: control group. Group P: propofol group. Group A: aminophylline group.
SD: standard deviation. NS: non-significant. *: Highly significant. n: number of parturients.

Regarding the mean arterial blood pressure (MAP), there was no statistically significant difference among the studied groups. While there was statistically significant decrease immediately after spinal anesthesia within each group compared to the baseline. Then MAP increased again after delivery and during infusion of the study drugs compared to its value after spinal anesthesia **(Table 4)**.

Table (4): Mean arterial blood pressure (mmHg) in the studied groups at different times

MAP (mmHg)	Group C (n=52)	Group P (n=52)	Group A (n=52)	P
Baseline: Mean ± SD	89.7 ± 4.6*	91± 4.2*	90.5 ± 4.6*	**<0.001***
After spinal anesthesia: Mean ± SD	70 ± 2.9	70.6 ± 2.7	71 ± 2.8	**0.190**
Immediately after delivery: Mean ± SD	79.9 ± 3.5	80.7 ± 3.4	80.5 ± 3.4	**0.467**
10 minutes after drug infusion: Mean ± SD	81.6 ± 2.6	81.2 ± 2.6	81.8 ± 2.7	**0.498**
20 minutes after drug infusion: Mean ± SD	81.8 ± 2.0	81.6 ± 2.1	82 ± 2.1	**0.616**
30 minutes after drug infusion: Mean ± SD	82.2 ± 2.7	81.7 ± 2.6	82.4 ± 2.9	**0.408**
40 minutes after drug infusion: Mean ± SD	82.8 ± 2.0	83.0 ± 2.1	83.2 ± 2.1	**0.036***
P	**<0.001**	**<0.001**	**<0.001**	

Group C: control group. Group P: propofol group. Group A: aminophylline group.
MAP: mean arterial blood pressure. *: Significant, n: number of parturients. SD: standard deviation.

Regarding intraoperative nausea and vomiting (IONV) there was a highly statistically significant difference among the studied groups in the occurrence of IONV, as group P had the least proportions of IONV compared to the other groups. The proportion of no nausea or vomiting (Grade 0) was highest in group P as compared to group C or group A **(Table 5).**

Table (5): The incidence of intraoperative nausea and vomiting (IONV) in the studied groups

Grades of IONV	Group C (n=52)	Group P (n=52)	Group A (n=52)	P
Grade 0: No nausea or vomiting n (%)	14 (26.9%)	42 (80.8%)	16 (30.8%)	**<0.001***
Grade 1: Nausea alone n (%)	10 (19.2%)	6 (11.5%)	8 (15.4%)	**[1]<0.001**
Grade 2: Nausea and vomiting n (%)	20 (38.5%)	4 (7.7%)	22 (42.3%)	**[2] 0.865**
Grade 3: Vomiting more than twice in 30 min. n (%)	8 (15.4%)	0 (0.0%)	6 (11.5%)	**[3]<0.001**

Group C: control group. Group P: propofol group. Group A: aminophylline group.
*: Significant, [1] Group C versus Group P. [2] Group C versus Group A. [3] Group P versus Group A.

There was no statistically significant difference among the studied groups regarding the incidence and the onset of PDPH. Regarding the severity of PDPH, group P recorded the least severity score compared to group C and group A. This represented a statistically significant difference. Regarding the duration of PDPH, group P recorded the shortest duration compared to group C and group A. This represented a statistically significant difference **(Table 6)**.

Table (6): Post-dural puncture headache (PDPH) characteristics in the studied groups.

Variables	Group C (n=52)	Group P (n=52)	Group A (n=52)	P
Incidence of headache: n (%)	12 (23.1%)	6 (11.5%)	8 (15.4%)	**0.275**
Onset of headache:	**(n=12)**	**(n=6)**	**(n=8)**	**0.577**
1st day n (%)	6 (50.0%)	4 (66.7%)	4 (50.0%)	
2nd day n (%)	4 (33.3%)	2 (33.3%)	4 (50.0%)	
3rd day n (%)	2 (16.7%)	0 (0.0%)	0 (0.0%)	
Severity (VAS): Median (Range)	5.5 (3 –6)	3 (2 – 4)	4.5 (4 – 5)	**1.000** **0.02**[1] 0.09[2] **0.04** [3]
Duration (days): Median (Range)	6.5 (5.0 –7.0)	4.0 (4.0 – 5.0)	5.5 (5.0 – 6.0)	**1.000** **0.005**[1] 0.07 [2] **0.03**[3]

Group C: control group. Group P: propofol group. Group A: aminophylline group.
*: Significant, n: number of parturients.
[1] Group C versus Group P. [2] Group C versus Group A. [3] Group P versus Group A.

