ORIGINAL ARTICLE ASIAN JOURNAL OF MEDICAL SCIENCES

Coagulation disorder in moderate to severe traumatic brain injuries

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Submitted: 08-07-2014 Revised: 16-09-2014 Published: 31-12-2014

ABSTRACT

Background: Significant proportions of patients presenting with moderate to severe traumatic brain injuries are diagnosed as having coagulation disorder and subsequent secondary brain injury. We evaluated the incidence of coagulopathy in patient with moderate to severe traumatic brain injury in this study. **Methods:** A prospective study of 100 patients with moderate to severe traumatic brain injury was carried out over a period of 2 years. Platelet count (PC), Bleeding time (BT), Clotting time (CT), Prothrombin time (PT), International Normalized ratio (INR), activated partial thromboplastin time (aPTT) and Fibrin degradation product (FDP) were measured at the time of admission and 12 hourly for 7 days. Daily D-dimer evaluation for DIC was performed in those who had abnormal value in any one of these parameters. Coagulopathy was classified as collectively 3 abnormal parameters. **Results:** Among the 100 patients, 43% had severe and 57% had moderate traumatic brain injury. Coagulopathy was detected in 63% of total patients; 76.7% (33/43) among severe traumatic brain injury and 52.7% (30/57) among moderate (p 0.013). Multivariate statistical analysis showed deranged FDP as a significant individual predictor of coagulopathy among others ($p<0.001$, Odds ratio 166.25; 95% confidence interval 31.7 ± 869.7). **Conclusion:** Coagulopathy is common in patients with moderate to severe traumatic brain injury. Evaluation of FDP can significantly predict coagulopathy in traumatic brain injury patients.

Key words: Traumatic brain injury, Coagulopathy, Fibrin Degradation Product, Secondary brain injury

Access this article online

Website: http://nepjol.info/index.php/AJMS

DOI: 10.3126/ajms.v6i3.10730

INTRODUCTION

Traumatic brain injury is a major cause of presentation to any neurosurgical centre. The outcomes of such injuries have been found to be affected by hemostatic derangements. Brain tissue is rich in thromboplastin, and activation of clotting pathways following traumatic brain injury is thought to occur leading to abnormal coagulation.[1] Many studies have suggested possible adverse effects of disseminated intravascular coagulation and other coagulopathies on outcome of the patients.[2-7] Post-traumatic coagulopathy, in particular, appears to be linked to secondary cerebral injury.[5,8] Although the extent of this process is yet to be elucidated fully, coagulation abnormalities are evident soon after trauma. This allows early identification of patients likely to suffer secondary complications and provides an opportunity to mitigate post traumatic disseminated intravascular coagulation and related pathologies in these patients.

MATERIALS AND METHODS

This prospective longitudinal analytical study was carried out from June 2010 to May 2012 at National Institute of Neurological and Allied Science, Bansbari, Kathmandu. All patients admitted to NINAS with moderate to severe traumatic brain injuries were included in the study. Patients on anti-coagulants before injury and previous history of coagulopathy were excluded from the study. Non-probability, purposive sampling technique was adopted to select the required samples.

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A total of 118 consecutive patients with moderate to severe traumatic brain injuries were enrolled in the study. Out of them, 18 patients died within 2 days of admission and hence were excluded from the study, leaving behind a cohort of 100 patients. Platelet count (PC), Bleeding time (BT), Clotting time (CT), Prothrombin time (PT), International Normalized ratio (INR), activated partial thromboplastin time (aPTT) and Fibrin degradation product (FDP) were measured at the time of admission and every 12 hourly thereafter for the first 7 days of admission. Patients with features suggestive of rapidly progressing coagulopathy were evaluated in the line of DIC by evaluating D-dimer every 24 hour. Any kind of therapeutic interventions for the management of the patient in the due course of study period were provided without bias. Such patients were still a part of the study thereafter.

Data were edited and analyzed using descriptive and inferential statistics. SPSS 16 was used for the analysis of data. All analyses with $p<0.05$ were regarded significant. Continuous variables were evaluated with the Wilcoxon two-sample test and [chi^2] test or two-sided Fisher's exact test wherever required. Values were reported as mean±standard deviation for continuous variables and as percentages for categorical variables.

