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Review Article

Trauma-induced coagulopathy in pediatric patients: an evidence-based approach

Coagulopatia do trauma em pacientes pediátricos: uma abordagem baseada em evidências

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ABSTRACT

Trauma is the leading pediatric public health problem worldwide. Immaturity of the hemostatic system in children increases the risk of Trauma-Induced Coagulopathy (TIC). Therefore, based on a literature review, a clinical protocol was developed. The literature analysis was conducted by selecting systematic reviews, randomized controlled trials, observational studies, and expert consensus statements. Grades of recommendation and levels of evidence were classified according to the 2014 Oxford University criteria. Laboratory monitoring during the first hour is of paramount importance. For fluid resuscitation, crystalloid solutions are recommended up to 20 mL/kg, with a transition to blood components as soon as they become available. The indication for blood component transfusion should be based on clinical signs and symptoms, rather than laboratory results alone. Thromboelastography may be useful to guide blood component transfusion. In patients refractory to 20 mL/kg of crystalloid infusion with severe hemorrhage, a massive transfusion protocol is recommended, with plasma–to–red blood cell ratios of 1:1 or 1:2. When available, whole blood should be used. With regard to tranexamic acid, there are unresolved issues; however, its use is recommended by experts in cases of severe hemorrhage. Deep vein thrombosis prophylaxis with enoxaparin should be considered after hemodynamic stabilization in patients older than 15 years with a low risk of bleeding, as well as in pubertal patients younger than 15 years who have sustained severe trauma and have a low bleeding risk.

Keywords: Pediatrics. Blood Coagulation Disorders. Multiple Trauma.

INTRODUCTION

Trauma is the top pediatric public health issue worldwide. Each year in Brazil, traumatic injuries cause more deaths among children and teens than the combined pediatric mortality from cancer, congenital anomalies, heart disease, respiratory illnesses, sepsis, and cerebrovascular conditions[1].

Pediatric patients are generally able to tolerate relatively greater blood loss than adults due to their higher physiological reserve[2]. However, the hemostatic system is underdeveloped at birth, with low levels of anticoagulant and procoagulant proteins[3]. In the pediatric age group, concentrations of plasminogen, tissue plasminogen activator, and α-antiplasmin are reduced. In contrast, tissue plasminogen activator inhibitor levels are elevated, reducing plasmin generation and fibrinolytic activity. Furthermore, although platelet counts are similar to those of the adult population, platelet function is often impaired, which may significantly contribute to an increased risk of TIC in children[4-6]. In the pediatric population, the reported incidence of TIC ranges from 5.8 to 77% and is associated with worse outcomes[7,8].

The main mechanisms associated with the development of TIC include endothelial injury, shock, hemodilution, hypothermia, acidemia, and inflammation[5]. In children, TIC may present as hypocoagulability or hypercoagulability and may vary according to the number of days after trauma[9]. Three fibrinolytic phenotypes following pediatric trauma have been described. Approximately 25% of patients develop

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hyperfibrinolysis, with mortality in this group ranging from 9 to 50%. About 45% of patients develop fibrinolytic shutdown following a period of hyperfibrinolysis. These patients frequently have associated Traumatic Brain Injury (TBI), and mortality in this group ranges from 8 to 10%. The remaining 30% exhibit physiologic fibrinolysis and have lower mortality rates (1 to 8%)[10].

There is a scarcity of methodologically robust studies on TIC, resulting in heterogeneous management primarily based on the experience of individual institutions. The development of a clinical protocol for the diagnosis and management of TIC may contribute to evidence-based care, reducing the likelihood of iatrogenic interventions and improving the quality and safety of care for pediatric trauma victims. The use of such a protocol will also enable research on the subject, as it promotes standardized management strategies[11]. Accordingly, this study aimed to develop a protocol for the diagnosis and management of TIC in pediatric patients based on the best available evidence. This study addresses the diagnostic approaches to TIC and its clinical management, with particular emphasis on indications for blood component transfusion, the use of antifibrinolytic agents, and thromboprophylaxis in pediatric and adolescent trauma patients.

