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Traumatic Induced Coagulopathy

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Introduction

Problem identification and scope

- "Trauma is the leading cause of death and disability between the ages of 5 and 44" (Noel, Cashen, Patel, 2013, p. 259).
- Coagulopathy is "the inability of blood to coagulate normally" (Katrancha, Gonzalez III, 2014, p. 54).
- One quarter of the patients with severe injury arrive in the emergency room already suffering from acute coagulopathy of trauma (ACOT) (Noel, Cashen, Bhavesh, 2013, p. 259).
- Of those suffering severe multisystem trauma who make it to the hospital 80% die within 24 hours (Noel, Cashen, Patel, 2013, p. 259).

The following scenario is played out daily in the United States. An otherwise healthy 30-year-old male suffers a traumatic insult from a motor vehicle accident. He presents to the emergency room hypotensive, cold, and acidotic with significant blood loss. He is aggressively resuscitated with multiple units of normal saline and packed red blood cells (PRBC's), and transferred to the ICU. There he continues to decline succumbing from his injures a short 12 hours later from coagulopathy and multiple organ failure. The cause of their death a condition known as acute coagulopathy of trauma (ACOT) or trauma induced coagulopathy (TIC). Complicated by hypothermia (many times iatrogenic in nature), hypoxia, and acidosis from anaerobic metabolism patients enter a vicious cycle ending in death. The condition results in depletion, dilution, and inactivation of normal clotting factors, and leads to the greatest risk from death in the first 24 hours following a traumatic incident (Katrancha & Gonzalez III, 2014, p. 54).

In over 30 years of treating trauma patients this nurse has personally seen the devastating effects of multi system blunt and penetrating trauma. With improved prehospital knowledge and skill, patients are arriving sooner than ever to trauma centers. Helicopter emergency medical service (HEMS), the profession occupied by this nurse, adds additional prehospital resources aiding in the expeditious transport individuals from remote areas to urban trauma centers.

Historically this nurse found it interesting that TIC may have been a contributing factor in the death of Jesus 2000 years ago.

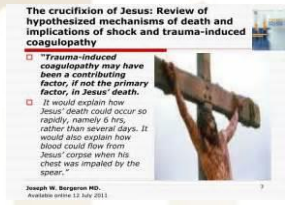

Figure 1: Proposed mechanism for the death of Jesus (Bergeron,2012)

Signs and symptoms

Patients who are severely injured appear acutely ill. This is most notable demonstrated by decrease in level of consciousness. The causes of patient presentation are as follows:

- Hypothermia – Hypothermia is many times iatrogenic, caused by removing clothing and exposing patients to the elements. The addition of ambient temperature fluids used in resuscitation further compounds the problem. Medications and anesthetics are also responsible for decrease in body temperature (Katrancha, Gonzalez III, 2014, p. 54). Noel, Cashen, and Patel, (2013), provide several interesting facts:
- ISS scores greater than 25 show mortality that increases from 10% to 100% when body temperature declined from 35 degrees Celsius to below 32 degrees Celsius (p.263).
- A 10% reduction in coagulation factor activity is seen for every 1 degree Celsius drop in temperature (p. 263).
- "Hypothermia < 33°C reduces factor activities below 33%" (p. 263).
- There is a drop of up to 10 percent in thrombin production for each degree below 36°C (p.263).
- Acidosis – Partially caused by both chloride containing fluids and citrate used to preserve blood. pH levels of less than 7.4 can reduce the activity of coagulation factors by as much as 40% (Katrancha, Gonzalez III, 2014, p. 54). Acidosis will contribute to ineffectiveness of administered medications. Vital signs will initially be elevated to compensate for hypoxemia and tissue ischemia. As Compensatory mechanisms fail vital signs will deteriorate rapidly and the patient will die.
- Hypoperfusion – This condition leads to an acidotic state with the accumulation of the byproducts of metabolism. This is also the primary condition leading to a decrease in mentation.