RESULTS

Among the 100 patients included in the study, age of patients ranged from 7 years to 77 years with mean age being 32.7 ± 14.5 years. Males comprised 84% of the population with a significant preponderance in all age groups. Severity of traumatic brain injury was graded according to the GCS of the patient at the time of presentation. GCS of 3 to 8 were grouped as severe and GCS of 9 to 12 as moderate traumatic brain injury. Among the patients included in the study, 43 had severe and 57 had moderate traumatic brain injury.

Abnormality of at least one hemostatic parameter among BT, CT, PT/INR, aPTT, Platelet Count and FDP and D-dimer, was seen in 73 patients, however, only 63 developed coagulopathy as evident by abnormality of any three of the parameters collectively.

Only 2 patients developed prolonged BT during the study period and both of them developed coagulopathy subsequently. However, the correlation of raised BT and development of coagulopathy was not significant (p=0.529). Twelve patients developed prolonged CT and all them developed coagulopathy which was statistically significant (p=0.03). Sixty three patients developed prolonged PT out of which 54 (85.7%) developed coagulopathy ($p<0.001$) while 9 had other haemostatic parameters within normal limit. Nineteen patients developed prolonged aPTT and all of them developed coagulopathy which was statistically significant ($p<0.001$). Thrombocytopenia was noted in 59 patients among whom 55 (93.2%) developed coagulopathy and the correlation was statistically significant with $p<0.001$. FDP levels were raised in 59 patients and 57 (96.6%) of them developed coagulopathy ($p < 0.001$). D-dimer was evaluated in 73 patients who had at least one abnormal haemostatic parameter abnormality. Out of the 73 patients, 56 (76.7%) had deranged D-dimer out of which 55 (98.2%) developed coagulopathy which was statistically significant with $p<0.001$ as shown in Table 1.

Among the haemostatic parameters mentioned above, CT, PT, aPTT, Platelet Count, FDP and D-dimer were found to be significant predictors of coagulopathy. Multivariate statistical analysis among these parameters however showed FDP as a significant individual predictor of coagulopathy among others ($p<0.001$, Odds ratio 166.25; 95% confidence interval 31.7 ± 869.7).

Abnormality in any three of the haemostatic parameters, defined as Coagulopathy, were found in 63 patients. Among the patients with coagulopathy, 34.9% of patient developed coagulopathy within 24 hours of admission. Coagulopathy was diagnosed from the time of admission to up to 5 days from admission during the study period. Table 2 shows the time of diagnosis of coagulopathy in the cohort of patient studied.

Among the patients developing coagulopathy, 34.9% (n=22) were in 20-30 years age group. When the age groups of patients were analyzed for development of coagulopathy, no significant correlation was found (p=0.735). Table 3 shows the development of coagulopathy in different age groups.

Table 1: Deranged haemostatic parameters and development of coagulopathy

Haemostatic parameters	Total number	Number of abnormality	Number of coagulopathy (%)	P-value
BT	100	2	2	0.529
CT	100	12	12	0.03
PT	100	63	54 (87)	0.000
aPTT	100	19	19	0.000
Platelet count	100	59	55 (93.2)	0.000
FDP	100	59	57 (96.6)	0.000
D-dimer	73	56	55 (98.2)	0.000

Table 2: Day of onset of coagulopathy

Day of onset of coagulopathy	Number (%)
1st day	22 (34.9)
2nd day	21 (33.3)
3rd day	8 (12.7)
4th day	4 (6.4)
5th day	8 (12.7)
Total	63

Coagulopathy was equally common in both the genders. Among the males, 63.1% and 62.5% of among females developed coagulopathy (p=0.964) as shown in Table 4.

Coagulopathy was present in 76.7% of severe traumatic brain injury patients compared to 52.7% in moderate traumatic brain injury (p=0.013) as shown in Table 5.

DISCUSSION

This prospective study included a wide range of patients, from 7 years to 77 years, and different types of head injuries. There was a striking predominance of male patients, total 84%, consistent with other studies as well.[4,9] A study by Talving P[10] including 436 patient with traumatic brain injury showed 78% males with overall mean age of 37 ± 20 years. Affonseca[11] had 69.1% males in her study too. Present study showed that coagulopathy was most common in age group of 20-30 as 22 patients in that age group developed coagulopathy. Coagulopathy was equally common in both genders as 63.1% of all males and 62.5% of all females developed coagulopathy.

