

Adverse Effects of Protamine Causes Hypotension

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Abstract

Protamine is a routinely used safe antidote for heparin reversal in cardiovascular surgery. Protamine was first utilized to extend the shelf life of insulin formulations. Only a little amount of protamine is used to neutralize heparin in plasma because it interacts with platelets and fibrinogen while still serving as an anticoagulant. Major Adverse Drug Reactions (ADRs) have been related to protamine; however they are uncommon, especially in patients with a history of protamine hypersensitivity. Protamine-induced pulmonary arterial hypertension and peripheral vascular collapse struck a 60-year-old diabetic male patient who had had on-pump coronary artery bypass grafting at a tertiary care center. This was a definite, non-preventable, severe ADR, according to the causality, preventability, and severity assessment scale.

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INTRODUCTION

Protamine is a polypeptide that comes from salmon sperm. Recombinant DNA technology is now used to make it. Protamine, a strong base, binds to and neutralises unfractionated heparin, a common anticoagulant. Protamine is rarely required to reverse heparin's activity because it is short-lived due to metabolism. It has, however, been safely used as an antidote in cardiovascular procedures where heparin's activity must be stopped rapidly for years. However, in a small percentage of cases, protamine can cause fatal Adverse Drug Reactions (ADRs).

An adverse drug reaction (ADR) is defined as "an appreciably harmful or unpleasant reaction resulting from an intervention related to the use of a medicinal product; adverse effects usually predict hazard from future administration and warrant prevention, specific treatment, dosage regimen modification, or product withdrawal." such as hypotension and pulmonary arterial hypertension (PAH).

Some of the negative consequences of protamine include hypotension, anaphylaxis, PAH, bradycardia, hepatic renal impairment, cardiovascular collapse, and death. The incidence rate varies between 0.06 percent and 10.6 percent. Immunologic and non-immune (pharmacogenetics variations) processes are hypothesized to play a role in the pathophysiology of ADRs. In this case, protamine was given through the peripheral (cephalic) vein because it produces histamine release and hypotension when given through the central vein. To detect any hemodynamic instability early, protamine is given as a small bolus (test dose). There were two episodes of hypotension and PAH in this patient. The first occurrence happened after

a 60 percent fresh protamine infusion. Protamine re-challenge produced the second episode, which occurred after a 10% protamine infusion. ADR caused by protamines is common.

Because protamine shares antigens with fish proteins, cross-reactivity develops. Vasectomy- (Vasectomy is a surgical treatment that is used to sterilize men or to provide long-term contraception. The male vasa deferential is cut and knotted or sealed during the surgery to prevent sperm from entering the urethra and so fertilization of a female through sexual intercourse. Vasectomies are normally conducted in a doctor's office, a medical clinic, or a veterinary clinic when performed on an animal) breaks down the blood-testis barrier, exposing the host to sperm antigens. NPH insulin is a crystalline suspension of protamine, zinc, and insulin. Chronic protamine exposure resulted in the formation of particular immunoglobulin E antibodies in half of the patients in this study, as well as a 95-fold increased risk of severe protamine hypersensitivity episodes. In this patient on recombinant protamine, none of the risk factors were present. The patient was given glimepiride as an anti-diabetic medication. Preoperative skin prick testing for hypersensitivity has a high rate of false negatives and is not 100 percent accurate. As a result, skin testing isn't done at our facilities on a regular basis. Protamine's negative inotropic effect and the release of nitric oxide cause hypotension.

To help prevent protamine-induced ADRs, advanced pharmacokinetic and pharmacogenetic testing could be developed and used. Newer chemicals, such as oligoethylene glycol functionalized guanidinocalixarene, which selectively neutralises heparin intended as an antidote while being highly biocompatible, may be a safer option.