METHODS

The study consisted of an integrative literature review followed by the development of a clinical protocol for the diagnosis and management of Trauma-Induced Coagulopathy (TIC) in pediatric patients. A bibliographic search was conducted on the PubMed platform using the following keywords: "pediatric trauma", "polytrauma", "pediatric massive transfusion protocol", and "coagulopathy of trauma".

Studies on the diagnosis and management of TIC in pediatric patients were identified. Articles were screened by abstract, and randomized controlled trials, prospective and retrospective observational studies, systematic reviews, and case-control studies, as well as expert consensus guidelines published in English, were selected for full-text review using the rayyan AI tool[12]. Two authors independently searched; the results were then combined and reviewed by a senior researcher. The search was limited to the past 15 years (2010–2025), and additional references were included based on the review of selected articles (Figure 1).

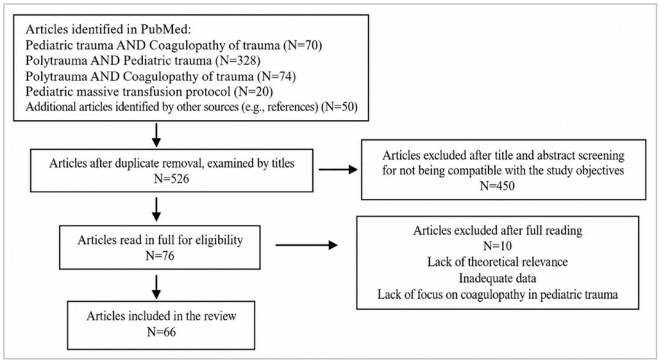

Figure 1: *Flow diagram of study selection.*

Based on the selected studies, a protocol was proposed for the diagnosis and management of TIC in pediatric patients. The protocol addresses the following:

a) Analysis of the main laboratory markers of TIC;

b) Initial clinical management based on the main phenotypes: hypercoagulability or hypocoagulability.

Grades of recommendation and levels of evidence were classified according to the 2014 Oxford University criteria[13].

RESULTS

Diagnosis of TIC

TIC should be diagnosed in patients who present with an international normalized ratio (INR) ≥1.3 and/or activated Partial Thromboplastin Time (aPTT) >36 seconds and/or platelet count <100,000/mm^3[3,14-16].

The following laboratory tests should be obtained within the first hour of care of the trauma patient: complete blood count, Prothrombin Time (PT)/ INR, aPTT, fibrinogen concentration, blood gas analysis, lactate, electrolytes, blood glucose, urea, creatinine, blood type, and crossmatch[17]. When available, Viscoelastic Hemostatic Assays (VHAs), which rapidly and accurately assess functional coagulation status at the bedside, may contribute to targeted TIC therapy[19-23].

Clinical Management

Early recognition of patients at high risk for massive bleeding and TIC is essential; these include patients with severe abdominal and/or thoracic visceral injuries, severe pelvic trauma, amputations, multiple bone fractures, or severe TBI.

The primary goal in managing patients with massive hemorrhage is to control bleeding, which almost always requires damage control surgical intervention. The second goal is to restore tissue perfusion, correct acidosis, reverse hypothermia, and manage coagulation[24].

Fluid Therapy

The goals of fluid resuscitation include achieving hemodynamic stability, maintaining urine output of at least 1mL/kg/h, preserving mental status, and normalizing tissue perfusion markers, such as serum lactate levels. Hypotension should not be used as a reference for volume resuscitation, as pediatric compensatory mechanisms, including tachycardia, increased cardiac output, and increased systemic vascular resistance, allow blood pressure to remain stable even in the presence of circulatory shock[24].

Use of Crystalloids

The use of warmed crystalloids should be considered in the initial post-trauma phase to prevent hypothermia and worsening of TIC, particularly while blood components are not yet available. Volume expansion should be administered in 10mL/kg aliquots of crystalloid solution, up to a maximum of 20mL/kg, with continuous assessment of hemodynamic status and signs of pulmonary congestion. As soon as blood components become available, resuscitation with crystalloid solution should be discontinued, as higher crystalloid volumes are associated with worse outcomes[25-29].

