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Effect of Tranexamic Acid on Coagulation Profile in Patients Undergoing Brain Tumour Resection Surgery

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ABSTRACT

Introduction; The majority of researchers currently believe that the haemostatic anomalies in brain tumour resection patients undergoing surgery are caused by hyperfibrinolysis, either primary or subsequent to a condition of disseminated intravascular coagulation. This Study explored the changes in haemostatic profile occurring during surgery for primary brain tumours and effect on Tranexamic acid on coagulogram.

Aims & objectives: To study effect of tranexamic acid on coagulation profile in brain tumour resection patients.

Materials & methods: Patients of either sex, aged 18-65 years were randomly allocated to either group - the study group and the control group (30 patients in each group) using computer generated random numbers in sealed envelopes. The investigator was present during the procedure for data collection purpose only and was not involved in the conduct of anaesthesia. Blood samples were collected preoperatively, 6hrs postoperatively and 24hrs postoperatively for coagulogram*;* fibrinogen levels; platelet count; D-dimer levels

Results: In our study we found that there were no significant differences in PT, INR, aPTT, D-dimer preoperatively and at 6 and 24 hrs postoperatively. However, fibrinogen levels increased in tranexamic group and significantly decreased in saline group as compared to preoperatively.

Conclusion: Tranexamic acid prevented decrease in levels of fibrinogen and even increased levels fibrinogen significantly during the operative and postoperative period in brain tumour resection surgery.

Key words: Coagulation profile, Meningioma

INTRODUCTION

Haemorrhagic irregularities and postoperative haemorrhages consistently lead to poor outcomes in neurosurgery, with one recent series reported only 13% with excellent outcomes, and 55% severe disability or fatality at six months [1]. Morozov was the first to suggest that variables related to brain tumours might be to blame in the 1960s [2]. The majority of researchers currently believe that these haemostatic anomalies are caused by hyperfibrinolysis, either primary or subsequent to a condition of disseminated intravascular coagulation [3]. The pathogenesis is believed to entail the release of tissue factors from damaged brain parenchyma after surgery or plasminogen activator factors from tumour cells [4,5]. In neurosurgical interventions TXA (1 g immediately after diagnosis of an aneurysmal subarachnoid hemorrhage [aSAH], followed by 1 g every 6 h up to the time the aneurysm has been clipped) reduced

the mortality risk and coagulopathy by 80% [6]. Data from randomized controlled studies on the efficacy and safety of antifibrinolytics in brain surgery are rare. A Cochrane review published in 2013 included all randomized controlled studies published between 1973 and 2002 [7]. The authors came to the conclusion that the short-term data were promising but felt that the studies were too heterogeneous to justify a general recommendation to use antifibrinolytics in the treatment of aSAH. Similarly, the European Stroke Organization is not ready to make such a recommendation on the basis of the data so far available [8]. This Study explored the changes in haemostatic profile occurring during surgery for primary brain tumours and effect on Tranexamic acid on coagulogram.

AIMS & OBJECTIVES

1. To study the changes in coagulogram during brain tumour resection surgery
2. To study the effect of tranexamic acid on coagulation profile during brain tumour resection surgery.

MATERIALS & METHODS

This observational study was conducted in Department of Anaesthesiology and Critical Care at Sher-i-Kashmir Institute of Medical Sciences, Soura for a period of two years. Approval by our institutional ethical committee was taken prior to the start of the study. A proper informed consent was obtained from all patients included in the study. The study included 30 patients aged 18-65 years of both genders, planned for brain tumour resection surgeries (meningiomas, astrocytomas, gliomas and other vascular tumours) under general anesthesia.

EXCLUSION CRITERIA

- Patients with abnormal liver function.
- Patients with known renal dysfunction (creatinine>1.5mg/dl).
- Patients with coagulopathy on anticoagulation therapy (abnormal PT/PTT).
- Patients with thromboembolic events.
- ASA IV patients.
- Patients with intraoperative bleeding due to vessel injury.

