



Coagulopathy in multiple traumas

Çoklu travmalarda koagülopati

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BACKGROUND

This study aimed at analyzing the effect on coagulation of head trauma and other local traumas in patients exposed to multiple traumas in the early stage, and also the relations of Glasgow Coma Scale (GCS) and Injury Severity Score (ISS) with coagulation parameters in these patients.

METHODS

Fifty consecutive patients (9 women, 41 men) with multiple traumas were included in this study. The GCS, ISS and coagulation parameter levels were measured. Presence of a correlation between GCS and ISS with coagulation parameters was analyzed. Patients exposed to multiple traumas were assessed in four categories as the patients with no significant traumas (A), only head traumas (B), head trauma and other local traumas (C), and no head traumas but other local traumas (D).

RESULTS

A marked relationship was found between ISS and international normalized ratio (INR), activated partial thromboplastin time (aPTT), D-dimer, fibrin degradation product (FDP), antithrombin (AT), and fibrinogen ($p<0.05$). There was a statistically significant difference between Group C and the other groups in INR, D-dimer, fibrinogen, aPTT, and AT parameters ($p<0.05$). There was also a statistically significant difference between the groups with and without head trauma in INR, D-dimer and fibrinogen ($p<0.05$).

CONCLUSION

The coagulation parameters were observed to diverge in patients with head trauma, but in cases with head injuries accompanying other local traumas, more coagulation parameters became abnormal.

Key Words: Blood coagulation; Injury Severity Score; multiple traumas.

AMAÇ

Erken dönemde genel vücut travmalı (GVT) hastalarda, kafa travmasının ve diğer bölge travmalarının koagülasyon üzerine etkisi ve bu hastalarda koagülasyon parametreleri ile Glasgow Koma Skoru (GCS) ve travma şiddet skoru (ISS) ilişkilerinin araştırılması amaçlandı.

GEREÇ VE YÖNTEM

Acil servise GVT ile başvuran, 50 hasta (9 kadın, 41 erkek) çalışmaya alındı. Hastaların GCS, ISS, koagülasyon parametreleri düzeyleri belirlendi. GCS, ISS ile koagülasyon parametreleri arasında korelasyon değerlendirildi. Hastalar; önemli bir travma tespit edilmeyen (A), sadece kafa travması olanlar (B), kafa travması ve diğer bölge travması olanlar (C), kafa travması olmayan ancak diğer bölge travmaları olanlar (D) olarak ayrıldı.

BULGULAR

ISS ile uluslararası normalize oranı (INR), aktif parsiyel tromboplastin zamanı (aPTT), D-dimer ve fibrin yıkım ürünleri (FDP) düzeyleri arasında pozitif, ISS ile antitrombin (AT) ve fibrinojen düzeyleri arasında negatif bir ilişki saptandı ($p<0,05$). C grubuyla diğer gruplardaki INR, D-dimer, fibrinojen, aPTT, AT parametreleri karşılaştırıldığında istatistiksel anlamlılık saptandı ($p<0,05$). Kafa travması olan ve olmayan gruplar arasındaki INR, D-dimer ve fibrinojen parametrelerinde istatistiksel anlamlılık saptandı ($p<0,05$).

SONUÇ

Kafa travması olan hastalarda koagülasyon parametrelerinin bozulduğu, ancak kafa travmasına diğer bölge travmaları eşlik ettiğinde koagülasyon parametrelerinin daha fazla anormalleştiği belirlendi.

Anahtar Sözcükler: Koagülasyon; travma şiddet skoru; genel vücut travması.

