Heparin Resistance and ATIII

Objectives:

- Understanding the mechanism of Heparin and Heparin Resistance
- Understanding potential factors responsible for Heparin Resistance
- Understanding the different therapeutic options for managing Heparin Resistance
- Understanding the role of ATIII in patients with Heparin Resistance

Heparin is the most commonly used drug to provide anticoagulation for initiation of cardiopulmonary bypass (CPB). It is also a commonly used drug in the hospital setting providing prophylaxis for venous thrombosis, treatment of acute cardiac syndrome, and numerous other clinical scenarios where rapid anticoagulation is necessary. Heparin is a negatively charged, sulphated glycosaminoglycan which is most commonly commercially prepared with porcine intestinal mucosa (bovine lung rarely available). Heparin exerts its anticoagulant effect via antithrombin III (AT) which results in a conformational change of ATIII and this inhibits factors II and Xa. The dosing of heparin is variable between patients and a single heparin dose results in vastly different degrees of anticoagulation as measured by aPTT or ACT between individuals of similar weight. This variability is in large part secondary to heparin’s alternate binding to plasma proteins. The binding of heparin to these plasma proteins can result in reducing the effects of heparin which is linked with heparin resistance. These proteins include: platelet factor 4 (PF4), fibrinogen, factor VIII and histidine-rich glycoprotein. An increase in any of these plasma proteins (which may occur in malignancy, very ill patients, and in the partituent) may cause a reduced response to a heparin dose. Other causes of heparin resistance are a decrease in the amount of ATIII available (congenital or more commonly acquired) or an increase in thrombin. A big part of heparin administration and dealing with resistance is the complexity of the different laboratory tests available and understanding their limitations.

In this presentation we will consider a number of variables responsible for heparin resistance. We will consider limitations of monitoring heparin and possible uses of ATIII in treating heparin resistance. It is also important to understand that there is a discrepancy among anesthesiologists as to what adequate anticoagulation is for a given patient. The ideal ACT and the appropriate heparin dosing for patients is highly variable between institutions. We will consider the different strategies of managing ACT and heparin administration.


Hattersley PG. Activated coagulation time of whole blood. JAMA 1966;196:436–40