

Heparin resistance and coagulation activation rebound effect after anticoagulant withdrawal - beneficiary effect of adjuvant antiplatelet therapy.

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Abstract

AIM:

To investigate biological resistance to enoxaparin and rebound effect after prophylaxis withdrawal, using Thrombin Generation (TG) assay.

METHODS:

Fifteen patients undergoing femoro-popliteal bypass grafting (enoxaparin 4000 antiXaIU+75mg clopidogrel), and 15 patients undergoing total-hip-replacement (THR) (enoxaparin alone). TG-assay parameters [lag-time, Endogenous-Thrombin-Potential, Peak-, time-to-Peak, and Mean-Rate-Index] were assessed to investigate heparin resistance and rebound effect after prophylaxis interruption. Measurements were obtained pre-op, post-op (before prophylaxis initiation), 8-days post-op, and 48-hours after anticoagulant withdrawal (Day 32).

RESULTS:

Surgery increased TG in vascular patients despite intra-operative unfractionated heparin administration when compared to orthopaedic patients (MRI:p=0.039, ETP:p=0.001, PGT:p=0.003), but this peri-operative pro-thrombotic status was reversed by post-operative thromboprophylaxis. No thromboembolic events were observed. Similar TG parameter values between the 8t h and 32n d post-op day indicate that vascular patients were adequately protected after prophylaxis withdrawal, probably due to the synergic action of clopidogrel, while orthopaedic patients increased TG on Day-32 compared to the 8t h post-op day (p=0.03, for both lag-time and ttPeak). Furthermore, on day-32, a prothrombotic status (increased TG) was observed in the orthopaedic patients (p=0.034, and 0.004 for ttPeak and lag-time, respectively). Inter-individual variability to enoxaparin response was observed in both groups: 7/15 vascular and 10/15 orthopaedic patients increased TG despite anticoagulant administration, which reveals heparin-resistance. Among the heparin-resistant patients, 4 Vascular and 6 Orthopaedic further increased TG after anticoagulant withdrawal depicting a rebound effect to activation of coagulation.

CONCLUSIONS:

Heparin-resistance is not a rare phenomenon in clinical practice and was found in about half of our patients. A rebound effect of coagulation activation after thromboprophylaxis withdrawal is observed in the extended post-operative period. This phenomenon is attenuated with the addition of concomitant anti-platelet (clopidogrel) treatment.