Blood Component Transfusion

Decisions regarding transfusion of blood components (packed red blood cells, plasma, platelets, and cryoprecipitate) should be guided by the overall clinical context, both in the prehospital setting and at emergency department admission, taking into account the presence of significant hemorrhage, the mechanism of injury, and persistent hemodynamic instability following an initial crystalloid bolus exceeding 20mL/kg[26,30,31].

In children with active bleeding but without signs of hemodynamic instability or life-threatening hemorrhage, transfusion of packed red blood cells is recommended when hemoglobin (Hb) is below 5g/dL and, based on clinical judgment, when Hb is between 5 and 7g/dL. In cases of TBI, priority should be given to maintaining Hb levels above 9g/dL[32].

There is insufficient evidence to recommend a specific laboratory test as a trigger or target for platelet and/or plasma transfusion for either therapeutic or prophylactic indications[33]. The use of thromboelastography and thromboelastometry data may assist in decision-making[20,21]. In patients with moderate to severe bleeding, the decision to transfuse plasma and/or platelets is based on clinical judgment. It is important to emphasize that plasma should not be used to correct INR in the absence of moderate to severe bleeding, especially in patients with TBI[34].

Cryoprecipitate administration is recommended only in patients with active bleeding and hypofibrinogenemia[35].

Transfusion of coagulation factor concentrates, such as prothrombin complex concentrate, activated factor VII, or fibrinogen concentrate, is not routinely indicated due to insufficient evidence demonstrating outcome benefit, except in specific cases, such as prior anticoagulant use[11,36,37].

Massive Transfusion

In patients with massive hemorrhage, activation of a Massive Transfusion Protocol (MTP) is indicated. MTPs are components of hemostatic resuscitation designed to correct hemorrhagic shock through balanced transfusion of plasma, platelets, and packed red blood cells[2].

Patients who may benefit from MTP include those who do not improve after infusion of 20mL/kg of crystalloid solution or 20mL/kg of blood components within one hour[38], those with evidence of coagulopathy or acidosis, hypofibrinogenemia at admission[39], associated

severe TBI[41], or severe trauma[42], particularly involving the abdomen and extremities, and hypotension at admission[43].

In pediatric patients with hemorrhagic shock after trauma, the resuscitation strategy with fresh frozen plasma and packed red blood cells in a 1:1 or 1:2 ratio should be considered[44-49].

Table 1 presents the recommended volumes of crystalloids and blood components in pediatric trauma patients.

Table 1 - *Recommended crystalloid and blood component volumes for pediatric trauma.*

Solution	Quantity
Crystalloids	10-20mL/kg
Packed Red Blood Cells	10-20mL/kg
Plasma	10-20mL/kg
Platelets	10mL/kg
Cryoprecipitate	1IU/10kg
Whole Blood	10-30mL/kg

Thromboelastography may be useful to guide transfusion, as shown in Table 2[50,51].

Table 2 - *Transfusion recommendation based on thromboelastography..*

TEG parameter	Normal Value	Transfusion Value	Product	Dose
ACT	86-118s	>128s	Plasma	20mL/kg
Alpha Angle	64-90	<60	Cryoprecipitate	1IU/10kg
K-value	0-2.5 min	>2.5 min	Cryoprecipitate	1IU/10kg
Maximum Amplitude	52-71 mm	<55 mm	Platelets	10mL/kg

Source: Adapted from ACS TQIP Massive Transfusion In Trauma Guidelines. Available at: https://www.facs.org/media/zcjdtrd1/transfusion_guildelines.pdf Key: ACT – ActivatedClotting Time.

Whole Blood

Whole blood transfusion in patients with massive hemorrhage is considered safer and more effective, offers greater logistical simplicity, and is less coagulopathic than MTPs using separated blood components[52-55]. Therefore, when available, whole blood should be used.

Tranexamic Acid (TXA)

TXA is an antifibrinolytic agent that binds to plasminogen, preventing fibrinogen degradation and promoting clot stability. TXA should be routinely administered within the first three hours after trauma in patients with poor response to crystalloid boluses and evident significant bleeding. In children under 12 years of age, the dose is 15mg/kg (maximum 1g) intravenously over 10 minutes, followed by a 2mg/kg/h infusion over eight hours or until bleeding stops. For adolescents aged 12 years and older, the same regimen used in adults is recommended: a 1g intravenous bolus over 10 minutes, followed by an infusion of 1g over 8 hours. Its use should also be considered in cases where LY30 analysis by thromboelastography is available[5]. Reported adverse effects include an increased risk of seizures[56].