As mild traumatic brain injuries were excluded from present study, moderate traumatic brain injury patients comprised the bulk of cohort (57%). Association of severity of traumatic brain injury with coagulopathy was found to be statistically significant as 76.7% of patients with severe head injuries in present study developed coagulopathy compared to 52.5% of patients with moderate head injuries. Affonseca[11] also included moderate to severe head injuries in his study which consisted of 37.2% patients with moderated traumatic brain injury and 62.8% severe traumatic brain injury and, similar to our findings, he had shown association of coagulopathy with GCS of the patient. Talving[10], in his study of 436 patients with traumatic traumatic brain injury, has shown statistically significant association of development of coagulopathy with GCS of the patient.

Table 3: Coagulopathy in different age groups

Age group	Coagulopathy		Total	P
	Absent	Present		
0-10	2	1	3	0.735
10-20	5	11	16	
20-30	12	22	34	
30-40	10	13	23	
40-50	4	5	9	0.735
50-60	4	7	11	
60-70	0	2	2	
70-80	0	2	2	
Total	37	63	100	

Table 4: Coagulopathy in different gender

Gender	Coagulopathy		Total	P
	Absent (%)	Present (%)		
Female	6 (37.5)	10 (62.5)	16	0.964
Male	31 (36.9)	53 (63.1)	84	0.964
Total	37	63	100	

Table 5: Coagulopathy in patients with moderate and severe head injuries

Severity of injury (GCS)	Coagulopathy		Total	P
	Absent (%)	Present (%)		
Severe (3-8)	10 (23.3)	33 (76.7)	43	0.013
Moderate (9-12)	27 (47.3)	30 (52.7)	57	0.013
Total	37	63	100	

The incidence of coagulopathy is difficult to define with the frequency ranging from 17% to 76% of traumatic brain injury depending upon the study group and laboratory criteria.[3,12-15] The wide variation may be due to the bias of the selection of patients, diversity of injury severities, varying criteria used to define coagulopathy, different sensitivities of the clotting tests used, different times at which coagulation was tested after injury and definition of coagulation abnormalities followed. Pondaag[3] defined coagulopathy as a fibrinogen level below 130 mg/dl and FDP values greater than 40 gm/ml. Halpern[6] defined coagulopathy in his study as PT above normal range of 10.3-13.4 seconds. Lozance,[4] Selladurai[8] and Olson[9] defined coagulopathy as a DIC score below 6. Preston[15] defined coagulopathy as decreased platelet counts and FDP, aPTT and PT increased from normal values. We have, in present study, defined coagulopathy as abnormality of three or more than three hemostatic parameters among BT, CT, PT, aPTT, FDP and D-Dimer.

Abnormality of at least one parameter was seen in 73 patients in the present study, which corroborates to the findings of Selladurai[8] who found that 71% of patients had at least one hemostatic parameter abnormal. However, only 63% in our study developed coagulopathy as evidenced by abnormality of any three haemostatic parameters, compared to 38% in the study by Selladurai.[8] This could be attributed to different criteria used for diagnosis of coagulopathy. Similar to our findings, Affonseca[11] observed coagulopathy in 77% of patients and that its presence was closely related to the severity of traumatic brain injury. Kuo[5] found in his study that the incidence of abnormal coagulation following traumatic brain injury was 72.1%. In patients who succumb to the injury, the incidence was 100% whereas it was 66% in those who survived. This indicates higher mortality among patients who develop coagulopathy after traumatic traumatic brain injury. An abnormality in the PT, aPTT, or Platelet count at admission was present

in 55% of 253 patients studied by Stein.[7] Harhangi,[17] in his review, found that one out of three patients with traumatic brain injury developed coagulopathy.

Abnormal Platelet count and FDP levels were seen in 59% patients in our study reflecting that these are the common parameters to be deranged in traumatic brain injury patients. In the study by Kuo,[5] 59% patients had abnormal D-dimer and 24.5% had abnormal aPTT making them commonest abnormalities. Contrary to our findings, they had thrombocytopenia in only 3.3% of patients. Statistically significant association between individual coagulopathy parameter and development of coagulopathy in present study was seen in patients with abnormal CT, PT, aPTT, Platelet counts, FDP and D-dimer. Multivariate study among these parameters showed that only FDP had statistically significant predictive capacity for development of coagulopathy.

Lustenberger[16] found in his study that coagulopathy occurred 23.1 ± 2.2 hours after admission and early coagulation abnormalities occurred within 12 hours of admission. He has shown that coagulopathy may ensue as late as 5 days after injury. Similarly, Talving[10] diagnosed coagulopathy on an average of 20.8 hours after admission, minimum being 10 minutes and maximum time to develop coagulopathy being 7.4 days. In this study as well, most patients with coagulopathy, 34.9%, developed it within 24 hours of admission. Coagulopathy was diagnosed from the time of admission to up to 5 days after admission in our study.

