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Case Report

Innovative Hemofiltration Approach to Protamine-Induced Shock After Cardiac Surgery in a Low-Resource Environment: A Case Report

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Abstract: Protamine sulfate is routinely administered to reverse heparin anticoagulation following cardiopulmonary bypass (CPB). Although generally well tolerated, protamine may elicit severe hypersensitivity reactions, including anaphylaxis. Managing such complications is especially challenging in resource-limited settings where access to blood products and advanced supportive therapies is constrained. A 61-year-old man with multiple comorbidities underwent elective coronary artery bypass grafting (CABG). Following a 50 mg test dose of protamine sulfate after CPB, the patient developed profound hypotension and refractory shock unresponsive to vasopressors. Cardiac arrest ensued, prompting reheparinization and emergent reinstitution of CPB. Protamine was withheld after the second decannulation. Postoperatively, the patient experienced massive hemorrhage (~7 liters over 3 hours). Autologous blood was salvaged using a gravity-driven hemofiltration system (HemoClear®), with reinfu-sion of washed, platelet-rich red blood cells. Four units of FFP and albumin were administered. After stabilization, a reduced protamine dose (0.5 mg/kg) was safely administered for 2 hours postoperatively. The patient recovered without recurrence of adverse events. This case illustrates the importance of early recognition and tailored management of protamine-induced hypersensitivity reactions. In low-resource settings, gravity-driven hemofiltration may offer a feasible method of autologous blood salvage during critical hemorrhagic events.

Keywords: Protamine Sulfate; Anaphylaxis; Cardiopulmonary Bypass; Hemofiltration; Autologous Transfusion; Low-Resource Settings.

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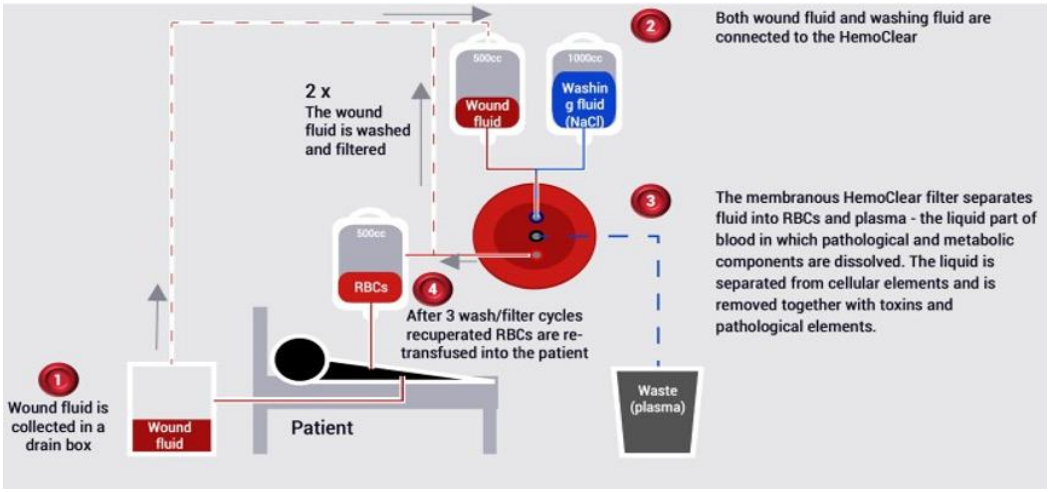
1. Introduction

Protamine sulfate, a cationic polypeptide derived from salmon sperm, is used to reverse heparin anticoagulation following cardiopulmonary bypass (CPB). Although generally safe, it can cause adverse reactions in 0.06–2.6% of cases [1,2], ranging from mild hypotension to life-threatening anaphylaxis and pulmonary vasoconstriction. Risk factors include prior use of neutral protamine hagedorn (NPH) insulin, fish allergy, vasectomy, or presence of anti-sperm antibodies [2,3]. Reactions may also occur unpredictably. In resource-limited environments, where access to transfusion and extracorporeal support is constrained, low-cost autologous salvage strategies like hemofiltration may be lifesaving [4,5].

2. Case Report

A 61-year-old male with non-insulin dependent diabetes mellitus, hypertension, prior percutaneous coronary intervention (PCI) (2017), a resolved ischemic stroke (2023), and an active diabetic foot ulcer underwent elective coronary artery bypass grafting (CABG) for three-vessel coronary artery disease. After CPB weaning, a bolus of 50 mg protamine was administered. Within 2 minutes, the patient developed profound hypotension with blood pressure decreasing to 58/34 mmHg and further down to 48/32 mmHg. He remained hypotensive despite escalating doses of norepinephrine 0.1 µg/kg/min, epinephrine 0.1 µg/kg/min, and dopamine 5 µg/kg/min. A 2 mg bolus of terlipressin was administered [6] due to ongoing vasoplegia. The patient experienced cardiac arrest shortly thereafter. Protamine infusion was immediately halted (Figure 1 and Figure 2), heparin was re-administered, and emergency reinstitution of CPB was performed.

Figure 1. Workflow of autologous blood salvage using gravity-driven hemofiltration (HemoClear®). Shed blood from postoperative hemorrhage was processed, yielding washed, platelet-rich red blood cells that were reinfused into the patient (own data).