Deep Vein Thrombosis Prophylaxis

Deep vein thrombosis (DVT) prophylaxis should be performed with enoxaparin 1mg/kg/day, administered subcutaneously once daily, in patients older than 15 years with low bleeding risk, or in pubertal patients younger than 15 years with severe trauma and low bleeding risk. Prophylactic enoxaparin should be initiated after hemodynamic stabilization, within the first 24-48 hours after trauma. In prepubertal children, venous thromboembolism prophylaxis is contraindicated[57-60].

The protocol for the diagnosis and management of TIC in pediatric patients is summarized in Table 3.

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DISCUSSION

Based on a comprehensive literature review, we developed a protocol for the diagnosis and management

of TIC in pediatric patients. Over the past 15 years, since the publication of landmark studies in adult trauma populations[61,62] demonstrating strategies such as balanced blood component transfusion and tranexamic acid use, which marked a paradigm shift in the management of severe trauma, there has been a growing body of literature focused on pediatric patients. However, studies involving the pediatric population generally have smaller sample sizes and less robust methodologies compared with adult studies. Therefore, proposing a protocol based on the best currently available evidence is both timely and relevant. In Brazil, a recent study found that fewer than half of surgeons involved in research reported that their hospitals had a massive transfusion protocol, and fewer than 20% reported using whole blood[63]. Thus, the proposed protocol may serve as a foundation for local institutional adaptations and help improve pediatric trauma care.

Table 3 - *Summary of the main topics related to trauma-induced coagulopathy in pediatric patients..*

Topics	Results and Guidelines	References	Grade of Recommendation and Level of Evidence
Prevalence of TIC	5.8 - 77%	Christiaans SC e cols[6] Hendrickson JE e cols[7] Strumwasser A e cols[8]	Not applicable
Mortality associated with TIC	14 - 40%	Nair e cols[4] Strumwasser A e cols[8] Morgan KM e cols[31] Reppucci ML e cols[67]	Not applicable
Diagnosis	TIC should be diagnosed in patients who have: INR greater than or equal to 1.3 and/or aPTT >36 seconds and/or platelet count <100,000/mm3	Burggraf M e cols[14] Davenport e cols[15]	A. 1b (Prospective Observational Studies)
Laboratory Tests at Admission	Complete blood count, prothrombin time/INR, aPTT, fibrinogen concentration, blood gas analysis, lactate, electrolytes, blood glucose, urea, creatinine, blood type, and counterproof	Gaessler H e cols[17]	A. 1b (Prospective Observational Study)
Viscoelastic Tests	When available, viscoelastic hemostatic assays can contribute to targeted TIC therapies	Lindsay C e cols[20]	A. 1b (Randomized Controlled Clinical Trial)
Fluid Therapy	Expansions should be performed in 10mL/kg aliquots of crystalloid solution up to a maximum of 20mL/kg, with continuous assessment of hemodynamic status and signs of pulmonary congestion	Polites SF e cols[27]	A. 1b (Prospective Observational Study)
Packed Red Blood Cells	In children with active bleeding but no signs of hemodynamic instability or life-threatening bleeding, transfusion of packed red blood cells is recommended when Hb is below 5g/dL and, according to clinical judgment, if the Hb concentration is between 5 and 7g/dL In the case of TBI, priority should be given to Hb concentrations above 9g/dL	Valentine SL e cols[32]	D. 5 (Expert Consensus)
Plasma and Platelets	In patients with moderate to severe bleeding, the decision regarding plasma and/or platelet transfusion is based on clinical judgment	Nellis ME e cols[33]	D. 5 (Expert Consensus)

