Chapter 11
Anticoagulation Options

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ABSTRACT

There are multiple indications for anticoagulation in the cardiac surgery intensive care unit including cardiac valve replacement, mechanical circulatory pumps (ECMO and ventricular assist devices), deep vein thrombosis prophylaxis, treatment of heparin-induced thrombocytopenia, and treatment of other thrombotic conditions including pulmonary embolism. Anticoagulant medications broadly fall into two categories: antiplatelet drugs and inhibitors of protein clotting factors. In this chapter we will review anticoagulant medications, therapeutic drug monitoring, common indications for anticoagulation, and the risks associated with anticoagulation after cardiac surgery.

INTRODUCTION

Human blood has the remarkable ability to transform from its normal fluid state to a semi-solid state known as clot. Over thousands of years, evolution selected for this highly specialized mechanism, which limits blood loss during injury and leads to wound healing. In a simplified paradigm coagulation can be thought of as primary and secondary. Primary coagulation occurs when a platelet plug adheres to a site of endothelial injury and secondary coagulation occurs when blood proteins solidify the plug creating a clot.

Although coagulation is a highly adaptive mechanism, it can also be pathologic. For example clots in coronary arteries, pulmonary arteries, or cerebral arteries can lead to permanent organ injury or death. Virchow described the classic triad for clot formation as: endothelial injury, changes in blood flow (stasis), and hypercoagulability. Because cardiac surgery often requires implantation of artificial surfaces (cardiac valves, graft material etc.) patients are at risk for pathologic clotting. Cardiac surgery also leads to disruption of the normal endothelium, stasis (due to immobility), and altered levels of common coagulant and anticoagulant factors.

This chapter will review anticoagulant drugs that are commonly used in the cardiac surgery intensive care unit, therapeutic monitoring for these drugs, indications for anticoagulation, and the risks associated with anticoagulation after cardiac surgery.

Background

Anticoagulation management is a frequent issue in cardiac surgery critical care. There are a bevy of drugs available to today's intensive care unit (ICU) practitioner allowing for maximal benefit and minimal risk when an anticoagulant is properly selected, dosed, and monitored. Available drugs work through different pathways, have different pharmacokinetic profiles, and have different routes of administration making them best suited for particular clinical scenarios. They also carry different levels of risk depending on a patient's hepatic and renal function. For these reasons, ICU practitioners must be facile in managing the various anticoagulant medications that are available.

Anti-platelet drugs are used frequently in the cardiac surgery ICU, particularly in patients who have had coronary artery bypass graft (CABG) surgery, aortic replacement surgery, or bioprosthetic cardiac valve replacement. Almost all of these patients require aspirin and select patients receive dual anti-platelet therapy, typically with a thienopyridine drug.

Drugs that inhibit protein coagulation factors are also used in the cardiac surgery ICU for mechanical valve replacement, mechanical circulatory support devices or ECMO, prolonged atrial fibrillation in high-risk patients, heparin induced thrombocytopenia (HIT), pulmonary embolism, and certain bioprosthetic valves. Recently novel oral anticoagulant drugs have become available which will likely change future anticoagulation practices (eg: apixiban, dabigatran, and rivaroxaban).

STATE OF THE ART APPROACHES

Anti-Platelet Drugs

Aspirin

Acetylsalicylic acid is an analgesic, anti-inflammatory, and anti-platelet drug that was first isolated from the bark of willow trees. The German pharmaceutical company Bayer began synthesizing the drug aspirin in the late 1800s. Since that time it has remained one of the most important and widely used drugs in medicine. Aspirin is a non-steroidal anti-inflammatory drug (NSAID) that irreversibly inhibits the enzyme cyclo-oxygenase (COX). COX has two isoforms COX-1 and COX-2 and aspirin is 170 times more potent at inhibiting COX-1 (Vane, Bakhle & Botting, 1998). The downstream effect of COX inhibition is decreased production of thromboxane A2, which leads to decreased platelet aggregation. Aspirin may also inhibit platelets through other mechanisms including inhibition of neutrophil-related platelet activation (Bolz & Pohl, 1997). The dose necessary for platelet inhibition in a given individual is debatable and it has been suggested that some patients are "aspirin resistant". In one study, doses as small as 37.5 mg per day decreased thromboxane A2 production by 98% 2-6 hours after the first dose (Perneby,

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