Protamine

Newborn use only

bleeding Reversal of low molecular weight heparin (e.g. enoxaparin) by protamine is incomplete. Rapid IV injection of protamine can cause anaphylactic reaction and cardiovascular collapse. Facilities for resuscitation and treatment of shock should be available. Protamine acts as an anticoagulant at very high doses. Protamine has variable dose-response and a narrow therapeutic window. Indication Reverses anticoagulant at very high doses. Protamine forms a neutral 1.1 complex and strips heparin from antithrombin fluction. Reverses anticoagulant at very high doses. Action Protamine forms a neutral 1.1 complex and strips heparin from antithrombin fluction. Reverses anticoagulant defects of unfraction and selectively precipitates fibrinogen. (2, 3) Drug type Antidote to heparin Protamine sulfate injection BP Presentation Ampoule contains 50 mg/S ml of protamine sulfate Dose 0 Time Since Last Heparin Dose Protamine dose per 100 units of heparin received in the last 2 hours 30-60 min 0.375-0.5 mg 30-60 min 0.375-0.37 mg 30-6120 min 0.375-0.37 mg 30-60 min 0.375-0.37 mg 30-800 min 0.375-0.37 mg 30-60 min 0.375-0.57 mg 30-800 min 0.375-0.37 mg 30-60 min </th <th>Alert</th> <th>1 Stopping untractionated henarin (LIFH) intus</th> <th>ion is adequate in most instances including overdose if no</th>	Alert	1 Stopping untractionated henarin (LIFH) intus	ion is adequate in most instances including overdose if no		
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Protamine

Newborn use only

	Device Accepteilling have deviced the effective effectiv		
	Drugs: Ampicillin, benzylpenicillin, cefazolin, cefotaxime, cefoxitin, ceftazidime, ceftriaxone,		
	dexamethasone, folic acid, furosemide, heparin sodium, hydrocortisone sodium succinate,		
	indometacin, insulin (Actrapid), ketorolac, methylprednisolone sodium succinate, pentamidine, phenobarbital, sugammadex (7)		
Stability	Diluted solutions should be used immediately and should not be stored as it contains no preservatives.		
Storage	Store below 25°C. (8)		
Excipients	Sodium chloride, hydrochloric acid, sodium hydroxide, water for injections. (8)		
Special	The rapid disappearance of protamine from the circulation could contribute to "heparin rebound" after		
comments	initial adequate reversal of heparin. Repeated doses may be required to neutralise		
Evidence	Efficacy		
	When titrated with heparinised plasma, protamine neutralises its anticoagulant activity and restores thrombin generation. (3, 9, 10) This pharmacological action is used for reversing the anticoagulant effect of unfractionated heparin and low molecular weight heparin following accidental overdose or procedures requiring anticoagulation of in vitro blood-circuits. In neonates and children anticoagulation reversal with heparin, when used with individualised heparin dosage significantly reduces activation of coagulation cascade, fibrinolysis, blood loss, need for transfusion, ventilatory support and hospital stay after cardiac surgery with cardiopulmonary bypass. (11, 12) Equimolar concentrations of protamine sulfate neutralize anti-Ila activity of LMWH but result in only partial neutralization of its anti-Xa activity. (13) The dose of protamine sulfate required depends on the dose and type of LMWH used. Repeat doses of protamine may be required after subcutaneous LMWH. (14) Safety In neonates, protamine has been used for reversal of heparin effect following cardiac surgery requiring cardiopulmonary bypass and accidental heparin overdose. (9, 15) Hypersensitivity reactions to protamine sulfate may occur in patients with known hypersensitivity reactions to fish or those previously exposed to protamine therapy or protamine-containing insulin. (5) Some studies recommend use of peripheral venous catheter for administration as protamine delivery through a central line can cause an increase in plasma histamine levels and a decrease in systemic vascular resistance. (16) Pharmacokinetics In vitro studies suggest a significant effect at protamine plasma concentrations of 0.02 to 0.5 mg/mL. Protamine sulfate and the heparin/protamine complex are partially metabolized by fibrinolysin and		
	free protamine is broken down by plasma protaminase. Half-life of protamine is reported to be 7.4		
	min, after a single intravenous dose of 0.5 mg/kg via infusion pump over 10 min in healthy volunteers.		
	(17)		
Practice points	 It is presumed that 1 mg of protamine neutralises anticoagulant effects of 1 mg (100 units) of heparin. 		
	• Half-life of heparin is short, so dose of protamine depends on time since the last heparin injection.		
	Obtain blood for PT and APTT 15 min after the administration of protamine sulphate.		
	• Effects of LMWH can persist for up to 24 hours after administration, so repeat doses of protamine may be required.		
	Prolonged infusion of protamine is necessary if heparin was administered subcutaneously.		
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Protamine

Newborn use only

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