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Efficacy of hemoperfusion with Seraph-100 in series with single pass albumin dialysis in acute hepatitis B infection: A case report

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Abstract

Acute and acute-on-chronic liver failure is a cause of death in patients suffering from viral hepatitis, and many cases need liver transplantation. Infection from hepatitis B virus may range from asymptomatic to severe acute and fulminant hepatitis. In this setting, treatment is mainly supportive as there is no consensus on antiviral therapy based on non-nucleoside reverse transcriptase inhibitors. Single-pass albumin dialysis is a liver-support technique for patients suffering from liver failure, that has shown effectiveness in the removal of both water-soluble and albumin-bound toxins, which accumulate due to impairment of the liver's cleansing function. We report here the case of a 62-year-old male who presented with a severe acute hepatitis B infection, liver failure, and marked hyperbilirubinemia. Treatment with single-pass albumin dialysis combined with a hemoperfusion device was successful in improving clinical, physiological, and laboratory parameters.

Keywords

Acute hepatitis B, hemoperfusion, albumin dialysis, liver failure, Seraph 100 filter.

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Introduction

Hepatitis B virus (HBV) has a high worldwide incidence, since it is estimated that about 30% of the population has been exposed and that 400 million of these are chronically infected.[1] Though in most patients HBV infection manifests in a subclinical or anicteric form, in some cases it can be severe or even fulminant. The diagnosis is based on the detection of HBsAg and IgM anti-HBc. Resolution of the infection is characterized by the disappearance of HBV DNA and seroconversion. A decrease in HBsAg concentrations by more than 50% within the first 4 weeks indicates resolving acute infection in >95% of cases.[2] Treatment for acute HBV is mainly supportive. There is yet no consensus to use non-nucleoside reverse transcriptase inhibitors (NNRTI).[3] Furthermore, the early administration of antiviral therapy might inhibit the production of neutralizing antibodies.[4,5]

Regardless of the underlying cause, patients with acute liver failure (ALF) accumulate albumin-related toxins including bilirubin, aromatic amino acids, indoles, and mercaptans. Blood bilirubin levels represent a marker for these toxins and correlate with mortality.[6] Since albumin-bound toxins exhibit strong binding to albumin and are difficult to remove with conventional hemodialytic treatments or plasmapheresis,[7] artificial extracorporeal liver devices have been developed and used as supportive therapy, to provide a bridge either to liver transplantation or to hepatic regeneration. Based on the concept of albumin dialysis, use of extracorporeal liver support systems has been shown to be effective in the removal of albumin-bound substances.[8,9]

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Table 1. Effects of combined treatment SPAD-Seraph 100 filter on serum blood concentration of bilirubin, viremia, and IL-6 levels.

Serum bilirubin	T0	T1	T2	T3
mg/dl	23.6	20.52	20.8	14.9
HBV-DNA	T0	T1	T2	T3
IU/dl	6901	2355	2095	924
IL-6	T0	T1	T2	T3
pg/ml	24.4	13.3	15.9	13.7

Single-pass albumin dialysis (SPAD) is a liver support system, characterized by blood circulation through a circuit containing a high cut-off membrane whereby the albumin solution flows on the other side of the membrane in the opposite direction. SPAD demonstrated to be effective in reducing bilirubin levels while maintaining good hemodynamic stability in the critical patient.[6,10–13]

We report here on a patient suffering from a severe acute HBV infection causing liver failure, successfully treated by SPAD combined with a new eextracorporeal blood purification (ECBP) device.

Case report

A 62-year-old male with sexual risk factors presented at the Hospital of Avezzano (L'Aquila, Italy) with a 10 days history of worsening upper-abdominal pain, nausea, and anorexia. Five days before referral, patient reported the appearance of jaundice, acholic stool, and hyperchromic urine.

He was otherwise healthy and had no family history of liver disease. His daily alcohol consumption was moderate and his history was consistent with behavioral risk factors.

On examination, the patient was afebrile, blood pressure was within normal values, heart rate was 100 beats per minute, respiratory rate was 20 breaths per minute, and his oxygen saturation was 98% on ambient air.

He was alert and oriented with icteric sclera and skin; there was no pitting edema of the lower extremities and abdominal examination was unremarkable.

At admission, laboratory blood exams revealed mildly elevated transaminases (GOT 101 IU/L; GPT 176 IU/L), moderate thrombocytopenia (69.000×10^3/ml platelets), markedly increased serum bilirubin (24 mg/dl), hypoalbuminemia (2.6 g/dl), and slightly elevated international normalized ratio (INR) (1.45), indicative of impaired liver function; ammonia levels were within normal range (78 mcg/dl), and C-reactive protein was moderately elevated (45 mg/l).

Acute viral hepatitis panel showed negative results for hepatitis C, HIV, hepatitis A antibodies (IgM), and delta antigen. The search for other hepatitis viruses such as CMV and EBV, or for toxoplasma, was also negative. Further testing revealed positivity of anti-HBc and anti-HBc IgM, negativity of HBe antigen and anti-HBe, HBs antigen of 797 UI/ml, negativity of anti-HBs, and HBV DNA of 6901 UI/ml, consistent with acute HBV infection.

An abdominal ultrasound and an abdominal CT scan revealed liver steatosis without liver fibrosis or portal hypertension.

A magnetic resonance cholangiography performed to characterize the biliary system, did not reveal biliary obstruction, stones, or biliary sludge.

