

Heparin Contamination and Patient Safety

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Unfractionated heparin (UFH) represents a universal anticoagulant which is widely used for several medical, surgical and interventional indications. Low molecular weight heparins (LMWHs) represent depolymerized versions of porcine mucosal heparin which are prepared by chemical and enzymatic processes. Mammalian sources such as the bovine, porcine and equine tissue are used to extract heparin. Heparin and related polymers are also widespread in non-mammalian tissues. The currently available UFH and LMWHs represent a heterogeneous mixture of glycosaminoglycan with structural identity. Only 20-30% of these components exhibit anticoagulant activity while the others remain uncharacterized. Although the currently available UFH and LMWHs have undergone refinements, some of these products may still contain carry-over contaminants such as dermatan sulfate and other non-heparin GAGs. More recently, the increased usage of UFH in the production of LMWHs has created a shortage of porcine mucosal heparin. Most of the raw material for the manufacturing of heparin represents porcine material from China. During the period 2007 and 2008, contaminant heparin was linked to at least 149 deaths and hundreds of adverse reactions. At the same time microbial contaminants were also reported in the UFH. More concerning were the reports that the Chinese supplies of heparin contained a semi-synthetic GAG, namely oversulfated chondroitin sulfate. This contaminant was mainly linked to the reported adverse reactions. Additional studies indicate that besides oversulfated chondroitin sulfate (OSCS) chemically sulfated heparin byproducts representing heparin sulfate, chondroitin sulfate and dermatan sulfate were also present in some of the recalled batches of heparin. Moreover, some of the recalled batches of heparin that produced adverse reactions and deaths were found to be free of OSCS, suggesting that this agent was not the sole contaminant responsible for the observed adverse reactions. Interestingly, the contaminated heparins were also found to contain different types of OSCS with marked differences in physico-chemical characteristics. Because of the availability of newer technology, it is possible to produce anticoagulant GAGs with comparable or better anticoagulant effects in comparison to heparin. While the OSCS is claimed to be the main contaminant in the recalled heparins, a dispute on the presence of other contaminants causing the adverse reaction is still debated. This presentation will provide an update on this topic and its implication on future heparin and related anticoagulant development. Despite several publications and intense investigations, the origin of heparin contaminants and product adulteration is not established.

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