Regarding the associated symptoms of PDPH, there was a statistically significant difference among the studied groups in concern of neck rigidity. Whereas, group P didn't record any case of neck rigidity, group C and A recorded (6) and (4) cases respectively. On the other hand, there was no statistically significant difference among the studied groups regarding tinnitus and dizziness as associated symptoms of PDPH **(Figure 1)**.

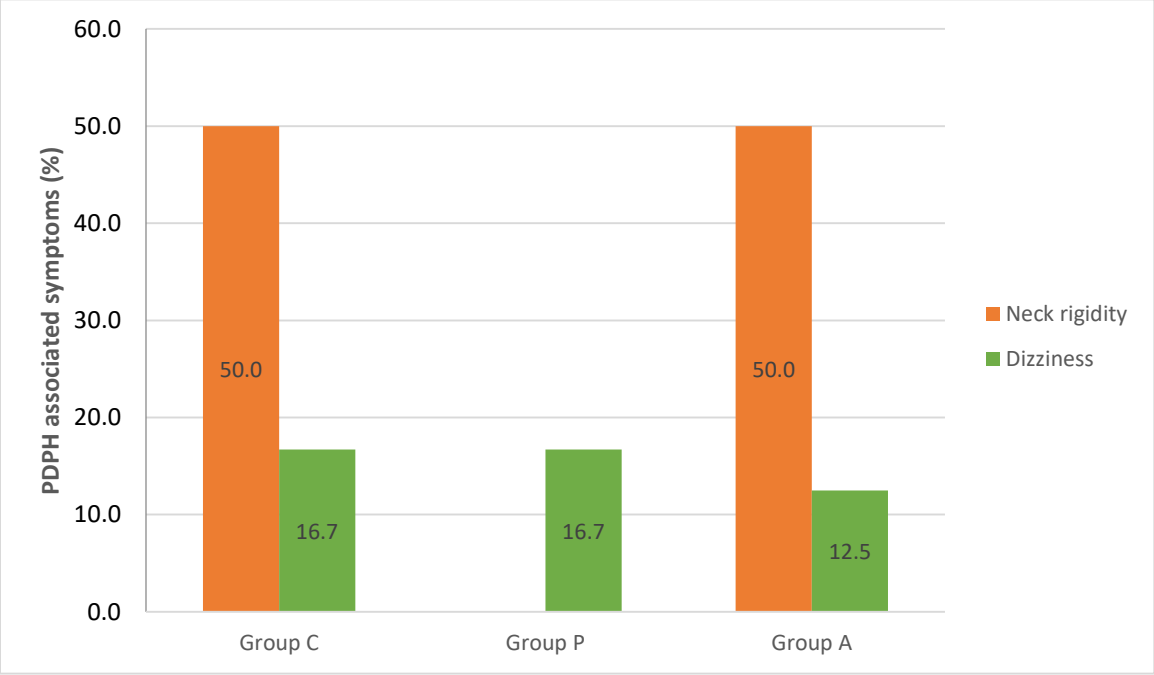

Figure (22): Incidence of PDPH associated symptoms in the studied groups.

DISCUSSION

There were no statistically significant differences in parturients' and surgical characteristics of the studied groups regarding age, gestational period, BMI, duration of the surgery and parity. The results of the current study revealed that values of SpO_2, HR and MAP didn't differ between the three groups and all of these values were within the normal range. Moreover, MAP decreased after spinal anesthesia then increased immediately after delivery, and after drug infusion, while HR increased after spinal anesthesia then decreased immediately after delivery, and after drug infusion.

Hypotension is the most common complication after spinal anesthesia especially in parturients undergoing cesarean section. This could be attributed to the sympathetic block induced by spinal anesthesia resulting in a decrease in the systemic vascular resistance, venous return and eventually the maternal cardiac output. Additionally, the vasodilator effect of progesterone may play a role in this complication[13].

The increased level of MAP immediately after delivery was attributed to the auto-transfusion of blood via the uterine contractions and the relief of aortocaval compression, increasing the cardiac output by as much as 60–80%[14].