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Despite the latest developments in intervening trauma, coagulopathy, which is resistant and life-threatening, remains a major problem and an unbeatable rival; accordingly, when present, it results in the death of the traumatized patient.^[1] The release of mediators after tissue trauma activates multiple humoral systems including coagulation, fibrinolysis, complement, and kallikrein cascades. Certain injuries in particular are known to interfere with the coagulation system. Brain injuries have been shown to lead to coagulopathy, caused in part by the release of brain tissue thromboplastins after neuronal injury.^[2,3] Similarly, long bone fractures may be associated with disorders of the hemostatic mechanisms.^[4] Coagulation disorders in brain injury are complex and can be characterized by a combination of coagulopathy and hypercoagulability. Hypercoagulability is the increased capacity of formation of fibrin in the blood vessels. The brain tissue contains large amounts of thromboplastin. This substance is released in high concentration into the blood stream after physical trauma to the parenchyma, causing disturbance in coagulation processes. Coagulopathies are independently correlated to an increased risk of mortality in patients with moderate to severe traumatic brain injury.^[2,5-9] In local traumas other than head injuries, an early coagulopathy is possible through the trauma itself and the release of mediators related with traumas, or through the aggregation of iatrogenic interventions.^[10-16]

In this study, we aimed at analyzing the effects of head traumas together with other local traumas on platelet counts (plt), activated partial thromboplastin time (aPTT), international normalized ratio (INR), antithrombin (AT), plasminogen activator inhibitor-1 (PAI-1), fibrin degradation products (FDP), D-dimer, and fibrinogen levels, all of which are among the coagulation parameters. In addition, we aimed at establishing the relation between the Glasgow Coma Scale (GCS) and Injury Severity Score (ISS) and these coagulation parameters. We also stress the necessity of monitoring the coagulation parameters in patients with multiple traumas in the early stages in an emergency room.

MATERIALS AND METHODS

The study protocol was approved by the ethics committee of the medical faculty. Prospectively, patients with multiple traumas who presented to İnönü University Hospital's emergency department over a four-month period (November 2003 - February 2004) within six hours of trauma were enrolled in this study. The cases were selected among patients without any medication history or a prior illness that could interfere with coagulation parameters. On admission of the traumatized patients, peripheral venous blood samples were taken from each patient to determine the plt,

aPTT, INR, AT, PAI-1, FDP, D-dimer, and fibrinogen levels. GCS was calculated. Injured areas were then established with the help of physical examination and imaging methods, and ISS was calculated. Correlations between GCS, ISS and coagulation parameters were analyzed. In addition, patients exposed to multiple traumas were divided into four categories as those with: no significant traumas (with soft tissue traumas) (A), only head traumas (B), head trauma and other local traumas (C), and no head traumas but other local traumas (D). Patients were also categorized as those with only head traumas and with no head traumas.

Statistical Analysis: GCS, ISS, Plt, INR, aPTT, AT, D-dimer, fibrinogen, PAI-1, and FDP values were compiled using SPSS for Windows® v.11.5 (SPSS Inc, Chicago, USA) software. Spearman's rho (r_s) correlation coefficients were calculated. In addition, GCS, ISS, plt, INR, aPTT, AT, D-dimer, fibrinogen, PAI-1, and FDP values were analyzed using Kruskal-Wallis and the Mann-Whitney U test. Findings were considered statistically significant at $p < 0.05$.

RESULTS

During the study period, 50 patients (82% male, mean age 37.8 ± 19.7 , range 1-79 years) with multiple traumas were enrolled in this study. Nine patients (4.5%) were younger than 18 years, with a mean age of 8.8 ± 5.7 years. Patients were divided into four groups according to the region of trauma (with no significant traumas (A), with only head traumas (B), with head trauma and other local traumas (C), and with no head traumas but other local traumas (D)) (Table 1). A significance was established in multiple comparisons among the groups between INR, D-dimer, fibrinogen, aPTT, and AT ($p < 0.05$). In dual comparisons, a significance level of $p < 0.05$ was found between A/C, A/D, B/C, C/D in INR; A/C, B/C, C/D in D-dimer; A/B, A/C, A/D, C/D in fibrinogen; A/C, B/C, C/D in aPTT; and A/C, B/C, C/D in AT. We observed more divergence in coagulation parameters of patients in Group C with head traumas and other local traumas. Patients with head injury ($n=27$) and without head trauma ($n=23$) had INR, D-dimer and fibrinogen levels of 2.4 ± 3.3 and 1.1 ± 0.1 ; 1496.1 ± 541.5 and 965.3 ± 649.4 $\mu\text{g/L}$; and 158.6 ± 93.5 and 270.5 ± 87.9 mg/dL , respectively (p values: 0.026, 0.008, 0.000, respectively). A marked positive relationship was found between ISS and INR, aPTT, D-dimer and FDP levels ($p < 0.05$). In addition, a negative relationship was found between ISS and AT and fibrinogen levels ($p < 0.05$). PAI-1 and plt levels did not correlate with ISS (Table 2). A marked negative relationship was found between GCS and INR, aPTT and D-dimer levels ($p < 0.05$). In addition, a positive relationship was found between GCS and fibrinogen level ($p < 0.05$). PAI-1, AT, FDP, and plt did not correlate with GCS (Table 3).

