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SCA39

IN VITRO EFFECT OF PROTAMINE EXCESS ON BLOOD COAGULATION ASSAYS

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Introduction. Coagulation assays that utilize artificial activation, while time-efficient, have limitations in the ability to assess hemostatic competency after cardiac surgery. On-site tests for protamine excess, which produces an anticoagulant effect and may prolong clotting time (1), have not been described. The objective of this investigation was to evaluate the *in vitro* effect of protamine excess on coagulation. For these studies, we have compared three assays: Hemochron Saline (HS), Medtronic kaolin-activated clotting time (ACT), and activated partial thromboplastin time (aPTT). With both ACT and aPTT, artificial activation occurs; however, in HS, no activators are present. Our hypothesis was that the sensitivity to possible subtle effects of protamine excess on clotting time would be greater in the HS assay than in either ACT or aPTT. In a previous study, the HS assay correlated strongly ($r = 0.938$) with Lee-White whole blood clotting time (2). The HS assay is fully automated, and is carried out in a small battery-operated apparatus; therefore, it has the potential to serve as an on-site test for protamine excess.

Methods. With IRB approval, a total of eight patients scheduled for cardiac surgery were studied. Five of the patients were evaluated for HS, ACT, and aPTT clotting time; three patients were evaluated for only HS and ACT. Blood was drawn from the patients post-bypass, following heparin reversal with protamine. Assuming a blood volume of 5.6 l per 70 kg body weight, a 25 mg "excess dose" of protamine per 70 kg -- beyond the amount necessary for heparin reversal -- would amount to 4.5 μ g per ml of blood. Excesses of 50 mg of protamine were also studied on the same basis. A set of three assays were prepared for each patient as follows: protamine sufficient for 3 ml of blood in the HS tubes; for 4 ml of blood for the aPTT assay; for 2 ml of blood for the ACT assay. Except for aPTT (assayed by the hospital laboratory) the other assays were carried out in the operating room.

Results. The results are summarized in the figures as means \pm S.E. The HS assay showed a marked sensitivity to increases in protamine excess ($r = 0.605$; $p = 0.0286$). ACT ($r = -0.014$) and aPTT ($r = 0.190$) did not correlate with protamine excess. The average baseline values for the assays were: HS =264 sec, ACT =117 sec, aPTT =33.8 sec.

Conclusions. The HS assay, which contains no artificial activators of coagulation, was highly sensitive to the anticoagulant effect of protamine. The basis for this unique sensitivity of the HS assay in this regard is not known.

References.

1. Mochizuki T, et al. *Anesth Analg* 87: 781-5, 1998.
2. Schriever, HG, et al., *Am J Clin Pathol* 60: 323-9, 1973.