The changes in HR in the current study were similar to the results of the study carried out by **Langesæter and Dyer**[15] in which, the onset of spinal anesthesia was associated with a rapid and profound drop in systemic vascular resistance with a compensatory increase in HR with no significant changes in the stroke volume. A less frequent response to spinal anesthesia is bradycardia with hypotension. This effect is known as the supine hypotensive syndrome and is believed to result from vena-caval obstruction or vagal reflex bradycardia associated with an inadequately filled heart "Bezold–Jarisch reflex"[16].

Moreover, There were no significant effects of either propofol or aminophylline infusion on the maternal hemodynamics. These results agreed with the studies carried out by **Golfam *et al.*** [17] which compared between the effects of propofol and placebo on the incidence and of PDPH in parturients undergoing spinal anesthesia for elective cesarean section, and **Yang *et al.*** [18] which compared between the effects of aminophylline and placebo on the incidence of PDPH in parturients undergoing combined spinal-epidural anesthesia for elective cesarean section.

To the best of our knowledge, this is the first study to directly compare the effect of both propofol and aminophylline simultaneously regarding the incidence, onset, severity, duration and associated symptoms of PDPH in parturients undergoing elective cesarean section under spinal anesthesia.

In the current study, there was two weeks follow up period of PDPH characteristics in the studied groups. However, in all the parturients who developed PDPH, the onset of headache was recorded only on the first three days after the dural puncture. This agreed with the international classification of headache disorders that stated that PDPH develops within five days after the dural puncture[19]. Moreover, there were no significant effects of the study drugs on the onset of headache among the studied groups.

The incidence of PDPH after spinal anesthesia for cesarean section varies greatly between the studies, this is mainly due to the difference in the size of the spinal needles used. In the current study we used a 25 G Quincke spinal needle for spinal anesthesia. The reported incidence of PDPH in other studies using the same needle for cesarean section ranged from 23% to 30% [17,20], and this agreed with the results of the present study.

In the present study, the incidence of PDPH was highest in the control group compared to the other two groups. Yet, this difference was statistically non-significant. Additionally, the incidence of PDPH on the first, second and third days after spinal anesthesia in the three groups didn't show any significant difference.

In accordance with the results of the current study, **Zajac *et al.*** [21] showed that aminophylline 250 mg once, when administered intravenously, was not effective in decreasing the incidence of PDPH in comparison to caffeine or magnesium sulphate premedication.

In their study, **Sirit *et al.*** [22] compared the effect of aminophylline and placebo on the incidence of PDPH after spinal anesthesia for elective cesarean section. They showed that aminophylline administration didn't reduce the incidence of headache compared to placebo. Moreover, another study compared between the effects of ondansetron and aminophylline on the incidence and severity of PDPH after spinal anesthesia for elective cesarean section, showed that aminophylline had no effect on reducing the incidence of PDPH[23].

On the contrary, in a study conducted by **Sadeghi *et al.*** [24] a single dose of intravenous aminophylline 1 mg/kg significantly decreased the incidence of PDPH in the parturients undergoing elective cesarean section compared to control group. Our study was different because they used meperidine as an adjuvant to the local anesthetic lidocaine which could play a role in decreasing the incidence of PDPH, and the duration of the follow up period was only 48 hours in their study.

A recent study was carried out by **Yang *et al.*** [18] on parturients undergoing cesarean section under combined spinal-epidural anesthesia. They recorded that the pre-administration of 250 mg aminophylline infusion after umbilical cord clamping significantly reduced the incidence of PDPH and it was not associated with any related side-effects. Indeed, these results were different from ours although they used the same size of the spinal needle (25G), but they didn't specify the type of the spinal needle they used whether it was a cutting or a pencil-point needle.

Regarding the incidence of PDPH with propofol, to the best of our knowledge, the only study done on propofol was carried out by Golfam and her colleagues. They showed that the incidence of PDPH was lower in propofol group compared to placebo group in parturients undergoing spinal anesthesia for elective cesarean section[17]. However, the current study showed that propofol decreased the incidence of PDPH compared to placebo, but this effect was statistically insignificant.

The current study showed that the severity of PDPH in the propofol group was lower compared to the other groups. This came in agreement with **Golfam *et al.*** [17] who showed that the severity of headache was reduced significantly in propofol group 6 hours after surgery compared to control group.

