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Original article

Effect of extra protamine infusion in underweight patients undergoing cardiac surgery

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Abstract

Introduction: The risk of post-operative bleeding was shown to be inversely correlated to Body Mass Index (BMI) in patients undergoing cardiac surgery.
Objective: To identify whether an additional dose of protamine infusion given to underweight patients undergoing cardiac surgery will reduce postoperative blood loss, transfusion requirement and need for re-exploration for bleeding.
Method: A prospective trial, where 100 underweight patients with BMI less than 20 kg/m^2, underwent open cardiac surgery from May 2013 till June 2015. Patients were divided into two equal groups; Group (A), 50 patients, received additional protamine infusion at a dose of 25 mg/h for the first 6 h following complete neutralization of heparin at the end of surgery and Group (B), 50 patients, did not received any additional protamine.
Results: Blood loss was less in group A 576 ml ± 310 versus group B 800 ml ± 241 (P = 0.001). Transfusion requirement was also lower in group A 1.2 unit ± 0.7 versus group B 3.4 unit ± 1.5 (P = 0.001). The ACT (Activated Clotting Time) levels at 0 h (time of heparin neutralization) were not significantly different in both groups 108 s ± 9.1 versus 112 s ± 10.9 in groups A and B respectively (P = 0.4). However, after 6 h, the ACT was significantly lower in group A 110 s ± 9.7 versus 145 s ± 6.7 in group B (P = 0.01).
Conclusion: Additional protamine infusion for 6 h significantly reduced the amount of blood loss, transfusion requirement and the ACT at 6 h in underweight patients undergoing open cardiac surgery.

Keywords: Protamine; Underweight patients; Post cardiac surgery bleeding

1. Introduction

The degree of obesity is assessed by the BMI which equals weight (in kilograms) divided by the square of height (in meters) [1]. BMI values are categorized into one of five groups: underweight (<20 kg/m^2); normal weight (≥20 and <25 kg/m^2); overweight (≥25 and <30 kg/m^2); obese (≥30 and <35 kg/m^2); severely obese (≥35 kg/m^2) as per the American Heart Association guidelines for defining overweight [2].

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Underweight patients were shown to bleed more post cardiac surgery and this may be caused by relatively increased hemo-dilution caused by the priming volume of the cardiopulmonary bypass (CPB) circuit which may exacerbate CPB – related coagulopathy or to the amount of heparin sequestrated in their internal organs during CPB [3,4].

The heart – lung machine cannot compensate for the pulsatile flow of the normal circulation. This leads to blood sequestrating in poorly perfused areas, mainly the spleen, liver, the splanchnic bed, skin and muscles [5]. The time of maximal heparin release is usually immediately following discontinuation of CPB, where the patient has a brief period of hemodynamic instability and peripheral hypo perfusion [6].

Impaired coagulation profile post cardiac surgery is a major cause of bleeding, mainly attributed to heparin rebound, several theories tried to explain this including release of heparin sequestered in tissues [7], delayed return of heparin to the circulation from the extracellular space via lymphatics [7], clearance of an unrecognized endogenous heparin antagonist [8] and more rapid clearance of protamine in relation to heparin [8]. Some studies demonstrated the release of heparin from the endothelial cells once the plasma levels have dropped to a certain level following protamine neutralisation. This raises the question of whether or not heparin rebound is responsible for the postoperative coagulopathy and subsequent bleeding following cardiac surgery [9].

2. Patient and method

2.1. Study population

This prospective study included 100 underweight adult patients (BMI less than 20 kg/m^2) undergoing cardiac surgery at Cardiothoracic surgery department, Ain Shams University hospital, Cairo, Egypt, during the period from May 2013 till June 2015.

2.2. Inclusion criteria

Selected patients were aged >18 years, of both sexes, with BMI <20 kg/m_2 and scheduled for cardiac surgery under CPB whether elective, urgent or emergency. Written consent was obtained.

2.3. Exclusion criteria

Patients with known coagulopathies such as haemophilia and Von Willebrand's disease, patients with liver cell failure with hypoalbuminemia and elevated PT and PTT, patients receiving unfractionated or low molecular weight heparin, thrombin inhibitors, warfarin, antiplatelet within the past 7 days, patients expected to undergo moderate and deep hypothermic CPB or circulatory arrest, patients undergoing surgery involving thoracic aorta, anaemic patients with preoperative haemoglobin less than 10 gm/dl, patients undergoing Re-do surgery and finally patients going for off pump procedures were excluded from this study.

2.4. Method

All patients received an initial dose of unfractionated heparin at a dose of 400 IU/kg to achieve an ACT above 480 s prior to initiation of CPB, if ACT did not reach the targeted level, an extra dose of 100 IU/kg heparin was given, ACT was regularly checked every 30 min during CPB time to make sure it is maintained above 480 s and extra doses of heparin were given if needed.

CPB was primed with crystalloid solution and the prime volume ranged from 1000 to 1500 ml and 5000 IU heparin was added to the prime volume. Haematocrit level was kept between 20 and 30 during CPB period and temperature was kept above 32 °C. Following termination of CPB, all patients were given protamine sulphate at a dose of 1.5 mg for each 100 IU of heparin in relation to the initial loading dose of heparin. ACT was repeated to make sure the pre-heparin baseline ACT was reached. Then, patients in group (A) (50 patients) were infused with protamine sulphate at a dose of 25 mg/h while patients in group (B) did not receive any additional protamine for the first 6 h. ACT was done to all patients in both groups at 0 and 6 h following complete neutralization of heparin by the end of surgery and recorded for all patients. Patients were transfused 2 units of packed RBC's if their haemoglobin level dropped below 8 gm/dl (threshold for blood transfusion), targeting a haemoglobin level between 8 and 10 gm/dl.

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