

TO OBSERVE THE EFFECT OF ORAL GABAPENTIN, THEOPHYLLINE AND CAFFEINE ON SBP, DBP, MAP AND HR.

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Abstract

After obtaining approval from institutional ethics committee, and written informed consent, the present study entitled "To Observe the Effect of Oral Gabapentin, Theophylline and Caffeine on SBP, DBP, MAP and HR" was conducted on 120 patients of ASA grade I & II scheduled for elective and emergency lower segment caesarean section under spinal anesthesia in the Department of Anesthesiology, J.A. Group of Hospitals & G.R. Medical College, Gwalior (M.P.) after getting written informed consent from the patients.

No significant effects on haemodynamic parameters were observed with all the study drugs. Recurrence of PDPH was significantly high with caffeine treatment. No serious untoward effects or complications of study drugs were observed in the study.

Keywords: Oral Gabapentin, Theophylline, Caffeine, SBP, DBP, MAP & HR.

Introduction

Gabapentin, a structural analogue of gamma amino butyric acid (GABA) is an antiepileptic drug and is widely used as a medication to relieve pain, especially neuropathic pain. It does not bind with plasma protein and is not metabolized in humans. After a single oral dose of 300 mg, mean maximum plasma concentration is attained in 2-3 hrs¹.

Theophylline a methylxanthine derivative having phosphodiesterase inhibiting activity leading to the relaxation of bronchial smooth muscles (bronchodilation) as well as cerebral vasoconstriction². Vasoconstriction through blocking of adenosine receptor along with induction of CSF production by stimulating Na⁺-K⁺ Pumps are the mechanism of relief in PDPH³.

Caffeine is a central nervous system stimulant that amongst other properties produces cerebral vasoconstriction. It is available in an oral and I.V. form. The oral form is well absorbed with peak levels reached in 30 min. Caffeine crosses blood- brain barrier and the long half-life of 3-7.5 allows for infrequent dosing schedules. The dose now recommended for the treatment of PDPH is 300-500 mg of oral or I.V. caffeine once or twice daily.

Caffeine may relieve PDPH because of its ability to increase cerebral vascular resistance, decrease cerebral CBF, and decrease cerebral blood volume⁴.

The aim of this study is to evaluate the effect of oral Gabapentin, Theophylline and Caffeine in the treatment of post dural puncture headache in patient of lower segment caesarian section under spinal anesthesia⁵.

Material & Method

After obtaining approval from institutional ethics committee, and written informed consent, the present study entitled "**To Observe the Effect of Oral Gabapentin, Theophylline and Caffeine on SBP, DBP, MAP and HR**" was conducted on 120 patients of ASA grade I & II scheduled for elective and emergency lower segment caesarean section under spinal anesthesia in the Department of Anesthesiology, J.A. Group of Hospitals & G.R. Medical College, Gwalior (M.P.) after getting written informed consent from the patients. The enrollments of patients were done in between Dec. 2015 to Oct. 2017.

The patients were enrolled based on following inclusion/exclusion criteria.

Inclusion criteria

1. Elective and emergency LSCS.
2. Patient of ASA Grade I & II.
3. Patient of age group 18-40 years, pregnant female, undergoing elective or emergency lower segment caesarean section, under spinal anesthesia.

Exclusion criteria:

1. Unwilling patients.
2. Any presence of local sepsis over sub-arachnoid block site.
3. Patients with spinal deformity or previous spinal surgeries.
4. Patients with severe cardiovascular, pulmonary, hepatic, renal and neurological diseases.
5. Patients on anticoagulants or antiplatelet therapy or with bleeding diathesis or coagulopathy.

6. Patients with history of headache or migraine.
7. Patients with raised intra-cranial tension.
8. Haemodynamic unstable patients
9. Pregnancy with fetal distress.
10. Patients requiring more than three attempts for subarachnoid block.

METHODOLOGY

The purpose and protocol of the study was explained to patients and informed written consent was taken.

Randomization: Patients were blinded by sealed envelope technique and observer anaesthesiologist was kept blinded to both drug and the patient thus avoiding observer's bias. The anaesthesiologist who gave the study drug took no further part in the study.