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Pathophysiology

Acute coagulopathy of trauma is a multifactorial process involving the dysfunction of multiple processes. Noel, Cashen, and Patel (2013) describe the drivers of ACOT as hypoperfusion, inflammation, and activation of the neurohumoral system (p.259). Platelet activation, endothelial activation, and the presence of chemical mediators are essential in the genesis of TIC. Katrancha and Gonzalez III, (2014) explain the cell based model of coagulation, a model which is supplanting the traditional intrinsic and extrinsic cascade models (pp. 54-55). In this model it is platelets, through initiation, amplification, and propagation, that lead to normal coagulation. Platelets were found to be "exhausted" in at least 45.5% of trauma patients who were admitted to the hospital (Noel, Cashen, Patel, 2013, p. 262). Protein C, interacts with this system, and depletion can lead to increased fibrinolysis and dysfunctional platelets. The glycocalyx is a thin layer of cells that lines the top of the endothelium. The glycocalyx is negatively charged, and when healthy resists adhesion and coagulation (Noel, Cashen, Patel, 2013, p.260). Damage causes a release of a variety of factors responsible for the effects of ACOT including (Noel, Cashen, Patel, 2013, pp. 260-262):

- Syndecan-1- endothelial permeability, increasing amount leads to protein C depletion and hyperfibrinolysis, increased level predicts poor outcomes
- Vascular endothelial growth factor (VEGF)
- Soluble vascular endothelial growth factor 1 (sVEGF1)
- Weibel-Palade body degranulation
  - Tissue plasminogen activator (tPA)
  - Angiopoietin 2 (Ang-2) – endothelial destabilization and permeability, increased levels predict poor outcome
- Catecholamine production – favors switch to a hypocoagulable state
- Angiopoietin 2 (Ang-2) – endothelial destabilization and permeability, increased levels predict poor outcome
- B-catenin – post-transcriptional silencing leads to hyperpermeability
- Heparin like substances – released from damaged glycocalyx
- Protein C – Activated by plasma membrane bound thrombin-thrombomodulin. Active form binds to endothelial cell protein C receptor increasing activation rate by 20-fold. Can remain bound to cell or dissociate and combine with protein S becoming an anticoagulant.
  a. Cleaves bonds in activated cofactors VIII and V that serve to activate X an II
  b. Promotes fibrinolysis by inhibition of plasminogen activator inhibitor 1
  c. Reduction of inflammation decreasing nuclear factor κβ
- Protein S – increase the activity of activated protein C

Hypoperfusion leads to the increased expression of thrombomodulin and activation of protein C. This activation cleaves bonds in both factor VIII and factor V making both mediators less active. Activated protein C (APC) also promotes fibrinolysis and inhibition of plasminogen activator inhibitor-1 (PAI-1) (Noel, Cashen, Patel, 2013, p.259). Protein C may be protective in states where the blood flow slows, and thus may inhibit thrombus formation. However, when systemic trauma is experienced the normal physiology between protein C and PAI-1 becomes pathologic, overwhelming the system leading to a state that inhibits clot formation (Ward, 2013, p 38). Severely injured patients were found to have less than 30% of normal coagulation activation. With studies showing abnormalities within 25 minutes from the time of injury (Noel, Cashen, Patel, 2013, p. 261). Low fibrinogen levels are found to be an indicator of mortality at 24 hours. Hyperfibrinolysis is another factor of increased mortality. Fulminant hyperfibrinolysis, defined as dissolution of a clot within 60 minutes, had a mortality rate of 87.5% (Noel, Cashen, Patel, 2013, p. 262). Inhibition of PAI-1 by activated protein C and tPA release from Weibel-Palade bodies after endothelial activation is the direct cause of hyperfibrinolysis (Noel, Cashen, Patel, 2013, p. 262). International Normalized Ratio (INR), was one of the first lab values showing coagulopathies in trauma patients, but is too slow to provide the needed information in a more real-time setting (White et. al., 2014, p. 978). White et.al., (2014) performed a cluster analysis which groups trauma patients according to injury severity score and laboratory parameters. Their study had 84 patients which were subsequently divided into three groups. Each group had increasing level of traumatic injury. While all three groups in the study had evidence of fibrinolysis only group three (the most severely injured group) had significant platelet dysfunction and inflammatory mediators (p. 983). Compounding the coagulopathy caused by trauma is the addition of what Cashen, Noel, and Patel (2013) term resuscitation associated coagulopathy (p. 262). Added to the triad of coagulopathy, hypothermia, and acidosis resulting from trauma, is the addition of hemodilution, forming what the authors state as the lethal quartet.

