Treatment of severe hyperbilirubinemia through coupled plasma filtration adsorption

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ABSTRACT

The development of severe hyperbilirubinemia after cardiac surgery performed with cardiopulmonary bypass is a possible life-threatening challenging complication because its mechanism is still not completely clarified, and there are only a few specific therapies available for acute hepatobiliary injury. Here, we report the case of an 80-year-old male scheduled for elective aortic valve replacement, during the 1st post-operative day (POD 1), developed acute systo-diastolic cardiac failure, with a severe aortic paravalvular leak. The surgeon decided reoperation to correct prosthesis dehiscence. There was a continuous total serum bilirubin increase, with a peak value of 24.50 mg/dl on POD 16. It was diagnosed as a "cholestatic post-cardiac surgery syndrome," and we performed seven cycles of coupled plasma filtration adsorption (CPFA), with definitive stable bilirubinemia reduction to 3.0 mg/dl at the discharge. CPFA was found to be a good hemodepurative technique to manage successfully severe hyperbilirubinemia of "cholestatic post-cardiac surgery syndrome."

Keywords: *Cardiac surgery, Coupled plasma filtration adsorption, Hemodepurative technique, Hyperbilirubinemia, Post-operative jaundice*

The development of severe hyperbilirubinemia after cardiac surgery performed with cardiopulmonary bypass (CPB) is a challenging complication because its mechanism is still not completely clarified, and there are so few specific therapies available for acute hepatobiliary injury [1].

Post-operative mortality well correlates with increasing total bilirubin values, particularly for bilirubin-associate acute kidney tubular necrosis [2]. The difficulty to reduce mortality is partially a consequence of not completely understood physiopathology [3-6]. It is obvious that long-lasting CPB plays an important role, in association with hemodilution, hypotension, ischemia-reperfusion, and increasing hematic level of endogenous catecholamine with reduction of hepatic blood flow [7]. These mechanisms, in the majority of cases, do not have any consequence because hepatocytes and biliary system well tolerate the reduction of blood flow, but rarely, and not exclusively following long-lasting CPB, total post-operative serum bilirubin can rise >3 mg/dl determining the "cholestatic post-cardiac surgery syndrome" [8-10].

Coupled plasma filtration adsorption (CPFA) is an extracorporeal technique used for blood purification in septic shock, severe sepsis, and multiple organ dysfunction syndrome, while the possibility of the resin in the cartridge to retain bilirubin was described as the second option of the technique and consequently used with success to treat hyperbilirubinemia after hepatic transplantation and multiple organ failure from hypoxic hepatitis [11,12]. We present the case of an 80-year-old cardiac patient with multiple organ failure, who was managed successfully using CPFA to remove conjugated bilirubin.

CASE REPORT

An 80-year-old male was scheduled for mini-sternotomy aortic valve replacement to correct severe stenosis with biological "suture-less" prosthesis in January 2018. He was diabetic, with pre-operative bilirubin value 0.4 mg/dl, recent evidence of severe dyspnea, and preoperative echocardiography showing low left ventricular ejection fraction. Operation was uneventful (cardiopulmonary by-pass time 59 min and aortic cross-clamp time 32 min), and the patient was moved to Intensive Care Unit (ICU) with satisfactory vital and hemodynamic parameters (invasive blood pressure 125/75 mmHg, central venous pressure 9 mmHg, and arterial oxygen saturation 100%) obtained with minimal inotropic support (dobutamine 4 µg/kg/min).

During the 1st postoperative day (POD 1), we noticed worsening hemodynamic profile, treated using different and stronger pharmacological support (noradrenaline 0.05 µg/kg/min and adrenaline 0.1 µg/kg/min). Transesophageal echocardiography showed acute systo-diastolic failure due to severe aortic paravalvular leak, so the patient was scheduled for immediate sternotomy reoperation (cardiopulmonary by-pass time 97 min and aortic cross-clamp time 27 min) and returned to

ICU with increased inotropic support (adrenaline 0.15 µg/kg/min and noradrenaline 0.15 µg/kg/min).