Patients of either sex, aged 18-65 years were randomly allocated to either group - the study group and the control group (30 patients in each group) using computer generated random numbers in sealed envelopes. The investigator was present during the procedure for data collection purpose only and was not involved in the conduct of anaesthesia. Blood samples were collected preoperatively, 6hrs postoperatively and 24hrs postoperatively for coagulogram; fibrinogen levels; platelet count; D-dimer levels. All patients were given standard general anesthesia consisting of propofol, an opioid (fentanyl and morphine), muscle relaxant (atracurium or vecuronium) and a volatile anesthetic (isoflurane or sevoflurane) with oxygen in nitrous oxide.

Statistical analysis

Statistical analysis was performed by our institutional biostatistician. The recorded data was compiled and entered in a spread-sheet (Microsoft Excel) and then exported to data editor of SPSS Version 20.0 (SPSS Inc., Chicago, Illinois, USA). Statistical software SPSS (version 20.0) and Microsoft Excel were used to carry out the statistical analysis of data. Continuous variables were summarized as Mean±SD and categorical variables were summarized as percentages. Student's independent t-test was employed for comparison of continuous variables. Chi-square test or Fisher's exact test, whichever appropriate, was used for comparison of categorical variables. Graphically the data was presented by bar diagrams. A P-value of less than 0.05 was considered statistically significant.

RESULTS

Table:6 Comparison based on preoperative coagulogram between the groups					
Preoperative Coagulogram	**TXA Group**		**Saline Group**		**P-value**
	Mean	**SD**	**Mean**	**SD**	
Platelets	2.16	3.92	1.97	2.73	0.828
PT	12.86	1.05	13.49	1.55	0.073
INR	1.04	0.07	1.10	0.15	0.078
APTT	30.23	3.14	29.83	2.81	0.614
Fibrinogen	337.12	43.15	331.16	39.71	0.579
D-Dimer	0.27	0.15	0.29	0.18	0.642

Before surgery, mean number of platelets in the tranexamic acid group was 2.16 lakhs/µl as compared to the platelets of 1.97lakhs/µl in the saline group (p=0.828) the mean PT in the tranexamic acid group was 12.86 seconds as compared to the PT of 13.49 seconds in the saline group (p=0.073). Before surgery the mean INR in the tranexamic acid group was 1.04 as compared to the INR of 1.10 in the saline group (p=0.07). Before surgery the mean APTT in the tranexamic acid group was 30.23 seconds as compared to the APTT of 29.83 seconds in the saline group (p=0.614). Before surgery the mean fibrinogen level in the tranexamic acid group was 337.12mg/dl as compared to the fibrinogen of 331.16 mg/dl in the saline group (p=0.579). Before surgery the mean D-dimer level in the tranexamic acid group was 0.27mcg/ml as compared to the D-dimer of 0.29mcg/ml in the saline group (p=0.642).

Table:7 Comparison based on postoperative coagulogram at 6 hours between two groups					
Postoperative Coagulogram	**TXA Group**		**Saline Group**		**P-value**
	Mean	**SD**	**Mean**	**SD**	
Platelets	2.31	3.82	2.12	4.16	0.854
PT	13.08	1.09	13.53	1.29	0.069
INR	1.09	0.09	1.13	0.12	0.158
APTT	29.27	6.82	29.35	2.97	0.972
Fibrinogen	363.41	47.82	302.72	51.62	<0.001*
D-Dimer	0.30	0.19	0.27	0.16	0.511

