Journal of Artificial Organs (2022) 25:270–273
https://doi.org/10.1007/s10047-022-01309-4

CASE REPORT

Artificial Heart (Clinical)

Single-pass albumin dialysis and hemoadsorption for bilirubin and bile acids removal for a child with hyperbilirubinemia after ventricular assist device implantation

Wun Fung Hui[1] · Kin Shing Lun[1] · Kam Lun Hon[1]

Received: 24 October 2021 / Accepted: 4 January 2022 / Published online: 17 January 2022

Abstract

We report the successful management of hyperbilirubinemia using two different modalities of extracorporeal bilirubin removal therapy for a pediatric patient. A 13-year-old boy with dilated cardiomyopathy requiring veno-arterial extracorporeal membrane oxygenation (VA-ECMO) developed acute kidney injury and was dependent on continuous renal replacement therapy. He developed hyperbilirubinemia with a peak total bilirubin level of 786 µmol/L after implantation of biventricular assist device (BiVAD). Extracorporeal bilirubin and bile acids removal using single-pass albumin dialysis (SPAD) with 4% albumin as dialysate brought down the bilirubin level to 672 µmol/L after 21 h of therapy. Subsequently, he was started on two sessions of hemoadsorption using the Cytosorb® column which further lowered the total bilirubin level to 306 µmol/ in 24 h and 173 µmol/ after the treatment. No complication was encountered. Our case illustrated that both SPAD and hemoadsorption can effectively and safely reduce the serum bilirubin and bile acid levels in pediatric patients with BiVAD implantation. The ease of set-up, faster rate of bilirubin decline and capability of cytokine removal make hemoadsorption a favorable alternative to albumin dialysis.

Keywords Hyperbilirubinemia · Ventricular assist device · Single-pass albumin dialysis · Hemoadsorption · Children

Introduction

Hyperbilirubinemia is commonly observed after ventricular assist device (VAD) implantation[1] and high serum bilirubin level after VAD implantation was associated with poor prognosis for survival [1, 2]. Several factors including ischemic and hypoxic hepatitis with splanchnic vasoconstriction, right ventricular dysfunction and gram-negative septicemia with the associated cytokines release have been postulated to cause hepatic dysfunction and intrahepatic cholestasis resulting in hyperbilirubinemia [3]. While there is no specific treatment, extracorporeal bilirubin removal by either single-pass albumin dialysis (SPAD) [4] or hemoadsorption [5] has been successfully applied for critically ill patients with hyperbilirubinemia. However, the application of extracorporeal bilirubin removal in patients with VAD has been limited and there is a paucity of information on pediatric patients. We here reported our experience of extracorporeal bilirubin removal in an adolescent male with VAD and hyperbilirubinemia.

Case report

A 13-year-old boy who was admitted for coryzal symptoms and chest pain developed cardiogenic shock with respiratory failure requiring multiple inotropes and mechanical ventilatory support. He was then put on VA-ECMO 10 h after admission. He underwent extensive workup and was finally concluded to have idiopathic dilated cardiomyopathy. He later developed acute kidney injury requiring continuous

✉ Wun Fung Hui
huiwf@ha.org.hk

✉ Kam Lun Hon
ehon@hotmail.com

[1] Present Address: Department of Paediatrics and Adolescent Medicine, The Hong Kong Children's Hospital, Doctor's Office, 9/F, Tower B, 1 Shing Cheong Road, Kowloon Bay, Kowloon, Hong Kong SAR

renal replacement therapy (CRRT). There were also elevated liver enzymes and conjugated hyperbilirubinemia with no identified secondary causes. He showed no recovery of both left and right ventricular function with echocardiogram showing the left ventricular fractional shortening of around 6–10% and right ventricular global longitudinal strain of around 7%. He was therefore put on biventricular assist device (BiVAD) with Heartmate III left VAD and extracorporeal right VAD using CentriMag pump after 16 days of ECMO therapy. Blood tests before BiVAD implantation showed hemoglobin 10.2 g/dL, urea 22 mmol/L, creatinine 90 µmol/L, total bilirubin 309 µmol/L, alkaline phosphatase (ALP) 121 IU/L, alanine aminotransferase (ALT) 150 IU/L and aspartate aminotransferase (AST) 94 IU/L. The implantation was uneventful with a bypass time of 2 h 49 min. The initial left VAD flow was set at 3.8L/min and maintained at 3.0–4.6L/min, whereas the right VAD flow was first set at 2.2L/min and maintained at 2.9–4.4L/min respectively. His mean blood pressure, central venous pressure, and oxygen saturation readings all along remained stable. Serial echocardiogram after insertion of BiVAD showed that the right ventricle was not dilated, and the left ventricular fractional shortening was around 20%. However, he was found to have a gradually rising trend of serum bilirubin level up to a peak level of 786 µmol/L. The ALT level was 75 IU/L and AST level was 288 IU/L, his MELD-Na score was 35, corresponding to a predicted mortality of 52.6%.

