Compliance of Trauma Team Leaders with Administering Tranexamic Acid for Significant Hemorrhage

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Background: Hyperfibrinolysis forms an integral component of the acute coagulopathy of trauma. This process can be blocked by antifibrinolytic drugs such as tranexamic acid (TXA).

Objective: To evaluate the current compliance rate of trauma team leaders (TTL) of administering TXA for eligible patients.

Design: A Retrospective Study.

Setting: Bahrain Defence Force Hospital, Bahrain.

Method: A retrospective clinical study was performed from October 2016 to March 2017. The patients data were retrieved from the trauma registry and only those ≥18 years old were included. Sixty-one patients were seen in the trauma bay. The compliance rate of administering TXA was documented. The inclusion criteria were as follows: adult trauma patients (>18 years) with evidence of ongoing hemorrhage on arrival to the trauma bay suggested by: systolic blood pressure (SBP) ≤ 90, heart rate (HR) ≥ 110, and patients transfused with 1 unit of O-PRBC (packed red blood cells). The exclusion criteria included age ≤18, hypersensitivity to TXA or any of its excipients, and frank hematuria.

Result: Twenty-six patients out of 58 (44.8%) had met the inclusion criteria and were supposed to receive TXA according to hospital guidelines. Only 8 (30.7%) received TXA as part of their initial resuscitation in the trauma bay.

Conclusion: A low compliance rate was observed. Current efforts can be directed towards adjusting guidelines and reinforcing seminars to improve adherence. Other interventions can be implemented in the long-term.

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Trauma is one of the leading causes of deaths worldwide, particularly in those under the age of 45[1,2]. Severe hemorrhage due to trauma is associated with preventable death[3]. Therefore, hemostatic agents have been widely used for minimizing post-traumatic bleeding.

Excessive fibrinolysis contributes to the coagulopathy following trauma and this accounts for the increased mortality and transfusion requirement[4]. It is suggested that hypoxia, hypoperfusion, and up-regulation of tissue plasminogen activator (tPA) act to disrupt the homeostatic balance towards 'hyperfibrinolysis'[4]. This process can be blocked by antifibrinolytic drugs such as tranexamic acid (TXA) which blocks the formation of plasmin from plasminogen; thus preventing clot degradation and reducing excessive bleeding[4].

TXA has various medical indications, one of which is the reduction of hemorrhage in elective surgical procedures[4]. Since similar hemostatic responses are elicited by surgery and trauma, an increased use of TXA has been observed in trauma patients undergoing elective surgery[4].

A study in 2010 involving 20,211 adult trauma patients revealed that mortality and bleeding were also significantly reduced after the use of TXA[1]. Another study revealed that mortality was lower in those who received TXA, especially in those who required massive transfusions[5].

Many hospitals have integrated the use of TXA in their trauma protocols and several guidelines recommended its early use in trauma patients[6]. Bahrain Defence Force (BDF) Hospital recommended TXA use in the management of the bleeding trauma patient[7].

The aim of this study is to evaluate the current level of compliance of trauma team leaders (TTL) of administering TXA for eligible patients. No previous study evaluated the use of TXA in Bahrain.

METHOD

A retrospective clinical study was performed from October 2016 to March 2017. The patients data were retrieved from the trauma registry and only those ≥18 years old were included. Sixty-one patients were seen in the trauma bay. However, both medications and transfusions were not available as part of the trauma registry data. The inclusion criteria were as follows: adult trauma patients (>18 years) with evidence of ongoing hemorrhage on arrival to the trauma bay suggested by: SBP ≤90, HR ≥110, and patients transfused with 1 unit of O-PRBC

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(packed red blood cells). The exclusion criteria included age ≤18, hypersensitivity to TXA or any of its excipients, and frank hematuria.

