Editorial

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Trauma & Acute Care

2016
Vol.1 No.3:19

Coagulopathy in Head Trauma – as Complicated as Ever

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Received date: February 29, 2016 **Accepted date:** March 1, 2016 **Published date:** March 4, 2016

Editorial

Many years ago, while I was a Chief Resident in my neurological surgery training program, I solicited the aid of my Department Chairman to have the Emergency Department add coagulation testing to the routine labs acquired on head trauma patients. Believe it or not, at that time, despite knowledge that coagulopathy frequently complicates traumatic brain injury (TBI), such testing was usually not performed until the neurosurgery service ordered the test. While understanding about coagulation deficits has increased over time, the problem has also become increasingly complicated by an older population, additional causes of coagulopathy (particularly in the form of new drugs), additional tests to define coagulopathy, and new (and expensive potential treatments).

Older literature suggested that some form of coagulopathy occurred in 40 to 86% of patients with TBI (depending on the nature of the injury) on the basis of elevated protime/international normalized ratio (INR), elevated partial thromboplastin time, or low platelet count [1-5]. Disseminated intravascular coagulation was present in 32.3% of patients with severe TBI [1]. More recent data provides similar incidence, with coagulopathy present in 10% to 90% of TBI patients during their hospital course; most studies have been retrospective series [6-8]. A recent prospective study placed the incidence at about 35% [9]. Clearly, coagulopathy after TBI remains a common problem.

A number of factors may contribute to the development of coagulopathy in TBI. Some are a direct consequence of the trauma. Release of tissue factor (thromboplastin) from injured brain activates the extrinsic coagulation pathway. Protein C activation from shock occurring after trauma and hypoperfusion may also contribute, as can hyperfibrinolysis. Shed microparticles reduce platelet functionality, and platelet count itself may be diminished. Other contribution derives from patient characteristics. Many patients, particularly the elderly, take medications for prevent or treat diagnosed cardiovascular or cerebrovascular disease. These drugs include older agents such as aspirin, warfarin, and clopidogrel, and newer agents which inhibit Factor Xa (rivaroxaban and apixaban) or directly inhibit thrombin (dabigatran). Older patients or those with neurological deficits related to previous stroke are more prone to fall and thereby suffer TBI. Acute alcohol consumption can reduce platelet function and cause coagulation deficits [10,11] while chronic alcohol abuse reduces liver production of clotting factors and causes thrombocytopenia, both conditions also play a role in causation of TBI by contributing to motor vehicle accident and fall occurrence.

Coagulopathy after TBI has significant impact on patient outcome. Coagulopathy increases secondary injury. Patients may experience delayed progression of hemorrhagic injuries or increased size of hemorrhages [12]. Surgery is more difficult if patients clot poorly. Blood loss is greater, operating time is longer, and re-accumulation of blood with mass effect is more likely. Neurological deficit and survival is worse [13]. Interventions may be delayed by attempts to correct coagulation deficits.

Measurement of coagulation profile has traditionally been with protime and INR, partial thromboplastin time (PTT), and platelet count, with coagulopathy defined as INR <1.5, PTT >35, and platelet count <100,000 cells/μL [14]. These assessments are good, but do not adequately assess platelet function, which is affected by many of the mechanisms of coagulopathy. The platelet function assay (PFA)-100 has been used to detect aspirin-induced platelet defects, but it has been shown to be unreliable in TBI [15]. Thrombelastography (TEG®) is becoming more widely available as a point-of care tool to determine clot strength, the final common pathway in the coagulation process, amongst other parameters. Its utility in head trauma is nascent, with few studies to show its effectiveness and reliability [16]. Anecdotally, the incidence of TEG abnormalities in the trauma patients I treat seems fairly high. Printz et al. [17] demonstrated that 50% of head trauma patients had coagulopathy using TEG for assessment. Sixta et al. [18] recently showed that a higher prevalence of coagulopathy was identified on TEG compared to traditional measures. But the importance of some of the abnormalities identified on TEG remains unclear.

Once coagulation deficits are identified, one must choose from amongst a number of therapeutic options without any clear guidelines for optimal use. Fresh frozen plasma (FFP) has been the traditional reversal agent for elevated INR. It must be thawed for use which takes time, and multiple units are often required, taking additional time. Recombinant Factor VIIa is another option which can correct coagulopathy more quickly than FFP, allowing patients to get to surgery more promptly

and with less transfusion of blood products. Despite its greater expense, Stein et al. [19] showed that recombinant Factor VIIa was more cost effective than FFP. Recombinant factor VIIa can also be used to reverse effects of dabigatran [20]. Its cost is high, and many initial receiving hospitals do not carry recombinant Factor VIIa on their formularies. Platelets can be administered to combat thrombocytopenia or impaired platelet function suggested by low maximal amplitude, adenine-diphosphate inhibition, or low platelet activation and aggregation on TEG studies. What platelet level is acceptable to prevent coagulopathy-related consequences is not certain. Concerns about development of antibodies with repetitive platelet transfusion are also present. It is not clear if antifibrinolytic medications such as tranexamic acid will be helpful [21]. 4-factor prothrombin complex concentrate has been shown to function as a coagulation antidote for rivaroxaban and apixaban [22]. Which solution is truly best is uncertain, and practice patterns vary greatly, creating the potential for suboptimal patient care [23].

The complexity of coagulopathy in TBI leads to the number of unanswered questions which remain. These questions include the following: 1) what are the best tests to assess coagulopathy in patients with TBI? 2) What do the results of testing mean to the patient? 3) What are the best agents for correction of coagulopathy? And 4) what are the best target levels for correction to prevent consequences? As we gain answers to these questions, we can hopefully simplify the problem and develop clear evaluation and treatment guidelines which can be widely shared to address coagulopathy in TBI.

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