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REFRACTORY HEPATOPULMONARY SRYNDROME AFTER LIVER TRANSPLANT: NEW THERAPEUTIC STRATEGIES WITH EXTRACORPOREAL MEMBRANE OXYGENATION. A CASE REPORT

Sanchez *et al*. ECMO in HPS after LT

Belinda Sánchez Pérez, María Pérez Reyes, Jose Aranda Narvaez, Julio Santoyo Villalba, Jose Antonio Perez Daga, Claudia Sanchez-Gonzalez, Julio Santoyo-Santoyo

Abstract

BACKGROUND

Due to the lack of literature published about treatment of refractory hepatopulmonary syndrome after liver transplant(LT), this case adds information and experience on this issue along with a treatment with positive outcomes.

The hepatopulmonary syndrome (HPS) is a complication of the end-stage liver disease, with a 10-30% incidence in cirrhotic patients. LT can reverse the physiopathology of this process and restore normal oxygenation. However, in some cases a refractory hypoxemia can persist, being extracorporeal membrane oxygenation (ECMO) used as a rescue therapy with good results.

CASE SUMMARY

59-year-old patient with enolic cirrhosis and portal hypertension. Good liver function (MELD 12, Child B7). Mild restrictive respiratory pattern with basal saturation 82%. Hepatopulmonary syndrome and pulmonary fibrosis. Macroaggregated albumin >30. Spirometry with FEV1 78%, FVC 74%, FEV1/FVC 81% DLCO 42% KCO57%.

Domiciliary oxygen 2L/min (16h/day). Liver transplant indication: hepatopulmonary syndrome.

Admitted to the ICU and extubated in the first 24h, needing high-flow therapy and non-invasive ventilation and inhaled nitric oxide afterwards. Reintubation was needed after 72 h. Due to the non-response to supportive therapies, installation of ECMO was decided with progressive recovery after 9 days. Extubation was possible on the tenth day, maintaining high-flow nasal cannula and de-escalating to conventional oxygen therapy after 48 h. Discharged from ICU on postoperative day (POD) 20 with 90-02% saturation. Steroid recycle was needed twice for acute rejection. Discharged from hospital on POD 27, asymptomatic with 89-90% saturation.

CONCLUSION

Due to the favorable results observed, ECMO could become the central axis of treatment of HPS and refractory hypoxemia after LT.

Key Words: Liver transplantation; Hepatopulmonary syndrome; Refractory hypoxemia; Treatment; Extracorporeal membrane oxygenation; case report

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Core Tip: ECMO has been used as a rescue therapy in refractory hypoxemia after liver transplantation in hepatopulmonary syndrome, with positive results. We present a patient with HPS who underwent TSH and developed refractory hipoxemia requiring postoperative ECMO support. The literature demonstrates an 80% survival rate with an acceptable morbi-mortality. ECMO can become the central axis in the treatment of

patients with hepatopulmonary syndrome which present with refractory hypoxemia after liver transplantation.

INTRODUCTION

In the recent years, extracorporeal membrane oxygenation (ECMO) has become the gold-standard method for the treatment of severe pulmonary/cardiac dysfunction or insufficiency in the peritransplant period in liver recipients unresponsive to previous therapies[1-2]. Conditions that can be treated with ECMO include hepato-pulmonary syndrome (HPS), porto-pulmonary hypertension (PPHTN), and pulmonary arterial hypertension (PAH)[3].

HPS is characterized as the triad of liver disease, intrapulmonary vascular dilatation, and arterial hypoxemia. Although HPS is most frequently associated with liver cirrhosis, it may be related to any acute/chronic terminal liver disease, with or without associated portal hypertension[4]. Around 10-30% of cirrhotic patients develop HPS[4]. Liver transplantation may reverse the physiopathology of this process and restore normal oxygenation. However, in some cases, refractory hypoxemia persists despite support therapy. It is in this scenario where ECMO gives the necessary time to revert pulmonary arteriovenous shunts and reduce morbimortality.

This is a case report and a literature review of adult liver recipients that received ECMO therapy for HPS during the peritransplant period.

CASE PRESENTATION

Chief complaints

We report the case of a 59-year-old male patient included in the liver transplant (LT) waiting list in March 2022 under the indication of hepatopulmonary syndrome admitted for liver transplantation.

History of present illness

The patient had a good liver function, with a MELD of 12 and a Child-Pugh of B7. The patient had concomitant chronic respiratory failure, with a mild restrictive ventilatory defect and bronchial hyperreactivity (with a previous positive bronchodilator test). The patient also had hepatopulmonary syndrome and slow progressive pulmonary fibrosis.

History of past illness

The patient had a history of alcohol-related liver cirrhosis and data of pulmonary hypertension.

Personal and family history

There was no familial history of interest.

Physical examination

The patient used home oxygen at 2 L/min for at least 16 h a day and a portable oxygen concentrator for walking. His baseline oxygen saturation (O_2Sa) was 82%.