Trauma sheet records were reviewed. These sheets documented the complete management details of each patient, including transfusions and medications. Data regarding blood transfusion and TXA were documented. However, the sheets of three patients were unavailable; therefore, they were excluded. The sample size was 58 patients. Twenty-six patients met the inclusion criteria and were included in this study.

All data collected were entered into an excel spreadsheet. Those who met at least one of the inclusion criteria (SBP ≤90, HR ≥110, and blood transfusion) were assessed for TXA administration. The compliance rate was calculated as a percentage of those who received TXA from those eligible.

Data were also analyzed using SPSS. Chi-square test and Fisher's exact tests were used to study the association between categorical data such as each of the 3 eligibility criteria against the likelihood of TXA administration.

RESULT

Twenty-six patients out of 58 (44.8%) had met the inclusion criteria and were supposed to receive TXA according to the guidelines. However, only 8 (30.7%) received TXA. Two (7.7%) patients met all 3 inclusion criteria, 5 (19.2%) met 2 of the criteria and 1 (3.8%) met only one criterion. The eight (30.7%) patients who received TXA were transfused with O negative, 5 (19.2%) had an HR≥110 and 4 (15.4%) had an SBP≤90, see figure 1. Statistical significance obtained through Fisher's exact existed between SBP and TXA, P-value 0.008. Fisher's exact test showed no statistical significance between heart rate and TXA, P-value 0.251).

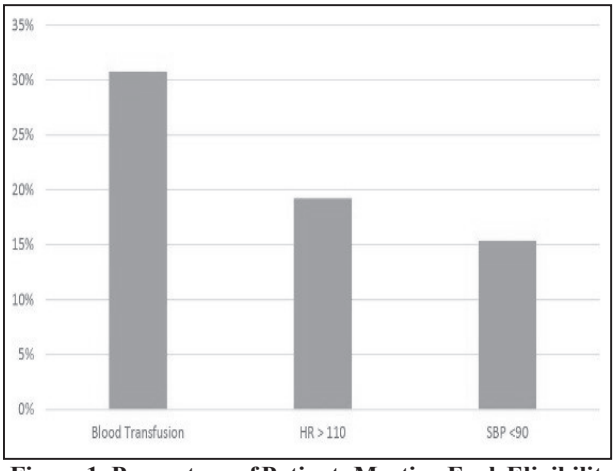

Figure 1: Percentage of Patients Meeting Each Eligibility Criteria in the Group Who Received TXA (n=8)

Table 1 shows age, injury severity score (ISS), and Glasgow coma scale (GCS) were almost the same in both groups. However, those who received TXA were more hypotensive (111.2 mmHg compared to 128.7 mmHg). Patients who did not receive TXA were more tachycardiac (118.6 bpm compared to who those who received, 110.2 bpm). Blunt trauma was high in both groups, as well as being the most common type of injury.

Female to male ratio in patients who met TXA criteria (N=26) was 23:3 and the age range was from 18 to 54 years.

Table 1: Patients Characteristic According to TXA Administration

	TXA	No TXA	Total
Total (%)	8 (30.7%)	18 (69.2%)	26 (100%)
Age, mean ±SD	30.3± 11.3	29.6± 2.1	29.8±1.8
Injury severity score (ISS), mean±SD	24.3±7.6	24.0±4.8	24.1 ±3.9
Heart rate bpm, mean±SD	110.2±9.4	118.6±5.6	116.0±4.8
Systolic blood pressure (mmHg), mean±SD	111.2±13.8	128.7±7.2	123.3±6.6
Received transfusion (%)	8 (53.3%)	7 (46.6%)	15 (100%)
Blunt trauma (%)	6 (37.5%)	10 (62.5%)	16 (100%)
Penetrating trauma (%)	1 (33.3%)	2 (66.6%)	3 (100%)
Other injury type (%)	1 (14.2%)	6 (85.7%)	7 (100%)
Glasgow coma scale (GCS), mean ±SD	11.3±1.5	11.1±1.1	11.1±0.8

DISCUSSION

In our study, the compliance rate of TXA was 30.7%. Other studies revealed TXA compliance rates of 66%, 38%, 27.1% and 18%[8,9,10,11].