Detection of this condition until now has frequently relied on standard lab values which may not be available quick enough to guide treatment. Thromboelastography (TEG) can now be used in the emergency room to screen for early indicators of TIC. TEG provides real time information about clot initiation, formation, and stability, and as such can help guide resuscitation and mass transfusion protocols (Liou et. al., 2014, p. 94).

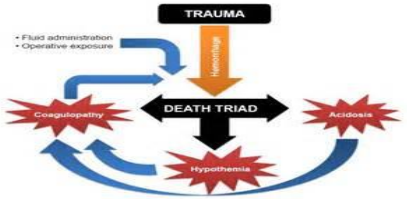

Figure 2: Graphic representation of TIC factors

Nursing implications

- Crystalloids, 0.9 normal saline and lactated ringers, the very fluids which have long been the gold standard for resuscitation are now being investigated as contributors to this deadly condition.
- With a substantial quantity of isotonic solutions diffusion out of the vascular space they contribute to interstitial edema, acute respiratory distress syndrome (ARDS), and multiple organ failure
- Crystalloids are being limited in many institutions to less than 4 liters in the first 24 hours (Holcomb, Pati, 2013, p. 656).
- The Department of Defense (DoD) is currently investigating the use of three dried plasma preparations (Pusateri, Given, Macdonald, Homer, 2016, p. 22).
- Part of the effectiveness of plasma has been its healing effect on the injured glycocalyx of endothelial cells (Holcomb, Pati, 2103, p. 657).
- The prehospital use of plasma in traumatic hemorrhage study (PUPTH) presents a protocol for use of plasma versus saline on survival of patients. The study will look at survival after all fluid administration 30 days post event. This study is again in cooperation with the Department of Defense (Reynolds, Michael, Cochran, Wegelin, and Spiess, 2015, (pp. 1-8).
- Agents such as tranexamic acid (TXA) are more frequently being administered help limit bleeding prior to arrival at a trauma center. By lessening the amount of blood lost, the effects of TIC can be ameliorated.
- Cornelius (2017), in a literature review found that TXA, by inhibiting fibrinolysis, significantly reduced mortality in trauma patients (p. 30).
- United States military use of TXA, prehospital plasma, and aeromedical evacuation have resulted in the lowest fatality rate on record (Cornelius, 2017, p. 30).
- Four factor prothrombin complex concentrate, which combines factors II, VII, IX, and X, has been used successfully in reversing major hemorrhage in vitamin K antagonists, like coumadin (Untold, Tormey, 2015, p. 1568).
- PCC use in experimental porcine trauma has yielded higher fibrinogen, hemoglobin, and platelet counts, with higher mean arterial pressure and decreased blood loss (Untold, Tormey, 2015, pp.1571-1572).
- Of note is that Ward describes swine as hypercoagulable which may make the findings with porcine models less relevant to humans (Ward, 2013, p. 39).

Conclusion

Death from traumatic incident remains a large problem for the American population. Growing research has delineated mechanisms associated with massive hemorrhage and hypotension. The blood which should be protective loses this ability due to a process known as coagulopathy of trauma. With optimization of transport, screening, and resuscitation practitioners can lessen the already devastating effects and help the patient recover as much function as possible. Professional vigilance is needed to stay abreast of the latest research providing all patients with state of the art care. This nurse has frequently been witnessed to the joy of having a patient who was clinging to life come back to say thank you for saving my life. Few rewards are greater for nurses caring for traumatically injured patients.

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