Hemodynamic stability was gradually restored with high-dose vasopressors and 100 mg prednisone. CPB was successfully weaned after 17 minutes, without re-administration of protamine. He was transferred to the intensive care unit (ICU), where he remained hypotensive (blood pressure ranging between 66/38 mmHg and 84/45 mmHg) despite continued vasopressor support. During the first 3 hours postoperatively, the patient experienced massive hemorrhage estimated at 7 liters. Blood was salvaged and processed using a gravity-driven hemofiltration system (HemoClear®). The total processing time was approximately 45–60 minutes. Laboratory analysis revealed a pre-filtration hematocrit of ~18% and a post-filtration hematocrit of ~34%. The pre-filtration platelet count was 54×10^9/L, which increased to 117×10^9/L post-filtration. The resulting product, washed platelet-rich red blood cells, was reinfused.

The patient also received four units of fresh frozen plasma and albumin. Approximately two hours after the initial reaction, once bleeding had been controlled and hemodynamic stability was observed, a reduced protamine dose (0.5 mg/kg) was cautiously administered. No adverse reactions occurred. The patient remained stable, was extubated on postoperative day one, transferred to the ward on day three, and discharged in good condition on postoperative day seven.

3. Discussion

Protamine-induced reactions encompass a spectrum of mechanisms, including IgE-mediated hypersensitivity, complement activation, and acute pulmonary vasoconstriction

[1,3]. In the present case, the extremely rapid onset of hypotension and cardiac arrest following protamine administration was clinically consistent with a severe hypersensitivity reaction [1,2] (Grade 4). However, the absence of confirmatory tests such as serum tryptase or advanced echocardiographic and pulmonary hemodynamic measurements limits the ability to definitively determine the pathophysiology. Alternative mechanisms such as complement activation or direct pulmonary vasoconstriction may have contributed to or even primarily caused the observed collapse.

Figura 2. Real setup procedure. Real set up Workflow procedure. Actual bedside setup of the HemoClear® device was used during the case, showing the collection bag, filtration unit, and reinfusion pathway.

The patient's subsequent tolerance to a reduced dose of protamine cannot be attributed to a single intervention [2,7]. It is far more likely that multiple factors contributed, including the administration of corticosteroids, volume resuscitation with fresh frozen plasma and albumin, and the natural resolution of the acute inflammatory cascade. While hemofiltration may have supported hemodynamic stabilization through reduction of circulating mediators and unbound protamine [4,5], its role in modifying antigen load or immune reactivity remains speculative. We present its use here as part of a multifactorial support strategy, not as a definitive mechanism for immune desensitization.

This case underscores the potential value of gravity-driven hemofiltration systems such as HemoClear® in environments where conventional blood salvage or extracorporeal devices are unavailable. The ability to rapidly process shed blood and reinfuse red cells and platelets, demonstrated by increases in hematocrit from ~18% to ~34%, and platelet count from 54×10^9/L to 117×10^9/L, suggests that such technologies can be lifesaving when transfusion resources are limited. However, their use should be contextualized within broader clinical support strategies, and outcomes must be interpreted cautiously given the complexity of critical care scenarios.

Protamine-induced anaphylaxis is rare but potentially fatal [1,2]. Proposed mechanisms include IgE-mediated hypersensitivity, complement activation, and acute pulmonary vasoconstriction [1,3], leading to right ventricular failure and shock. Acute manage-

ment entails stopping protamine, administering epinephrine, corticosteroids, antihistamines, and methylene blue if vasoplegia persists [8,9]. In refractory cases, reheparinization with CPB or ECMO may be required [7]. For future procedures, bivalirudin may be used to avoid protamine [2]. In LMICs, hemofiltration-based salvage (HemoClear, Zwolle, The Netherlands) offers a low-cost, electricity-independent solution [4]. A major additional advantage is that more than 50% of platelets are recollected together with the washed RBCs [5]. Z-BUF used in high-income settings achieves similar results [10,11] but requires active perfusion. Protamine, which remains largely unbound in plasma, can be effectively removed by filtration or plasma exchange [12]. In this case, hemofiltration followed by cautious reintroduction of protamine after stabilization (with FFP and albumin) likely reduced antigen burden and allowed tolerance of a reduced dose.

4. Conclusion

Severe protamine reactions are rare but potentially fatal events requiring prompt diagnosis and tailored intervention. In this case, emergency reheparinization, CPB reinitiation, corticosteroid therapy, and hemodynamic support were essential to the patient's survival. The use of a gravity-driven hemofiltration device enabled autologous blood salvage that contributed to volume resuscitation and recovery. In low-resource environments, such technologies offer feasible adjuncts to conventional care. Their application, however, must be integrated into a multifaceted response that addresses the full spectrum of hemodynamic, hematologic, and immunologic needs. Further clinical studies are needed to evaluate their effectiveness and clarify their role in the context of severe transfusion- and allergy-related emergencies.

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Research Ethics Committee Approval: The patient provided written informed consent for participation, and the study was conducted in accordance with the ethical guidelines outlined in the Declaration of Helsinki.

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Conflicts of Interest: Arno P. Nierich is the inventor of the HemoClear filter and holds stock ownership in HemoClear BV, Ceintuurbaan 28, 8024 AA Zwolle, The Netherlands. He has not been involved in the clinical treatment of the patient described in this study. All other authors declare no conflicts of interest.

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