Several factors were previously identified that might have contributed to the low compliance encountered. Some of which are inadequate documentation of TXA administration[10]. In addition, it is the stressful nature of dealing with traumatic patients, where the physicians tend to follow a 'heuristic' decision-making processes in order to minimize cognitive load[8]. In addition, the uncertainty attached to trauma care tends to create gaps between knowledge and routine practice[8].

The Bahrain Defence Force Hospital (BDF) guideline recommended TXA administration within 8 hours of injury. However, the optimum time interval for TXA administration remains unsettled. A study found that both early treatment (≤ 1 h) and treatment within 1 and 3 hours significantly reduced the risk of death, but treatment after 3 hours increased the risk of death due to bleeding[12]. NICE guidelines published in 2016 recommend: "Management of hemorrhage in pre-hospital and hospital settings". They had recommended not to use TXA 3 hours after injury, unless there's evidence of hyperfibrinolysis[13].

A controversy exists in the literature between the recommended time interval for TXA administration due to the early Disseminated Intravascular Coagulation (DIC) phase with the fibrinolytic phenotype in trauma patients; a phase of fibrinolytic shutdown follows by several hours where the use of antifibrinolytic could be detrimental[6]. This may account for the low compliance levels, where the TTL faces an uncertainty regarding the positive effect of TXA usage.

Furthermore, concerns about possible adverse events associated with TXA such as venous thromboembolism (VTE) might have impeded its administration. Various studies have looked into TXA and VTE; it remains controversial and further research is required to address the subject[6]. Barriers identified by previous studies included staff being unfamiliar with the medication[9].

The low compliance rate in this study could be attributed to the guideline which states "at discretion of the trauma team leader based on clinical suspicion/objective evidence of on-going hemorrhage". This statement is subjected to the interpretation

of the TTL clinical judgment. In our study, blood transfusion was the main indication for TXA administration.

The compliance was higher in those who fulfilled more than one eligibility criteria, as the results show that 7 (87.5%) of those who received TXA have met at least 2 criterions and only one (12.5%) met a single criterion. Similar results were obtained in a study which showed that as compliance rates increased, more criteria were fulfilled[10].

The trauma registry is relatively new in the BDF hospital, data entered was for a 6-month period; hence, the sample was limited. A bigger sample would be advisable in a future study.

It is recommended to add a third criterion to the guidelines for those transfused with at least 1 unit of PRBC. The administration of TXA is currently part of the BDF hospital's massive transfusion protocol.

Specific measures of hyperfibrinolysis (HF) such as thrombo-elastography and thrombo-elastometry can be applied as a point of care testing to support the clinical decision of TXA administration; however, given the dynamic process of the coagulopathy in acute trauma, significant limitations exist within these techniques[14].

Several studies had examined the benefit of pre-hospital TXA in civilian and military settings, but none provided any robust evidence[15]. Nevertheless, certain ambulance services such as the Royal Ambulance Service in the UK have implemented its use in the pre-hospital civilian setting, and policies for pre-hospital TXA use were incorporated in the emergency medical services of several armies such as the British, French and Norwegian[15].

Since most studies suggested that giving TXA within 3 hours of injury is most beneficial, theoretically, pre-hospital TXA would facilitate adhering to the recommended time interval and thus, having better outcomes. Further evidence is needed to support this recommendation, and this might be provided by two ongoing studies examining this subject which are "STAAMP" and "PATCH" [15]. Both are multi-center RCT trials which are expected to provide a valuable evidence that is needed in this area.

CONCLUSION

Overall, a low compliance rate was observed in BDF hospital. However, results were comparable with other reported TXA compliance rates. Current efforts can be directed towards adjusting guidelines and reinforcing seminars to improve adherence. Other interventions can be implemented in the long-term.

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