Table 1. Coagulation parameters according to trauma regions

Significant parameters	With no significant traumas A (n=8)	With only head trauma B (n=13)	With head trauma and other local traumas C (n=14)	With no head trauma but other local traumas D (n=15)	p
INR	1.09±0.08	1.22±0.25	3.53±4.38	1.23±0.13	0.000
D-dimer (µg/L)	811.2±618.4	1285±535	1639±506	1047±671	0.009
Fibrinogen (mg/dL)	330.2±56.5	195.31±98.4	124.6±77.1	238.6±86.2	0.000
aPTT (sec)	25.6±4.0	26.7±6.6	55.8±38.3	35.6±35.2	0.037
AT (%)	82±10	77±16	60±21	77±13	0.02

INR: International normalized ratio; aPTT: Activated partial thromboplastin time; AT: Antithrombin.

DISCUSSION

Post-traumatic activation of the blood coagulation system simultaneously with tissue destruction is a vital physiological defense mechanism. Strong inhibitor formation and (-) feedback mechanism protect against over-reactions and maintain a balance between hemorrhage and intravascular fibrin formation.^[16] Coagulopathy upon emergency admission was present in one-third of the patients studied.^[10,14] Patients with traumatic brain injury are at risk of developing abnormalities of both coagulation and fibrinolysis.^[3,17-20] In our study, among the coagulation parameters, the INR, D-dimer, and fibrinogen levels were found to be affected in patients with head trauma. The nature of the coagulation abnormalities differs between patients with isolated head injury and those with multiple injuries.^[21] Recently, Gando and co-workers^[22] demonstrated higher levels of tissue factor in head-injured patients than in non-head-injured trauma patients. To date, coagulopathy following trauma has been attributed mainly to the amount of bleeding itself and subsequently to trauma-hemorrhage associated dilution phenomena from intravenous fluid therapy, massive blood transfusion, progressive hypothermia, and acidosis.^[23-27] There are numerous studies concerning the fact that head traumas mar coagulation parameters. Studies on

coagulation disorders in patients with multiple traumas also exist; however, there are no sufficient data categorizing whether head traumas and other regional traumas accompany multiple traumas and studying their effect on coagulation. In our study, we found more divergence in coagulation parameters at the time of admission in patients with both head trauma and other local traumas. This makes the monitoring of coagulation parameters important not just in isolated head traumas in terms of initial coagulopathy but also in other local traumas together with head traumas. Furthermore, a close follow-up of coagulation parameters in the early stages might prove to be helpful in early treatments that cure coagulation disorders. In addition to brain traumas, long bone fractures may be associated with disorders of the hemostatic mechanism.^[4] In this study, we were unable to evaluate the effects of other regional traumas on coagulation parameters separately due to the small number of cases. Patients with multiple traumas were assessed in the emergency room in the early stages. Postmortem analyses were not carried out. Brohi et al.^[10] found that coagulopathy might develop independently from fluid replacement in patients with acute traumas. Tissue injury leads to release of tissue factor, which activates the coagulation pathways. Extensive tissue factor release that results in widespread or systemic activation eventuates in a consumption co-