Laboratory examinations

Macro aggregated albumin test was > 30. Spirometry demonstrated a FEV1 of 78%, FVC of 74%, FEV1/FVC of 81%, DLCO of 42%, and KCO of 57%.

Imaging examinations

No imaging examinations relevant to this case.

FINAL DIAGNOSIS

Refractory hypoxemia.

TREATMENT

LT was performed with a matched cadaveric donor. A temporary porto-cava shunt and piggy-back technique were used.

The patient was admitted to the ICU. Extubation was performed within the first 24 post-transplant hours, and the patient immediately needed high-flow nasal tubes, which was escalated to noninvasive mechanical ventilation (NIMV) plus inhaled nitric oxide. At 72 h, reintubation was required due to severe hypoxemia. Protective mechanical ventilation with high FiO_2 was initiated. Inhaled nitric oxide and support with inhaled ilioprost were maintained to reach an O_2Sat of 88-92%. As the patient was unresponsive to support therapies, veno-venous ECMO (VV ECMO) was initiated. Anticoagulation with continuous perfusion of heparin sodium was also started to reach an ACT (activated clotting time) of 140 s.

OUTCOME AND FOLLOW-UP

ECMO was maintained for nine days, with progressive improvement of right-to-left shunt lesions and oxemia. The patient was extubated after 10 days on high-flow ventilation (HFNO). Clinical course was excellent, with successful de-escalation to conventional nasal tubes in 48 h. The patient was discharged from the ICU at 20 postoperative days (POD) with an O_2Sat of 90-92%. In relation to liver function, the patient required steroid recycling two times, due to acute cellular rejection in the ICU. The patient was discharged at 27 POD without any respiratory symptoms, with a constant O_2Sat of 89-90% and very good tolerance.

Respiratory symptoms have disappeared since transplantation, with the patient showing a good liver graft function. Lung function has improved with respect to pre-transplant status, with a basal O_2Sat of 98%. The patient no longer needs home oxygen therapy.

DISCUSSION

In the last decades, HPS has gone from being a contraindication to becoming an indication for transplant. This has been made possible by our better understanding of the physiopathology of the disease, added to constant improvements in support therapies. However, in liver recipients with severe oxygenation deficit (severe

hypoxemia PaO2<50 mmHg), post-transplant mortality remains high, with a higher occurrence in the immediate postoperative period[8]. VV ECMO removes non-oxygenated blood, transfers it through devices that add oxygen to the blood, and returns it to the venous system. By this technique, arterial oxygen is controlled to ensure optimal oxygenation and support tissue metabolism[5] in the presence of standard cardiac output. This technique provides the time necessary to reverse lung disease.

VV ECMO had never been used before in our hospital to treat HPS, since liver transplantation had always been effective. However, as this patient developed refractory hypoxemia, the multidisciplinary team decided to use VV ECMO, despite the little scientific evidence available on the use of this support therapy in HPS. Ten cases have been reported (ours included) in the literature on adult liver recipients who received VV ECMO during the peritransplant period as a treatment for HPS (Table 1). In 80% of cases, ECMO was used to treat post transplant refractory hypoxemia[-11], intraoperatively in 20%[12-13], and as bridge-to-transplant therapy in 10%[6]. In all cases, the indication of ECMO was hypoxemia refractory to mechanical ventilation combined with conventional measures. Measured pretransplant $Pa0_2$ was 48.12 mmHg (r:35-57 mmHg). Mortality in these patients is high, with 60% of the series having required kidney replacement therapy, and 70% a tracheostomy. Complications included hepatic infarction/hematoma secondary to migration of the cannula [7] and hemothorax that required reintervention[8].

Despite the use of anticoagulation in this setting, no hemorrhages or hematomas were reported, as described previously[7-8], which we explain by good graft function at that moment (INR: 1.31, VF 98, PT:68%). In total, 80% of our patients were discharged. Two patients died (20%); a patient had multiorgan failure; and another patient had hepatic infarction followed by a biliary fistula and sepsis with multiorgan failure, which occurred after withdrawal of ECMO therapy. The mean time to initiation and mean duration of ECMO therapy was 7 days and 13.7 days, respectively. Early initiation of ECMO has been reported to reduce therapy duration, thereby decreasing the occurrence of associated complications and increasing survival[14].

CONCLUSION

ECMO therapy emerges as a cornerstone of perioperative support that improves survival in patients with HPS undergoing liver transplantation. In the light of the growing evidence available and good outcomes reported, ECMO will certainly become the gold standard treatment for severe pulmonary dysfunction/insufficiency in liver recipients during the peritransplant period.

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3	Bianca Mitricof, Alin Kraft, Florentina Anton, Alexandru Barcu et al. "Severe liver trauma with complex portal and common bile duct avulsion: A case report and review of the literature", World Journal of Clinical Cases, 2023 Crossref	13 words — 1%

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