In view of the worsening hyperbilirubinemia, SPAD was started for bilirubin removal using the Prismaflex system. The SPAD was carried out using a parallel system to the BiVAD through the left internal jugular vein, and 4% albumin was used as dialysate. No specific complication was encountered, and the bilirubin level dropped to 672 µmol/L after 21 h of therapy. The serum bile acids level also decreased from 107.6 µmol/L to 66.4 µmol/L (Fig. 1). However, with an intention to hasten the bilirubin and bile acids removal, SPAD was stopped and hemoadsorption using a CytoSorb® column attached post-filter in the conventional CRRT circuit was employed (Fig. 2). The CRRT prescription remained the same during SPAD and hemoadsorption. A dramatic reduction of serum bilirubin and bile acids levels was then observed. The serum bilirubin and bile acids level 24 h after starting hemoadsoprtion were 306 µmol/L and 48.4 µmol/L respectively with a nadir level achieved at around 53 h. A new column of Cytosorb® was then used for another 22 h. The serum bilirubin and bile acids levels after two sessions of hemoadsorption were 173 µmol/L and 26.4 µmol/L, and the respective MELD-Na score was 30 with a predicted mortality of 19.6%. His bilirubin level experienced a slow and transient rebound after stopping the hemoadsorption, which subsided spontaneously in a week. The serum bilirubin level thereafter maintained at around 50 µmol/L and no further bilirubin removal was performed. The BiVAD was functioning well all along. He failed the attempt to wean the right VAD two weeks afterwards and was later put back on BiVAD as a bridge for heart transplantation.

Comment

Bilirubin is a surrogate marker of hepatic dysfunction and cholestasis. In recent years, extracorporeal liver support for removal of bilirubin, bile acids and other toxic substances in patients with acute or acute-on-chronic liver failure has attracted much attention as accumulation of these substances

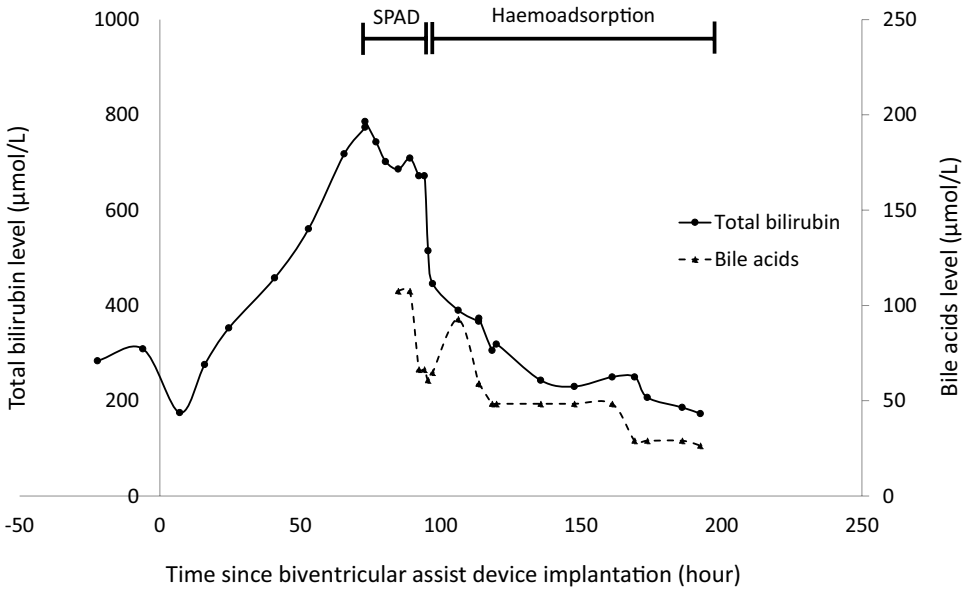

Fig. 1 The trend of serum bilirubin and bile acids levels. CRRT prescription during SPAD and hemoadsorption remained unchanged. Blood flow rate: 200 ml/min, Replacement rate: 1357 ml/1.73m^2/hour, Dialysate rate: 1583 ml/1.73m^2/hour and Heparin infusion: 18units/kg/hour

