Fibrinolytic proteins in human bile accelerate lysis of plasma clots and induce breakdown of fibrin sealants.

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Abstract:

OBJECTIVE: We investigated the effect of human bile on the stability of plasma clots and of fibrin sealants.

BACKGROUND: Fibrin sealants are extensively used in liver surgery, for example, during liver resections. Although these sealants have been developed to induce hemostasis, in practice these products are actually mainly used to seal dissected bile ducts to prevent postsurgical bile leakage.

METHODS: We performed in vitro assays in which clotting and lysis of human plasma clots or fibrin sealants was studied in presence or absence of human bile.

RESULTS: Addition of bile to human plasma resulted in a dose-dependent increase in clotting time, and a dose-dependent decrease in clot lysis time. Bile also accelerated lysis of in vitro clotted fibrin sealants. Immunodepletion of tissue-type plasminogen activator (tPA) resulted in partial depletion of the lysis promoting activity of bile. Immunodepletion of both tPA and lysine-binding proteins from bile fully abolished the lytic activity, suggesting that tPA and plasminogen present in human bile are responsible for the lysis-promoting effect. Surprisingly, addition of high dose plasminogen activator inhibitor type 1 (PAI-1) to bile did not attenuate the lytic activity toward fibrin sealants, which suggested that tPA in a biliary environment may be unsusceptible to PAI-1 inhibition. Indeed, bile acids were shown to prevent tPA from interacting with PAI-1, although preformed complexes were

not destabilized upon addition of bile acids.

CONCLUSIONS: These combined results suggest that the presence of tPA and other fibrinolytic proteins in human bile results in lysis of plasma clots or fibrin sealants, which potentially could affect the efficacy of the latter products.