Because there was no consensus on anti-viral treatment, we chose conservative therapy and support of liver function.

Due to the severe hyperbilirubinemia patient was treated with two SPAD sessions with EMIC-2 filter (Fresenius, Bad Homburg, Germany), a polysulfone-based membrane with medium cut-off (45 kDa), at the Dialysis Unit of L'Aquila Hospital. Each session lasted 5 h using a blood flow of 80 ml/min, a dialysate flow of 1000 ml/min with albumin solution at 3% concentration. SPAD sessions were carried out in series with a Seraph-100 Microbind Affinity Blood Filter (ExThera Medical Corporation, Martinez, CA, USA), and with supportive intravenous hydration.

Blood levels of interleukin (IL)-6, HBV DNA, and bilirubin levels were determined at T0 (before first treatment), T1 (immediately after the first treatment), T2 (before second treatment) and T3 (immediately after the second treatment).

As shown in Table 1, bilirubin decreased significantly after each extracorporeal session. Likewise, a drop of HBV-DNA viral load levels (2355 and 924 IU/ml, after the first and second session, respectively) was found. IL-6 levels also proved to decrease after each session, as shown in Table 1.

Patient was discharged with a bilirubin level down trend and normalization of hepatic cytonecrosis indices. One month after the combined treatment serum bilirubin had decreased to 5 mg/dl. We could not follow-up the patient for a longer period, but he is clinically stable as we know by the time this case report is written.

Discussion

Infections are the second cause of hospitalizations and death in critically ill patients.[14] High-level viremia has been associated with pro-inflammatory cytokines and increased mortality.[15] ECBP devices are potentially beneficial for treatment of severe infectious diseases. Hemoperfusion techniques aim to remove directly the pathogen and pro-inflammatory cytokines such as IL-6, and to reduce leukocyte activation and pro-inflammatory pathways by preventing molecular patterns pathogen-associated - pattern recognition receptors interaction (PAMPs-PRR). A limitation of these techniques is their

non-selectivity. However, during the infectious process there is imbalance of pro-inflammatory cytokines, and hemoperfusion techniques can restore the balance between pro-inflammatory and regulatory cytokines.

The new ECBP Seraph-100 is an extracorporeal hemoperfusion device, which can bind a wide range of bacteria, viruses, pro-inflammatory cytokines, and certain drugs.[15–17] The device is composed of ultrahigh molecular weight polyethylene beads with end point-attached heparin. Like the interaction with heparan sulfate (HS) on the cell surface, pathogens bind irreversibly to the immobilized heparin and are thereby removed from the bloodstream.[16] Heparin is a negatively charged biopolymer mainly composed of trisulfated disaccharide units.[18] The anticoagulant activity of heparin is a consequence of its ability to inhibit both thrombin generation and thrombin activity. In addition, heparin has numerous other effects, mainly anti-inflammatory and antiviral, which occur through interactions with a number of mediators.[18] The Food and Drug Administration (FDA) has approved the use of Seraph 100 or hemoperfusion, alone or in series with filters for hemodialysis or continuous renal replacement techniques. Treatment duration is dependent on blood flow rate (BFR), varying from 4 h for a BFR of 400 ml/min to 8–24 h with a 200 ml/min BFR. The maximum duration with a single filter is 24 h.

Seraph 100 device was used in several studies targeting the removal of SARS-Cov—2 from the bloodstream of critically ill patients.[15,17,19–21] Indeed, the spike protein of SARS-Cov-2 binds to cellular HS (and heparin) through its receptor-binding domain.[22] The concentration of SARS-Cov-2 nucleocapsid protein (N-Protein) after treatment with Seraph-100 proved to be consistently reduced,[19] a finding of potential significance since N-Protein concentration seems to be associated with viral load in blood and with disease severity.[23]

To the best of our knowledge, this is the first report on the use of Seraph 100 device for ALF due to severe acute HBV infection. HBV infection is featured by the initial binding to HS proteoglycans on the surface of host cells which serve as attachment receptor.[24] Neutralizing infection caused by viruses which use HS for cellular attachment through competitive inhibition for binding by Seraph can be envisaged. Hemoperfusion with the device was in series with SPAD to contemporarily treat viremia, hyperbilirubinemia, and IL-6 levels. Extracorporeal albumin dialysis is considered as being a therapeutic option during critical care to reduce endogenous toxic agents such as bile acids which are albumin-bound.[25] Specifically, by using standard dialysis machines SPAD allows easy access to extracorporeal liver support.[26] In our patient, just after two sessions of the extracorporeal treatment a marked reduction in blood bilirubin and viral load was observed. HBV-DNA is a virological marker that reflects HBV replication levels and has a central role in maintaining persistent infection. HBV DNA levels are associated with fibrosis severity.[27] To be noted that Seraph-100 filter resulted to be effective despite the use of a low flow hemofiltration.

Efficacy of artificial liver support systems such as SPAD to replace at least partially the liver detoxification function, and to correct several biochemical abnormalities, has been demonstrated.[8] Although data on survival benefit remain scarce and uncertain, artificial liver support systems can be considered as "salvage" therapy in patients suffering from ALF.[8] In case of ALF due to acute HBV infection as the present report, combined use of a device with high microbial affinity may improve the clinical outcome. Clearly, this issue requires further studies.

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Informed consent

Written informed consent from the patient for publication of the study was obtained.

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