Topics	Results and Guidelines	References	Grade of Recommendation and Level of Evidence
Cryoprecipitate	Cryoprecipitate administration is recommended only in patients with active bleeding and hypofibrinogenemia	Burt T e cols[35]	A. 1a (Systematic Review)
Coagulation Factor Concentrate	Transfusion of coagulation factor concentrate, such as prothrombin complex, activated factor VII, or fibrinogen concentrate, is not routinely indicated except in specific cases, such as prior anticoagulant use	Hannadjas I e cols[36] Itagaki Y e cols[37]	A. 1a (Systematic Reviews)
Massive Transfusion	Patients who may benefit from MTP include those who do not improve after infusion of 20mL/kg of crystalloid solution or 20mL/kg of blood components in 1 hour, who have evidence of altered coagulation or acidosis, hypofibrinogenemia on admission, associated severe TBI or severe trauma, and arterial hypotension on admission	Morgan KM e cols[38] Meizoso JP e cols[39] Samuels JM e cols[40] Leeper CM e cols[41] Hesling JD e cols[42] Zhu CS e cols[43]	B. 2b (Retrospective Cohort Studies)
Balancing of Blood Components	In pediatric patients with hemorrhagic shock after trauma, the resuscitation strategy with fresh frozen plasma and packed red blood cells in a 1:1 or 1:2 ratio should be considered	Spinella PC e cols[44] Mehl SC e cols[46]	A. 1b (Prospective Observational Studies)
Whole Blood	When available, group O whole blood with low anti-A and anti-B titers should be used	Gaines BA e cols[55]	A. 1b (Prospective Observational Study)
Tranexamic Acid	TXA should be routinely administered within the first three hours after trauma in patients with poor response to crystalloid boluses and evident significant bleeding. In children under 12 years of age, the dose is 15mg/kg (maximum 1g) intravenously over 10 minutes, followed by a 2mg/kg/h infusion over 8 hours or until bleeding stops. In adolescents, from 12 years of age, the same regimen used in adults is recommended: a 1g intravenous bolus dose over 10 minutes, followed by an infusion of 1g over 8 hours	Spinella PC e cols[5]	A. 1b (Prospective Observational Study)
DVT Prophylaxis	DVT prophylaxis should be performed with enoxaparin 1mg/kg/day, subcutaneously, once a day, in patients older than 15 years with a low risk of bleeding or in children under 15 years of age who are pubertal, with severe trauma and a low risk of bleeding 24-48 hours after the trauma	Leeper CM e cols[59]	A. 1b. (Prospective Observational Study)

Key: TIC – trauma-induced coagulopathy, INR – international normalized ratio, aPTT – activated partial thromboplastin time, Hb – hemoglobin concentration, TBI – traumatic brain injury, MTP – massive transfusion protocol, TXA – tranexamic acid, DVT – deep vein thrombosis.

Within the first 24 hours after trauma, hemorrhage is the leading cause of death[64]. Accordingly, laboratory monitoring is of paramount importance and should include a complete blood count and coagulation studies, as well as tissue perfusion markers, a metabolic panel, and pretransfusion testing[11,17,65]. Viscoelastic

assays have increased the proportion of patients receiving TIC-directed protocols[27,51], although their use still requires further validation in pediatric patients[23]. Special attention should be given to ionized calcium, which acts as a cofactor in the coagulation cascade and may be consumed or inactivated by blood components containing citrate[64].

The recommendation to restrict crystalloid use in trauma patients is justified by the deleterious effects of large-volume administration, including dilution of coagulation factors, disruption of the hemostatic thrombus, hypothermia, cellular edema, alterations in inflammatory mechanisms and metabolic processes, myocardial depression, development of acute respiratory distress syndrome, abdominal compartment syndrome, and multiple organ dysfunction[66].

Blood components should be considered judiciously and early in patients with suspected or confirmed bleeding associated with clinical deterioration. It is important to emphasize that the administration of large volumes of blood components (>40mL/kg) is associated with adverse effects, including DVT, increased risk of infection, and acute kidney injury[67].

Regarding early empirical transfusion (<4 hours from admission) of cryoprecipitate or fibrinogen concentrate, a systematic review of studies involving patients older than 16 years found no impact on mortality[35]. However, a retrospective cohort study of pediatric patients undergoing massive transfusion demonstrated that early administration (<4 hours from admission) of cryoprecipitate was associated with lower 24-hour mortality[68].