Results**TABLE 1: INTRA-GROUP STATISTICAL ANALYSIS OF PULSE RATE (bpm) BETWEEN FOUR GROUPS**

Sr. No.	Time	Group G		Group T		Group C		Group P	
		t –value	p – value	t- value	p – value	t – value	p – value	t – value	p – value
1.	B ₀	--	--	--	--	--	--	--	--
2.	T ₆	1.58	0.12	0.08	0.93	2.0	0.04	0.81	0.42
3.	T ₁₂	2.90	0.007	0.56	0.57	8.4	0.0001	0.49	0.62
4.	T ₂₄	3.95	0.0004	2.84	0.008	12.5	0.0001	1.51	0.14
5.	T ₄₈	3.79	0.0007	4.38	0.001	12.5	0.0001	2.38	0.02
6.	T ₇₂	4.34	0.0002	5.30	0.0001	9.4	0.0001	3.53	0.001

Above table shows that the changes in pulse rate were statistically highly significant ($p < 0.01$) in the four groups, after administration of drugs there was decrease in pulse rate in group G, T and C compared to group P at T₂₄, T₄₈, and T₇₂ which were statistically highly significant ($p \leq 0.05$). $p > 0.05$ – Not significant, $p \leq 0.05$ – Significant(S), $p < 0.01$ – Highly significant(HS).

TABLE 2: STATISTICAL ANALYSIS OF SYSTOLIC BLOOD PRESSURE (mm Hg) IN FOUR STUDY GROUPS

Sr. No.	Time	Group G (MEAN \pm SD)	Group T (MEAN \pm SD)	Group C (MEAN \pm SD)	Group P (MEAN \pm SD)
1.	B ₀	124.7 \pm 13.7	123 \pm 11	121.2 \pm 10.4	124 \pm 12
2.	T ₆	120.3 \pm 12.5	123 \pm 11	118 \pm 8.3	125 \pm 10
3.	T ₁₂	120.06 \pm 10.4	123 \pm 9.9	114 \pm 6.5	124 \pm 11
4.	T ₂₄	120 \pm 8.6	121 \pm 8.4	111.9 \pm 7	124 \pm 8.6
5.	T ₄₈	120.2 \pm 7.0	120 \pm 6.7	114 \pm 5.2	123 \pm 8.1
6.	T ₇₂	120.1 \pm 5.7	120 \pm 5.3	115 \pm 5.6	122 \pm 7.7

Above table is showing statistical analysis of mean (\pm SD) systolic blood pressure (mmHg) between four groups at different time intervals. Compared to baseline values (Bo), there was maximum decrease in systolic blood pressure at T₆ h after Gabapentin administration in group G. In group C increase in systolic blood pressure was noted at 48 and 72 h after caffeine administration in comparison to group P.

TABLE 3: STATISTICAL ANALYSIS OF DIASTOLIC BLOOD PRESSURE (mm Hg) IN FOUR STUDY GROUPS

Sr. No.	Time	Group G (MEAN \pm SD)	Group T (MEAN \pm SD)	Group C (MEAN \pm SD)	Group P (MEAN \pm SD)
1.	B ₀	77.2 \pm 9.1	76 \pm 7.5	79.7 \pm 9.6	77 \pm 7.7
2.	T ₆	75.2 \pm 7.7	75.5 \pm 6.5	77 \pm 9.4	77 \pm 7.2
3.	T ₁₂	75 \pm 6.5	76.3 \pm 5.5	74 \pm 8	76 \pm 6.8
4.	T ₂₄	74.6 \pm 6.3	75 \pm 5	72 \pm 7.9	75 \pm 6.4
5.	T ₄₈	74.3 \pm 4.6	73.7 \pm 4.89	73 \pm 5.5	76 \pm 6.3
6.	T ₇₂	74.6 \pm 4.2	73 \pm 3.9	74 \pm 5.5	74 \pm 5.4

Above table is showing statistical analysis of mean (\pm SD) diastolic blood pressure (mmHg) between four groups at different time intervals. Compared to baseline values (Bo), there was decrease in diastolic blood pressure after drugs administration in all the four groups. In group G decrease in diastolic blood pressure was marked in comparison to group P. In group C after drug administration there was increase in DBP at 72h. While in group P there is less decrease in DBP compared to other study groups.