**Statistically Significant Difference (P-value<0.05)*

In the immediate postoperative period at 6hours, mean number of platelets in the tranexamic acid group was 2.31 lakhs/µl as compared to the platelets of 2.12 lakhs/µl in the saline group (p=0.854), the mean PT in the tranexamic acid group was 13.08 seconds as compared to the PT of 13.53 seconds in the saline group (p=0.069), the mean INR in the tranexamic acid group was 1.08 as compared to the INR of 1.13 in the saline group (p=0.158) and the mean APTT in the tranexamic acid group was 29.27 seconds as compared to the APTT of 29.35 seconds in the saline group (p=0.972). Postoperatively, the mean fibrinogen level in the tranexamic acid group was 363.41mg/dl as compared to the fibrinogen level of 302.72 mg/dl in the saline group (p<0.001). Postoperatively, the mean D-dimer level in the tranexamic acid group was 0.30mcg/ml as compared to the D-dimer level of 0.27mcg/ml in the saline group (p=0.511).

Table:8 Comparison based on postoperative coagulogram at 24 hours between two groups					
Postperative Coagulogram	**TXA Group**		**Saline Group**		**P-value**
	Mean	**SD**	**Mean**	**SD**	
Platelets	1.96	2.97	1.91	3.45	0.952
PT	14.01	1.51	14.62	1.78	0.158
INR	1.10	0.29	1.15	0.42	0.594
APTT	29.67	6.07	29.42	2.52	0.836
Fibrinogen	340.13	41.82	332.17	48.15	0.497
D-Dimer	0.29	0.21	0.28	0.18	0.844

In the postoperative period at 24hours, mean number of platelets in the tranexamic acid group was 1.96 lakhs/µl as compared to the platelets of 1.91 lakhs/µl in the saline group

(p=0.952), the mean PT in the tranexamic acid group was 14.01 seconds as compared to the PT of 14.62 seconds in the saline group (p=0.158) , the mean INR in the tranexamic acid group was 1.10 as compared to the INR of 1.15 in the saline group (p=0.594) and the mean APTT in the tranexamic acid group was 29.67 seconds as compared to the APTT of 29.42 seconds in the saline group (p=0.836). Postoperatively, the mean fibrinogen level in the tranexamic acid group was 340.13mg/dl as compared to the fibrinogen level of 332.17 mg/dl in the saline group (p=0.497). Postoperatively, the mean D-dimer level in the tranexamic acid group was 0.29mcg/ml as compared to the D-dimer level of 0.28mcg/ml in the saline group (p=0.844).

DISCUSSION

In our study we found that there were no significant differences in PT, INR, aPTT, D-dimer at 6 and 24 hrs as compared to preoperative levels. However fibrinogen levels increased in tranexamic group and significantly decreased in saline group as compared to preoperatively. But different results were found by Ravi et al [9], coagulation profile in his meningioma patients was assessed preoperative, intraoperative, and postoperatively. The PT was within the normal limits in both the groups preoperatively, but they were found to be significantly prolonged in the placebo group intraoperatively and postoperatively ($P < 0.001$) as compared to tranexamic group. The intraoperatively and postoperative PT in patient receiving tranexamic acid were better than those who did not receive Tranexamic acid ($P = 0.002$, $P = 0.008$, respectively). This difference can be explained because of the fact that brain tissue is rich in tissue factor and these factors are released during tissue dissection in brain.[18] Meningiomas are also associated with high content of tissue plasminogen activator and studies have shown that these patients can have deranged coagulation in perioperative period [10,11]. Tranexamic acid use has shown that the PT did not increase further compared to placebo group. The preoperative APTT in both groups of patients in this study was within normal limits, but the intraoperative and postoperative values were prolonged in the placebo group compared to the tranexamic group ($P < 0.05$). Fibrinogen levels in our tranexamic acid group showed statistically significant elevation at 6 hrs postoperatively. This finding was consistent with findings of Ramya Vel et al [12], who found fibrinogen levels were significantly higher in TXA group compared to saline group at 3, 6 and 9 h ($P< 0.05$).

CONCLUSION

Tranexamic acid prevented decrease in the levels of fibrinogen and even increased levels fibrinogen significantly during the operative and postoperative period in brain tumour resection surgery.

Declaration by Authors

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