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Protamine Sulphate: An Antidote for Bleeding caused by Heparin

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ABSTRACT

Protamine is also used in the context of dialysis, invasive vascular procedures, and acute ischemic strokes to reverse the anticoagulation effects of unfractionated heparin. Protamine sulfate is a fairly strong basic protein that binds with the strongly acidic heparin to create a stable and inactive complex (salt) when given as an antidote to heparin. It is a highly cationic peptide that forms a stable ion pair without any anticoagulant properties when it binds to either heparin or low molecular weight heparin (LMWH). The positive cationic arginine peptide of protamine reacts with unfractionated heparin, a strongly anionic anticoagulant, to form a salt aggregate. The metabolism of the heparin-protamine salt aggregate is poorly understood.

Keywords: protamine sulphate, antidote, bleeding, heparin, stroke, anticoagulation

INTRODUCTION

Protamine sulfate is a medication used to reverse the effects of heparin that is specifically used in heparin overdose and has a low molecular weight heparin due to overdose. It is also capable of reversing the effects of heparin when given by injection into a vein during delivery and heart surgery, with the onset of effects coming in typically five minutes [1]. Protamine is also used in the context of dialysis, invasive vascular procedures, and acute ischemic strokes to reverse the anticoagulation effects of unfractionated heparin [2-5]. Protamine sulfate was first produced from salmon sperm, according to the American Society of Health-System Pharmacists in 2016, and it is currently primarily produced using recombinant biotechnology [7]. It was first authorized for medical use in the United States in 1969. Since hexadimethrine bromide, another cationic agent, was the original heparin reversal agent in the early days of heart surgery, until studies in the 1960s suggested that hexadimethrine bromide might cause kidney failure when used in doses above its therapeutic range, Protamine sulphate was substituted [8]. It is strongly alkaline with nearly two-thirds of the amino acid composition being poly-cationic arginine.

Toxicity

The positive charge of protamine is thought to be the cause of its toxicity. In bovine pulmonary endothelial cells, it has been demonstrated to reduce ATP production by endothelial cells and to cause progressive mitochondrial injury [9]. According to the theory, the salt that is created when protamine and heparin combine to effectively neutralize the positively charged molecule of protamine while also providing some intracellular protection against toxicity. This salt is also thought to have a toxic effect on myocardial cells because of its positive charge, which is thought to affect mitochondrial cells within the cells [10].

Medical uses

During some surgeries, particularly heart surgeries where anticoagulation is required to prevent clot formation within the cardiopulmonary bypass pump apparatus, protamine sulfate is typically given to reverse the large dose of

heparin administered during those surgeries. When the patient is off the pump and no longer requires extracorporeal circulation or anticoagulation, a protamine dose is administered by drip over a period of time. Additionally, it is utilized in tissue cultures as a cross-linker for viral transduction, gene transfer, protein purification, and other processes. Protamine sulfate has been investigated in the context of gene therapy as a means of enhancing transduction rates by viral and nonviral mediated delivery mechanisms [11].

Monitoring

Protamine should be administered gradually, and patients should be closely watched for anaphylaxis, rapid hypotension, or an increase in pulmonary artery pressures. In addition to hypotension, a rash, wheezing, or trouble breathing, anaphylaxis can result in an increase in peak airway pressures. It is advantageous to have an arterial line for invasive blood pressure monitoring and/or a pulmonary artery catheter to track changes in pulmonary artery pressures in order to detect protamine administration's early adverse effects [12].

Mechanism of action

Protamine sulfate is a fairly strong basic protein that binds with the strongly acidic heparin to create a stable and inactive complex (salt) when given as an antidote to heparin. It is a highly cationic peptide that forms a stable ion pair without any anticoagulant properties when it binds to either heparin or low molecular weight heparin (LMWH). The reticuloendothelial system removes and disintegrates the ionic complex after that. The positive cationic arginine peptide of protamine reacts with unfractionated heparin, a strongly anionic anticoagulant, to form a salt aggregate. The salt aggregate that forms is dormant and has no anticoagulant qualities. Protamine has a quick onset of action, a 5-minute half-life, and a 10-minute half-life, all of which are sufficient to neutralize unfractionated heparin. The metabolism of the heparin-protamine salt aggregate is poorly understood. Some authors have described the salt's metabolism in the liver, while others have claimed that the kidneys are responsible for the salt's metabolism and excretion. Protamine should only be used in the proper dosage; in excess, it has been shown to have anticoagulant properties, which can lead to bleeding and increased transfusion needs [13].

CONCLUSION

Protamine sulfate is a fairly strong basic protein that binds with the strongly acidic heparin to create a stable and inactive complex (salt) when given as an antidote to heparin.It is a highly cationic peptide that forms a stable ion pair without any anticoagulant properties when it binds to either heparin or low molecular weight heparin (LMWH).The positive cationic arginine peptide of protamine reacts with unfractionated heparin, a strongly anionic anticoagulant, to form a salt aggregate.The metabolism of the heparin-protamine salt aggregate is poorly understood.

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