Soleimanpour *et al.* [25] studied the effectiveness of intravenous dexamethasone or propofol on pain relief in migraine headache. They concluded that propofol is safe and effective medication for the treatment of migraine in emergency departments. In a similar study carried out on patients with refractory migraine headache, propofol in sub-hypnotic dose was administered intravenously, headache was dramatically eliminated in all patients[26].

The results of the current study revealed that aminophylline didn't decrease the severity of PDPH compared to the control group. This agreed with **Dehghanpisheh *et al.*** [23] who showed that aminophylline also didn't reduce the severity of headache when compared to ondansetron or placebo in parturients undergoing spinal anesthesia for cesarean section. Moreover, **Sirit *et al.*** [22] showed that aminophylline didn't show a significant effect on the severity of PDPH when compared with placebo. However, another study examined the effect of theophylline on PDPH treatment, revealed that headache was reduced more in 6 patients taking oral theophylline than in 5 patients receiving no theophylline from among 11patients with PDPH[27].

Regarding the duration of PDPH, to the best of our knowledge, there were no available studies on the effect of aminophylline (when administered during spinal anesthesia) on the duration of PDPH. In the current study, propofol group recorded the shortest duration of headache compared to the control and aminophylline groups. This agreed with **Golfam *et al.*** [17] who found out that propofol decreased the duration of PDPH.

As regards the associated symptoms of PDPH, the results of this study revealed that propofol group had no cases of neck rigidity compared to aminophylline and control groups. However, there was no statistically significant difference among the three groups regarding the tinnitus and dizziness associated with PDPH.

In the current study, the occurrence of intraoperative nausea and vomiting (IONV) was significantly decreased in the propofol group compared to the other groups. This was similar to a study carried out by **Rasooli *et al.*** [28] who reported that propofol decreased the incidence of IONV compared to placebo without any complications in parturients undergoing spinal anesthesia for elective cesarean section. This may be attributed to the anti-emetic effect of propofol. This also agreed with the results of the study conducted by **Niu *et al.*** [29], as they showed that the incidence of IONV was lower in the propofol group when compared to placebo in parturients undergoing spinal anesthesia for elective cesarean section.

No adverse reactions of aminophylline were recorded in the current study, clinical pharmacological studies showed that the adverse reactions of aminophylline were mainly allergy, arrhythmia and convulsions. Some studies suggested that 250 mg of aminophylline can be effective in the treatment of PDPH without significant side-effects and it can be used in parturients without affecting lactation[18].

CONCLUSIONS

We can conclude that propofol reduced the severity, the duration and the associated symptoms of post-dural puncture headache compared to aminophylline in parturients undergoing spinal anesthesia for elective cesarean section. Further studies are recommended to using different drug concentrations, performed including larger number of parturients from more than one center. Regular and close follow up of parturients undergoing CS is recommende for early detection of complications.

REFERENCES

1. **Ye J , Betrán A, Guerrero-Vela M *et al.* (2014):** Searching for the optimal rate of medically necessary cesarean delivery. Birth, 41(3): 237-244.
2. **Khan Z, Eftekhar N, Barrak R (2019):** General versus spinal anesthesia during cesarean section: a narrative review. Archives of Anesthesiology and Critical Care, 5(1): 18-21.
3. **Dranser K, Larson M (2011):** Spinal and Epidural Anesthesia. In:Miller RD, Pardo MC, editors. Basics of Anesthesia. 6th ed.Philadelphia (PA): Elsevier, Pp. 270-278.
4. **Choi P, Galinski S, Takeuchi L *et al.* (2003):** PDPH is a common complication of neuraxial blockade in parturients: a meta-analysis of obstetrical studies. Canadian Journal of Anesthesia, 50(5): 460-469.
5. **Kuczkowski K (2007):** The management of accidental dural puncture in pregnant women: what does an obstetrician need to know? Archives of Gynecology and Obstetrics, 275(2): 125-131.
6. **Morewood G (1993):** A rational approach to the cause, prevention and treatment of postdural puncture headache. CMAJ., 149:1087–1093.
7. **Grant R, Condon B, Hart I *et al.* (1991):** Changes in intracranial CSF volume after lumbar puncture and their relationship to post-LP headache. Journal of Neurology, Neurosurgery & Psychiatry, 54(5): 440-442.
8. **Kuczkowski K (2004):** Post-dural puncture headache in the obstetric patient: an old problem. New solutions. Minerva Anestesiologica, 70(12): 823-830.