Table 2. Correlation (Spearman’s rho coefficient, r_s) between ISS and coagulation parameters in patients with multiple traumas

ISS	r _s	p
PAI-1 (IU/ml)	0.047	0.74
AT (%)	-0.388	0.005
D-dimer (µg/L)	0.552	0.000
Fibrinogen (mg/dL)	-0.608	0.000
FDP (µg/mL)	0.340	0.016
INR	0.575	0.000
aPTT (sec)	0.290	0.041
Plt (x10 ⁹ /L)	0.027	0.85

AT: Antithrombin; FDP: Fibrinogen degradation product; INR: International normalized ratio; aPTT: Activated partial thromboplastin time; Plt: Platelets.

Table 3. Correlation (Spearman’s rho coefficient, r_s) between GCS and coagulation parameters in patients with multiple traumas

GCS	r _s	p
PAI-1 (IU/ml)	-0.092	0.52
AT (%)	0.279	0.05
D-dimer (µg/L)	-0.339	0.016
Fibrinogen (mg/dL)	0.386	0.006
FDP (µg/mL)	-0.098	0.49
INR	-0.338	0.016
aPTT (sec)	-0.308	0.029
Plt (x10 ⁹ /L)	-0.118	0.41

GCS: Glasgow Coma Scale; PAI-1: Plasminogen activator inhibitor-1; AT: Antithrombin; FDP: Fibrinogen degradation product; INR: International normalized ratio; aPTT: Activated partial thromboplastin time; Plt: Platelets.

agulopathy.^[12,13] In disseminated intravascular coagulations (DIC) associated with massive trauma, plasma fibrinogen level, aPTT, PT, platelet count, and estimates of FDP or D-dimer are cornerstones on which the diagnosis of DIC is based. Thrombocytopenia is an early and consistent sign of acute DIC.^[28] In our cases, thrombocyte levels at first showed no statistically significant differences between the groups. Thus, we can suppose predisposition to coagulopathy in subjects without clinical findings of acute DIC. Excessive fibrinolysis may also be a result of extensive tissue trauma.^[11,16] Levels of FDP, including cross-linked FDPs (D-dimer), are usually increased in the presence of acute venous thromboembolism.^[29] In our study, we established that coagulation parameters diverge as the severity of traumas increase. Inflammatory mediators have been implicated in activation of the coagulation pathways.^[30,31] Gando et al.^[32] demonstrated that plasmin activation and its inhibition after isolated head injury are similar to those in trauma patients without head injury. In a study by Becker and colleagues,^[33] a decrease in fibrinogen, AT and PAI-1 was observed on admission in children with severe head trauma. In our study, we did not establish a relation between PAI-1 and trauma areas with ISS and GCS. AT showed a decrease in Group C on a higher level. As the severity of trauma increases based on ISS, AT consumption also grows accordingly. Brohi et al.^[10] estimated the cut-off value as >45. Magele et al.^[34] found that patients with coagulopathy had an ISS ≥ 16 upon hospital admission, and frequency of coagulopathy increased with higher ISS scores. In our patient group, coagulopathy increased in conjunction with an increase in the ISS. Due to the small number of cases, we were unable to establish a cut-off value. Children with GCS <14 after traumatic brain injury are at greater risk for coagulopathy, and the risk is even further increased at lower GCS levels.^[35] In our study, we found a significant relation between GCS and coagulation parameters in terms of aPTT, INR, D-dimer, and fibrinogen levels, and fibrinolytic system activation increased as GCS decreased. We came to the conclusion that these scores can be utilized in predicting coagulation disorders due to the significant relation between coagulation parameters and ISS and GCS.

In conclusion, coagulopathy develops for many reasons in patients with multiple traumas. Coagulation parameters must be monitored closely in the initial stage in the presence of head trauma together with other local traumas. There is a necessity for prospective studies on the course of treatment and how the results are affected in patients with coagulation disorder in an early stage.

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