TABLE 4: STATISTICAL ANALYSIS OF MEAN (\pm SD) MEAN ARTERIAL PRESSURE (mmHg) IN FOUR STUDY GROUPS

Sr. No.	Time	Group G (MEAN \pm SD)	Group T (MEAN \pm SD)	Group C (MEAN \pm SD)	Group P (MEAN \pm SD)
1.	B ₀	93.3 \pm 10.1	91 \pm 8.2	93 \pm 9.3	93 \pm 8.9
2.	T ₆	89.9 \pm 9.0	91.1 \pm 7.3	90 \pm 8.4	92.5 \pm 8.1
3.	T ₁₂	89.6 \pm 7.5	91.5 \pm 6.4	87 \pm 6.7	91.5 \pm 7.5
4.	T ₂₄	90.3 \pm 6.7	89.7 \pm 5.8	84.9 \pm 7.1	91 \pm 7.1
5.	T ₄₈	89.2 \pm 4.9	89.2 \pm 5.5	86.23 \pm 6	91 \pm 6.6
6.	T ₇₂	89.7 \pm 3.9	88.3 \pm 3.8	87.7 \pm 4.6	89.4 \pm 5.3

Above table is showing statistical analysis of mean (\pm SD), mean arterial pressure (mmHg) between four groups at different time intervals. Compared to baseline values (Bo), there was marked decrease in mean arterial pressure in group G after drugs administration at 6h compared to group P.

Discussion

PULSE RATE (PR)

The mean (\pm SD) HR (bpm) at baseline was 85.6 \pm 13.8 bpm in group G. The maximum decrease in heart rate (81.9 \pm 9.1) was seen at 12 h after administration of study drugs. Heart rate progressively decreases further in the study period which was highly significant (p=0.00).

In group T the mean (\pm SD) HR (bpm) at baseline was 85.9 \pm 12.18 bpm. Heart rate progressively decreases further in the study period which was highly significant (p=0.00)⁶.

DIASTOLIC BLOOD PRESSURE (DBP)

In the present study, according to the mean (\pm SD) DBP (mmHg) at baseline was 77.2 \pm 9.1 mm Hg in the group G which decreased to 74.6 \pm 4.2 mm Hg at 72h

after administration of study drug, the fall in DBP was significant (p \leq 0.05).

In group T the mean (\pm SD) DBP (mmHg) at baseline was 76 \pm 7.5 mm Hg which decreased to 73 \pm 3.9 mm Hg at 72h after administration of study drug the fall in DBP was significant at 48h and 72h (p \leq 0.05)⁷.

In group C the mean (\pm SD) DBP (mmHg) at baseline was 79.7 \pm 9.6 mm Hg which decreased to 74 \pm 5.5 mm Hg at 72h after administration of study drug the fall in DBP was significant at 24, 48 and 72h (p \leq 0.05).

SYSTOLIC BLOOD PRESSURE (SBP)

In the present study, as shown in table no. 10, 11 and 12 the mean (\pm SD) SBP (mmHg) at baseline was 124.7 \pm 13.7 mm Hg in the group G, which decreased to 120.3 \pm 12.5 mm Hg at 6h after administration of study drug, which was highly significant (p=0.00). While in group C the mean (\pm SD) SBP (mmHg) at baseline was 121.2 \pm 10.4 mm Hg there was highly significant difference in SBP after administration of drugs (p=0.00)⁸.

In group T and group P the mean (\pm SD) SBP (mmHg) at baseline was 123 ± 11 mm Hg and 124 ± 12 respectively and there was no significant difference in SBP after administration of drugs ($p > 0.05$).

In inter-group statistical analysis, the fall in systolic blood pressure was highly significant on comparison of group G with group C, group T with group C and group C with group P at 12, 24, 48 and 72h after treatment ($p = 0.00$). While on comparing group G with group T, group G with group P and group T with group the fall in systolic blood pressure was not significant after administration of study drug ($p > 0.05$).

MEAN ARTERIAL PRESSURE (MAP)

In the present study, according to the mean (\pm SD) MAP (mmHg) at baseline was 93.3 ± 10.1 mm Hg in the group G which decreased to 89.7 ± 3.9 mm Hg at 72h after administration of study drug, the fall in MAP was highly significant ($p = 0.00$).

In group T the mean (\pm SD) MAP (mmHg) at baseline was 91 ± 8.2 mm Hg which decreased to 88.3 ± 3.8 mm Hg at 72h after administration of study drug, the fall in MAP was significant ($p \leq 0.05$)⁹.

In group C the mean (\pm SD) MAP (mmHg) at baseline was 93 ± 9.3 mm Hg which decreased to 87.7 ± 4.6 mm Hg at 72h after administration of study drug, there was highly significant difference in fall of MAP ($p = 0.00$)¹⁰.

Conclusion

No significant effects on haemodynamic parameters were observed with all the study drugs. Recurrence of PDPH was significantly high with caffeine treatment. No serious untoward effects or

complications of study drugs were observed in the study.

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