Impact of Tranexamic Acid on Posttraumatic Coagulation and Inflammation

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Introduction: Posttraumatic coagulopathy and inflammation can exacerbate secondary cerebral damage after traumatic brain injury (TBI). Tranexamic acid (TXA) has the potential to mitigate secondary brain injury with its reported anti-fibrinolytic and anti-inflammatory properties. We hypothesized that TXA would improve posttraumatic coagulation and inflammation in a murine model of TBI alone, and in a combined injury model of TBI and hemorrhage (TBI/H).

Methods: An established weight-drop model was used to induce moderate TBI. Mice were administered intraperitoneal injections of 10mg/kg TXA or equivalent volume of saline 10 minutes after injury. An additional group of mice was subjected to TBI followed by hemorrhagic shock using a pressure-controlled model. TBI/H mice were given intraperitoneal injections of TXA or saline during resuscitation. Blood was collected at intervals after injury to assess coagulation by thromboelastometry (ROTEM®), inflammation by multiplex ELISA, soluble P-selectin and serum neuron specific enolase. Brain tissue was analyzed for inflammatory changes by multiplex ELISA, and splenic tissue was collected for splenic cell population assessment by flow cytometry.

Results: There were no coagulation, serum or cerebral cytokine, P-selectin, or neuron specific enolase differences between mice treated with TXA or saline after TBI or TBI/H. At 24 hours post-TBI, mice given TXA demonstrated lower splenic total cell counts (93.6 vs. 130.1, TXA vs. saline, $p = 0.01$), central memory CD8 (0.2 v. 0.3, TXA vs. saline, $p = 0.001$), effector CD8 (0.04 vs. 0.1, TXA vs. saline, $p = 0.006$), B cell (48.5 vs. 72.9, TXA vs. saline, $p = 0.001$), and increased naïve CD4 (14.6 vs. 11.5, TXA vs. saline, $p = 0.04$) cell populations. By contrast, TXA did not affect splenic leukocyte populations after combined TBI/H.

Conclusions: Despite clinical data suggesting a mortality benefit, TXA did not modulate the coagulation effects, inflammatory changes, or biomarker generation in either the TBI or TBI/hemorrhage murine models. Administration of TXA following TBI alone altered splenic leukocyte populations, which may contribute to a change in posttraumatic immune status. Future studies should be done to investigate the role of TXA in the development of posttraumatic immunosuppression and risk of nosocomial infections.

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