Fibrinogen, platelet and factor XIII supplementation in cardiac surgery

In vitro and *in vivo* studies

AKADEMISK AVHANDLING

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Fakultetsopponent: Docent Agneta Wikman

Institutionen för Laboratoriemedicin, Karolinska Institutet

Avhandlingen baseras på följande delarbeten

I. Shams Hakimi C, Fagerberg Blixter I, Hansson EC, Hesse C, Wallén H, Jeppsson A. Effects of fibrinogen and platelet supplementation on clot formation and platelet aggregation in blood samples from cardiac surgery patients. *Thromb Res*. 2014; 134: 985-900.

II. Shams Hakimi C, Singh S, Hesse C, Jeppsson A. Effects of fibrinogen and platelet transfusion on hemostasis in cardiac surgery patients with ongoing bleeding. In manuscript.

III. Shams Hakimi C, Carling MS, Hansson EC, Brisby H, Hesse C, Radulovic V, Jeppsson A. The effect of ex vivo factor XIII supplementation on clot formation in blood samples from cardiac and scoliosis surgery patients. *Clin Appl Thromb Hemost*. doi: 10.1177/1076029617713872. [Epub ahead of print].

IV. Hansson EC*, Shams Hakimi C*, Åström-Olsson K, Hesse C, Wallén H, Dellborg M, Albertsson P, Jeppsson A. Effects of ex vivo platelet supplementation on platelet aggregability in blood samples from patients treated with acetylsalicylic acid, clopidogrel, or ticagrelor. *Br J Anaesth*. 2014; 112: 570-575. *Shared first authorship.

V. Shams Hakimi C*, Hesse C*, Wallén H, Boulund F, Grahn A, Jeppsson A. In vitro assessment of platelet concentrates with multiple electrode aggregometry. *Platelets*. 2015; 26: 132-137. *Shared first authorship.

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ABSTRACT

Background: There is a high risk of bleeding complications in cardiac surgery. Fibrinogen and platelet concentrates are often used to treat perioperative bleeding, but there is little information about its efficacy. The overall aim of this thesis project was to study the effects of fibrinogen, platelet and factor XIII concentrates on markers of hemostasis in blood samples from cardiac surgery patients.

Methods: Increasing doses of fibrinogen, platelets, and factor XIII were added to blood samples from patients or healthy volunteers (study I, III–V). In study II, blood samples from cardiac surgery patients with ongoing bleeding were analyzed before and after transfusion of fibrinogen and/or platelet concentrates. In all studies, platelet function was assessed with impedance aggregometry, and clot formation with thromboelastometry.

Results: Supplementation with fibrinogen improved clot formation while platelets improved both platelet aggregation and clot formation in blood samples form cardiac surgery patients (I). Fibrinogen to patients with ongoing bleeding improved clot formation and platelets improved platelet aggregation (II). Factor XIII supplementation to blood samples from cardiac and scoliosis surgery patients improved clot formation moderately (III). Supplementation with platelets improved platelet aggregation independently of antiplatelet therapy (IV). Time-dependent changes in platelet concentrates were detected with impedance aggregometry *in vitro* (V). The results predicted with moderate accuracy changes in aggregation after addition of the platelet concentrates to whole blood samples.

Conclusions: The results suggest that transfusion with fibrinogen or platelets improve hemostasis, whereas factor XIII should remain a secondary tool in the treatment of perioperative bleeding. Impedance aggregometry may be used to monitor the quality of stored platelet concentrates *in vitro*.

Keywords: Fibrinogen, platelets, factor XIII, platelet aggregation, clot formation, cardiac surgery.

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