CONCLUSION

Traumatic brain injury is often complicated by presence of coagulopathy. In moderate to severe head traumatic brain injury, coagulopathy is present in about 2/3rd of the patients. Coagulopathy was found to develop from the time of onset of injury to up to 5 days after injury. Coagulopathy was equally common in both the genders and was not affected by the mode of injury. This study showed that evaluation of FDP can significantly predict coagulopathy in traumatic brain injury patients.

REFERENCES

1. Nekludov M, Bellander BM, Blombäck M and Wallen HN. Platelet Dysfunction in Patients with Severe Traumatic Brain Injury. J Neurotrauma 2007;1699-1706.
2. Lannoo E, Van Rietvelde F and Colardyn F. Early predictors of mortality and morbidity after severe closed head injury. J Neurotrauma 2000; 17:403-414.
3. Pondaag W. Disseminated intravascular coagulation related to outcome in head injury. Acta Neurochir (Wien) suppl 1979; 28:98-102.
4. Lozance K, Dejanov I and Mircevski M. Role of coagulopathy in patients with head trauma. J Clin Neurnsci 1998; 5(4):394-398.
5. Kuo JR, Chou TJ and Chio CC. Coagulopathy as a parameter to predict the outcome in head injury patients-analysis of 61 cases. J Clin Neurosci 2004; 11(7):710-714.
6. Halpern CH, Reilly PM, Turtz AR and Stein SC. Traumatic Coagulopathy: The Effect of Brain Injury. J Neurotrauma 2008; 25:997-1001.
7. Stein SC, Young GS, Talucci RC, Greenbaum BH and Ross SE. Delayed brain injury after head trauma: Significance of coagulopathy. Neurosurgery 1992; 30: 160-165.
8. Selladurai BM, Vickneswaran M, Duraisamy S and Atan M. Coagulopathy in acute head injury: A study of its role as a prognostic indicator. Br Jour Neurosur 1997; 11(5):398-404.
9. Olson JD, Kaufmann HH, Moake J, O'Gormann TW, Hoots K and Wagner K. Incidence and significance of coagulation abnormalities in patients with head injury. Neurosurgery 1989; 24:825-832.
10. Talving P, Benfield R, Hadjizacharia P, Inaba K, Chan LS and Demetriades D. Coagulopathy in Severe Traumatic Brain Injury: A Prospective Study. J Trauma 2009; 66(1):55-62.
11. Affonseca CA, Carvalho LF, Guerra SD, Ferreira AR and Goulart EM. Coagulation disorder in children and adolescents with moderate to severe traumatic brain injury. J Pediatr (Rio J) 2007; 83(3):274-282.
12. Penick GD and McLendon WW. Disorders of the hemostatic mechanism. Int Rev Med 1960; 173:491- 496.
13. Kumura E, Sato M and Fukuda A. Coagulation disorders following acute head injury. Acta Neurochir (Wien) 1987; 85:23-28.
14. Kaufmann HH, Moake JL, Olson JD, Miner ME, du Cret RP and Pruessner JL. Delayed and recurrent intracranial hematoma related to disseminated intravascular coagulation and fibrinolysis. Neurosurgery 1980; 7:445-449.
15. Preston FR, Malia RG, Sworn MJ, Timperley WR and Blackburn ER. Disseminated intravascular coagulation as a consequence of cerebral damage. J Neurol Neurosurg Psychiatry 1974; 37:241-248.
16. Lustenberger T, Talving P, Kobayashi L, Inaba K, Lam L, Plurad D and Demetriades D. Time course of coagulopathy in isolated severe traumatic head injury. Injury 2010; 9(41): 924-928.
17. Harhangi BS, Kompanje EJO, Leebeek FWG and Maas AIR. Coagulation disorders after traumatic brain injury. Acta Neurochir (Wien) 2008; 150:165-175.

Authors Contribution:
AS - Designed the study, collected and analyzed the data, drafted the manuscript, and reviewed the manuscript; **RMJ -** Contributed in collection of data and editing of manuscript; **UPD -** Guided the study, Reviewed the data and manuscript.

Source of Support: Nil, **Conflict of Interest:** None declared.