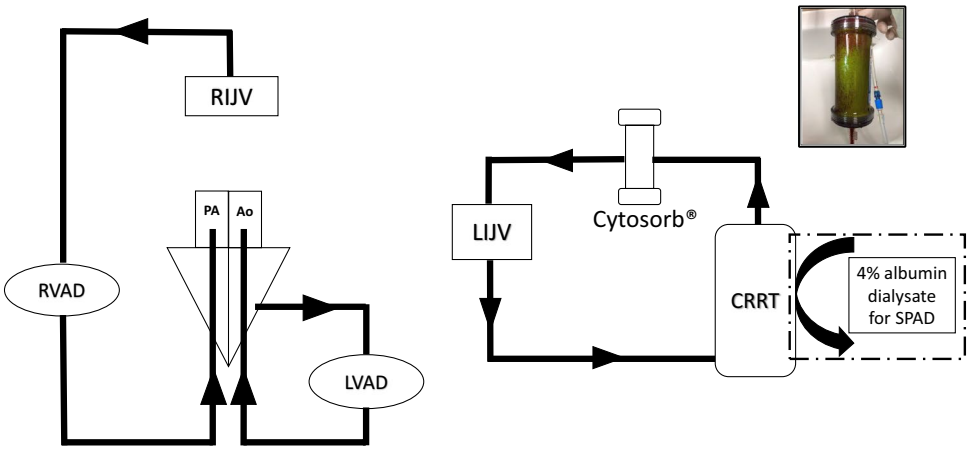

Fig. 2 The set-up of the BiVAD, SPAD and hemoadsorption. The BiVAD and extracorporeal bilirubin removal circuit were running as parallel systems. The picture at the corner showed the greenish Cytosorb® column after one session of bilirubin removal. *Ao* Aorta, *CRRT* Continuous renal replacement therapy, *LIJV* Left internal jugular vein, *LVAD* Left ventricular assist device, *PA* Pulmonary artery, *RIJV* Right internal jugular vein, *RVAD* Right ventricular assist device, *SPAD* Single-pass albumin dialysis

can lead to organ damage [6, 7], and a recent meta-analysis has demonstrated its association with mortality reduction [8]. However, no single modality was found to be superior to the others.

Albumin dialysis, including SPAD, is one of the most studied modalities for removal of albumin-bound and water-soluble toxins in both adults and children. On the contrary, hemoadsorption for bilirubin removal has regained interest in recent years with the availability of a new adsorption column CytoSorb® [9]. CytoSorb® is a hemoadsorption column having a surface area of 40,000 m^2. It is made of biocompatible porous polymer beads that can eliminate hydrophobic molecules up to the size of 55 kDa. The molecular weight of bilirubin is 580 daltons only, but it is bound to albumin in serum, whereas the molecular weights of bile acids range from 25-67 kDa. Hence both substances should be removable by CytoSorb®. In-vitro study has nicely depicted the kinetics of bilirubin removal using CytoSorb® [10], also it was found to have comparable efficacy to the molecular adsorbent recirculating system for bilirubin and bile acids removal [11]. However, clinical study comparing both modalities is lacking.

Our case demonstrated that both modalities were effective in lowering serum bilirubin and bile acids levels, but it appeared that the rate of decline was faster using hemoadsoprtion for our patient. On a closer look, the dramatic reduction of bilirubin level was mostly attributed to the initial drop right after starting hemoadsorption. Subsequently, the rate of decline decreased, and a plateau level was achieved at around 40 h after initiation of therapy, which could be due to saturation of the column. When using the SPAD, we maintained the albumin concentration in the dialysate at 4% with a fixed dialysate rate of > 1000 ml/m^2/hour for maximal efficacy [12]. However, it was labor-intensive for such frequent dialysate exchange (every 3–4 h on average). In addition, the ease of incorporating an adsorption column to the existing CRRT circuit and the additional benefit of removing cytokines made hemoadosprtion a favorable alternative in this circumstance.

Scharf et al. recently reported the efficacy of hemoadsorption using Cystosorb® versus advanced organ support system (ADVOS) for bilirubin removal among a group of critically ill adults with serum bilirubin > 10 mg/dL (~ 170 µmol/L) [13]. It was found that both modalities were effective for bilirubin removal with no significant difference of the efficacy. ADVOS comprises a sophisticated system that incorporates albumin dialysis as a mean of liver support. The authors concurred that the ease of setting up and a comparable efficacy would be the main advantage of using hemoadsoprtion column for bilirubin removal.

It is difficult to conclude the relative efficacy of SPAD and hemoadsoprtion for bilirubin removal from one single case. The limitations of our case included firstly, the difference of initial bilirubin concentration may render comparison difficult as the kinetics was concentration-dependent. Besides, the difference in treatment duration and failure to measure both bile acids and bilirubin level at constant time interval should be considered. However, we believed that the constant CRRT prescription and relatively stable VAD flow rate and physiological parameters during the treatment may provide some clues about the performance of the two modalities in clinical application, especially for pediatric patients.

In summary, our case demonstrated that both SPAD and hemoadsorption can safely and effectively reduce the bilirubin and bile acids levels in children after VAD implantation,

and the latter using a Cytosorb® column appeared to offer a faster rate of decline and was less labor-intensive. More prospective data would be required to compare the efficacy between different modalities of extracorporeal bilirubin removal.

Declarations

Conflict of interest The authors have no conflict of interest to declare.

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