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COMMENTARY

Trauma is an exhausting platelet experience

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Platelets are an essential part of the hemostatic process and tight regulation of platelet activity is key to maintaining normal hemostatic function in the vessel. Platelet dysfunction is typically thought of as being associated with an increased risk for occlusive thrombotic events leading to life-threatening pathophysiological conditions such as myocardial infarction and stroke. Hallmarks of platelet hyperreactivity include (1) increased alpha granule secretion leading to P-selectin expression on the platelet surface, (2) increased dense granule secretion leading to an increase in the release of prothrombotic small molecules into the blood such as ADP, calcium, and 5-HT, and (3) increased inside-out activation of the integrin αIIbβ3 on the platelet surfaced resulting in platelet–platelet and platelet–extracellular matrix adhesion and inside-out activation of the platelet.[1] For this reason, much of the work on platelets to date has been focused on ways in which to minimize platelet reactivity through targeting the various receptors and intracellular signaling pathways.[2] Interestingly, platelet hyporeactivity is also frequently observed in the clinic, leading to an increased risk for bleeding due to incomplete clot formation, reduced clot strength, and/or altered thrombolysis. The molecular mechanisms underlying impaired platelet function, however, are not well understood.

Trauma-induced coagulopathy (TIC) is a pathologic condition whereby blunt or acute trauma results in a serious and uncontrolled coagulation condition in the blood and an inability to form normal clots resulting in an increased risk for hemorrhage and often death.[3] Few clinical options exist due in part to our limited understanding of the mechanism causing the altered platelet reactivity and clot structure.[4,5] In the current issue, Matthay and colleagues demonstrate for the first time that the previously reported increase in catecholamine may be one of the mechanisms leading to decreased platelet function in trauma (Matthay et al. in press). To address this question, the authors designed a prospective study of trauma patients whereby they assessed the blood levels of two important catecholamines, epinephrine and norepinephrine. In parallel, the platelets from these patients was assessed for their ability to be activated. Consistent with previously published work, the catecholamines were elevated in blood of trauma patients.[6] These patients were also observed to have a decreased platelet response and clot strength potential. While the latter observation alone is intriguing, it is associative in nature and may not be directly related to the change in level of catecholamines in the blood.

In fact, previous studies demonstrated that epinephrine is a platelet agonist, not an antagonist.[7,8] The authors confirm those earlier findings showing in platelets from healthy subjects that addition of epinephrine or norepinephrine results in activation of specific platelet signaling pathways and platelet aggregation. Trauma, however, leads to long-term increased catecholamine levels in the blood, suggesting that the duration of exposure is a critical factor. The authors investigated this hypothesis and could nicely demonstrate that platelet reactivity is diminished with longer exposure to catecholamines. Together, these studies clearly demonstrate that catecholamine levels are increased in the blood of trauma patients and that a chronic exposure to these catecholamines results in a desensitization or exhaustion of the platelets in circulation. The result is a diminished ability of platelets to secure vascular integrity upon inflammation, insult, or injury.

This study provides important new information on the molecular mechanisms underlying impaired platelet function in trauma. The key finding is that platelets respond differently to acute and chronic exposure to catecholamines, the latter leading to impaired platelet function and prolonged bleeding following trauma. However, several

important mechanistic questions remain, including a deeper understanding as to how long-term exposure to epinephrine and norepinephrine alters collagen-induced platelet activation. Whether this is due to an internalization of the adrenoceptors on the platelet surface or is linked to changes in intraplatelet signaling remains to be determined. It will also be important to determine whether elevated levels of catecholamines affect all platelets equally, or if the effect is dependent on age of the platelets.[9] Regardless of the mechanism, this study brings us closer to understanding why bleeding, hemorrhage and risk of increased morbidity and mortality occurs in patients following trauma.

AUTHOR CONTRIBUTIONS

M. Holinstat wrote the manuscript and approves of the final draft.

CONFLICT OF INTEREST

The Author declares no relevant conflict of interest for this publication.

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