There is no consensus on the triggers for massive transfusion protocol activation[69]. Some molecules released from damaged tissue and involved in the post-trauma inflammatory response may serve as promising markers for the need for MTP activation, such as amphoterin and syndecan-1[70,71]. Until these biomarkers are validated and widely available, decisions regarding MTP activation should be based on clinical and laboratory data[72]. In patients requiring massive transfusion, balancing fresh frozen plasma and packed red blood cells in a 1:1 or 1:2 ratio appears to be beneficial[44-49].

Evidence also suggests an association between the use of whole blood and improved outcomes in pediatric patients[54,55]. The main concern regarding the routine use of whole blood in trauma centers is the risk of alloimmune transfusion reactions and massive hemolysis. To mitigate this risk, some trauma centers have implemented the use of group O whole blood with low anti-A and anti-B titers[52,73].

With respect to tranexamic acid use in the pediatric population, mortality benefits comparable to those observed in adult studies have not been demonstrated[62], as indicated by a 2022 meta-analysis that included only retrospective studies[74]. However, a multicenter prospective observational study demonstrated the benefits of antifibrinolytic agents in pediatric patients with life-threatening hemorrhage[5]. Unresolved questions remain regarding optimal dosing, timing, and fibrinolytic phenotypes that may benefit, which are currently being addressed in an ongoing randomized clinical trial[75].

TIC may also manifest as a hypercoagulable state, particularly 24–48 hours after trauma. In pediatric patients, several risk factors have been identified, including age >13 years, trauma severity, use of central venous catheters, parenteral nutrition, fibrinolytic abnormalities at admission, immobility, need for inotropic support, massive transfusion, TBI, and nonaccidental trauma[67,57-60].

Among the limitations of this review are the inclusion of retrospective, single-center studies and some meta-analyses involving adult patients, as well as the absence of national studies. A major strength of this article is its focus on an issue of undeniable public health relevance that lacks standardized protocols in Brazil. Future studies should evaluate the impact of institutional implementation of this protocol on pediatric trauma outcomes.

CONCLUSION

This clinical protocol for the management of trauma-induced coagulopathy in pediatric patients is grounded in the best evidence published over the past 15 years. It represents a practical advance with potential educational and scientific value for standardizing clinical practice in Brazil.

R E S U M O

Introdução: *O trauma é o principal problema de saúde pública pediátrica em todo o mundo. A imaturidade do sistema hemostático de crianças aumenta o risco de coagulopatia induzida pelo trauma. Portanto, a partir de uma revisão de literatura foi possível a elaboração de um protocolo clínico. A análise bibliográfica foi realizada com a seleção de revisões sistemáticas, estudos randomizados controlados, observacionais e consensos de especialistas. Os graus de recomendações e os níveis de evidência foram classificados de acordo com os critérios da Universidade de Oxford de 2014. A monitorização laboratorial na primeira hora é de suma importância. Em relação à fluidoterapia, recomenda-se o uso de soluções cristaloides até, no máximo, 20mL/kg, com substituição para os hemocomponentes, assim que estiverem disponíveis. A indicação da transfusão de hemocomponentes deve se basear nos sinais, sintomas e não apenas em resultados laboratoriais. A tromboelastografia pode ser útil para guiar a transfusão de hemocomponentes. Nos pacientes refratários à infusão de 20mL/kg de cristaloides com hemorragia grave, recomenda-se o protocolo de transfusão maciça com as proporções entre plasma e hemácias de 1:1 ou 1:2. Quando disponível, o sangue total deve ser utilizado. Em relação ao ácido tranexâmico, há questões não elucidadas, mas seu uso é recomendado por especialistas em casos de hemorragia grave. A profilaxia para trombose venosa profunda com enoxaparina deve ser considerada nos pacientes maiores de 15 anos com baixo risco de sangramento ou em menores de 15 anos púberes, com traumas graves e baixo risco de sangramento, após estabilização hemodinâmica.*

Palavras-chave: *Pediatria. Transtornos de Coagulação Sanguínea. Traumatismo Múltiplo.*

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Datasets related to this article will be available upon request to the corresponding author.

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