9. **Gisore E, Mung'ayi V, Sharif T (2010):** Incidence of post dural puncture headache following cesarean section under spinal anaesthesia at the Aga Khan University Hospital, Nairobi. East Afr Med J., 87(6):227-30.
10. **Essayan D (2001):** Cyclic nucleotide phosphodiesterases. Journal of Allergy and Clinical Immunology, 108(5): 671-680.
11. **Wu C, Guan D, Ren M *et al.* (2018):** Aminophylline for treatment of postdural puncture headache: A randomized clinical trial. Neurology, 90(17): 1523-1529.
12. **Krusz J, Scott V, Belanger J (2000):** Intravenous propofol: unique effectiveness in treating intractable migraine. Headache: The Journal of Head and Face Pain, 40(3): 224-230.
13. **Hwang J, Oh A, Song I *et al.* (2014):** Influence of a prolonged lateral position on induction of spinal anesthesia for cesarean delivery: a randomized controlled trial. Minerva Anestesiologica, 78(6): 646-53.
14. **Smith R, Young S, Greer I (2008):** The Parturient with coronary heart disease. Int J Obstet Anesth., 17: 46–52.
15. **Langesæter E, Dyer R (2011):** Maternal haemodynamic changes during spinal anesthesia for cesarean section. Curr Opin Anaesthesiol., 24(3):242–248.
16. **Kinsella S, Lohmann G (1994):** Supine hypotensive syndrome. Obstet Gynecol., 83:774–788.
17. **Golfam P, Yari M, Mansour R *et al.* (2016):** The effect of intravenous propofol on the incidence of post-dural puncture headache following spinal anesthesia in cesarean section. Journal of Kermanshah University of Medical Sciences, 20: 51-55.
18. **Yang C, Chen T, Ni X *et al.* (2019):** Effect of pre-administration with aminophylline on the occurrence of post-dural puncture headache in women undergoing cesarean section by combined spinal-epidural anaesthesia. Journal of International Medical Research, 47(1): 420-426.
19. **Headache Classification Subcommittee of the International Headache Society (2018):** The International Classification of Headache Disorders 3rd edition (ICHD-3). Cephalalgia, 38(1): 1–211.
20. **Sumaya S, Nargis Q, Shazia N *et al.* (2017):** Comparison of post-dural puncture headache incidence and severity in obstetric patients after spinal anesthesia for cesarean section with 25G and 27G quincke needle. International Journal of Research in Medical Sciences, 5: 596-603.
21. **Zajac K, Zajac M, Hładki W *et al.* (2012):** Is there any point in pharmacological prophylaxis of PDPH (post-dural puncture headache) after spinal anaesthesia for Cesaren section? Przeglad Lekarski, 69(1): 19-24.
22. **Sirit I, Ozturk I, Yazicioglu D (2015):** Aminophylline does not prevent postdural puncture headache in cesarean section. Int J Anesthetic Anesthesiol., 2(3): 31-33.
23. **Dehghanpisheh L, Bayani S, Azemati S *et al.* (2019):** The effect of intravenous administration of ondansetron compared to aminophylline on incidence and severity of post-dural puncture headache (PDPH) in cesarean section surgeries. Biomedical Research, 30: 1-6.
24. **Sadeghi S, Abdollahifard G, Nasabi N *et al.* (2012):** 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., 7(1): 13-16
25. **Soleimanpour H, Ghafouri R, Taheraghdam A *et al.* (2012):** Effectiveness of intravenous dexamethasone versus propofol for pain relief in the migraine headache: a prospective double blind randomized clinical trial. BMC Neurol., 12:114-119.
26. **Mosier J, Roper G, Hays D *et al.* (2013):** Sedative dosing of propofol for treatment of migraine headache in the emergency department: a case series. West J Emerg Med., 14(6):646-649.
27. **Mahoori A, Hassani E, Noroozinia H *et al.* (2013):** Theophylline versus acetaminophen in the treatment of post-dural puncture headache (PDPH). Middle East J Anaesthesiol., 22(3): 289-292.
28. **Rasooli S, Moslemi F, Khaki A (2014):** Effect of subhypnotic doses of propofol and midazolam for nausea and vomiting during spinal anesthesia for cesarean section. Anesth Pain Med., 4(4): 19384-88.
29. **Niu K, Liu H, Chen R *et al.* (2018):** Use of propofol for prevention of post-delivery nausea during cesarean section: a double-blind, randomized, placebo-controlled trial. J Anesth., 32(5):748-755.