On POD 3, we performed continuous veno-venous hemodiafiltration to reduce serum creatinine (4.0 mg/dl) and serum urea (151 mg/dl); during the following days, urine output and consequently patient's kidney function parameters were satisfactory without new renal replacement therapy (Fig. 1). In the course of hospitalization, the patient became jaundiced with progressive total serum bilirubin increased to 24.50 mg/dl (conjugated bilirubin 19.80 mg/dl and unconjugated bilirubin 4.70 mg/dl) on POD 16, and consequently, we performed CPFA, four cycles between POD 16 and POD 18, with total serum bilirubin reduction to 8.20 (conjugated bilirubin 6.36 mg/dl and unconjugated bilirubin 1.84 mg/dl) and three cycles between POD 22 and POD 24; as a consequence of first-treatment rebound due to extracellular shift of bilirubin, total serum bilirubin increases to 18.50 mg/dl (conjugated bilirubin 14.95 mg/dl and unconjugated bilirubin 3.55 mg/dl) with following reduction to 9.1 mg/dl (conjugated bilirubin 6.45 mg/dl and unconjugated bilirubin 2.65 mg/dl) (Fig. 1).

We used four-pump, modular extracorporeal blood purification system (Lynda® Bellco spa) consisting of plasma filter (0.45 m^2 polyethersulfone) to separate plasma from blood, unselective hydrophobic resin cartridge (140 ml for 70 g, with a surface of about 700 m^2/g), and synthetic, high-permeability, 1.4 m^2 polyethersulfone hemofilter where plasma treated from unselective hydrophobic resin cartridge came back with blood cells coming from plasma filter [13]. A follow-up of the patient was done after 3 months of discharge; the patient was asymptomatic with actual total serum bilirubin 0.6 mg/dl.

DISCUSSION

The pathogenesis of "cholestatic post-cardiac surgery syndrome" is still not completely understood but seems to be multifactorial [1,14,15]. Several factors are main predictors of post-operative hyperbilirubinemia: Overproduction of bilirubin caused by blood transfusions during and shortly after surgery [14,15], decreased intraoperative hepatic flow, acute systo-diastolic cardiac failure, and administration of drugs that constrict the hepatic vasculature such as norepinephrine and epinephrine [7], and hemolysis after prolonged CPB and aortic cross-clamp time [10,14,15].

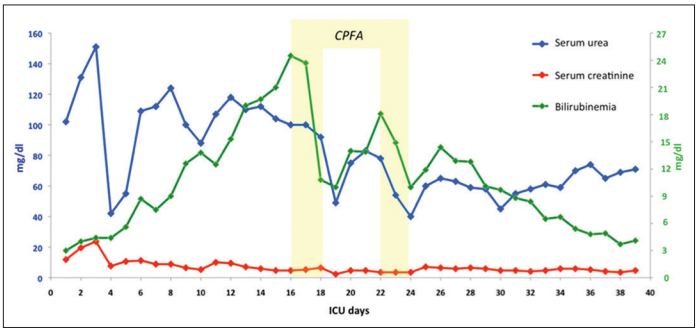

Figure 1: Total serum bilirubin levels in relation with kidney function indicators

We observed only mild hepatic transaminases elevation but marked total serum bilirubin increase, and these laboratory data showed that biliary system was more sensible than hepatocyte to ischemic damage because it worked against gradient to pump conjugate bilirubin from hepatocytes into biliary canaliculi and, consequently, the first sign of hepatic sufferance was total and particularly conjugated bilirubin increase. Meticulous post-operative pharmacological management, optimizing hemodynamics to maintain satisfactory cardiac output, and using a renal dosage of dopamine and continuous furosemide infusion were useful to preserve diuresis and avoid progression to hepatic renal failure.

We performed seven cycles of CPFA (lasting 6 h each-one until all the resins were adsorbed on the sorbent cartridge) using four-pump, modular extracorporeal blood purification system (Lynda® Bellco spa), with blood flow rate of 150 ml/min, plasma flow rate of 30 ml/min (20% of blood flow rate), and ultrafiltration rate of 35 ml/kg/h.

The observed reduction of total serum bilirubin was 67% from peak value after the first treatment (four cycles of CPFA) and 51% after the second one (three cycles of CPFA) with definitive stable bilirubinemia of 3.0 mg/dl (conjugated bilirubin 2.27 mg/dl and unconjugated bilirubin 0.73 mg/dl) when the patient was discharged from the ICU. The effectiveness of our treatment is clinically proved indeed the patient is well and alive 3 months after the discharge from ICU, with actual total serum bilirubin 0.6 mg/dl.

CONCLUSION

The development of severe hyperbilirubinemia after cardiac surgery performed with CPB is a rare and challenging complication. The results of our report suggest that CPFA is a good hemodepurative technique to manage successfully severe hyperbilirubinemia of "cholestatic post-cardiac surgery syndrome."

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