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LEVOSIMENDAN IN LUNG TRANSPLANT RECIPIENTS ON VA-ECMO

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Chronic heart failure is one of the most dreadful complications in the early postoperative period following lung transplantation. At the same time, the effect of using levosimendan in the early post-lung transplant period is currently insignificant and remains debatable. This paper presents a clinical case where levosimendan was successfully used in a patient with right ventricular heart failure during lung transplantation undergoing central venoarterial extracorporeal membrane oxygenation (VA-ECMO).

Keywords: levosimendan, lung transplantation, right ventricular heart failure.

INTRODUCTION

Lung transplantation (LT) is usually the final treatment option for end-stage lung disease, when other treatment methods are ineffective [1–3].

Russian Transplant Society reports that the country has only 4 LT centers [4]. As of the end of 2019, the Sklifosovsky Research Institute of Emergency Care had completed over 60 bilateral lung transplants. The early postoperative period in lung recipients can be accompanied by complications. The most common are bleeding, graft dysfunction, and failed bronchial anastomoses. Up to 20–30% of lung transplant recipients develop acute kidney injury (AKI), with indications for renal replacement therapy (RRT); 40% of the recipients develop neurocognitive disorders in the early postoperative period [5–8]. Cardiovascular disease is one of the most dreadful complications. Lung recipients often have delayed restoration of right ventricular (RV) function due to high pulmonary hypertension, as well as isolated left ventricular (LV) dysfunction with slight involvement of the right ventricle. Levosimendan is used in intensive care for managing left-sided heart failure (LSHF) and clinically significant RV dysfunction [9–11].

At the same time, the effect of levosimendan in the early post-LT period is currently insignificant and remains debatable. There are isolated cases of successful use of levosimendan.

We present a clinical case of successful use of levosimendan in right-sided heart failure (RSHF) during lung transplantation. The patient was under central venoarterial extracorporeal membrane oxygenation (VA-ECMO).

CLINICAL CASE

A 41-year-old patient diagnosed with pulmonary non-Langerhans cell histiocytosis (group 3 pulmonary hypertension) successfully underwent lung transplantation at Sklifosovsky Research Institute of Emergency Care.

Intraoperative monitoring in LT included continuous electrocardiographic (ECG) monitoring, heart rate (HR) measurement, pulse oximetry (SpO_2), invasive hemodynamic monitoring: blood pressure (systolic blood pressure, diastolic blood pressure, mean arterial pressure), central venous pressure (CVP) and pulmonary artery pressure with a Swan–Ganz catheter (pulmonary artery pressure, pulmonary wedge pressure / pulmonary capillary wedge pressure, cardiac output).

Induction anesthesia was carried out with propofol (2 mg/kg), fentanyl (4 μg/kg) and cisatracurium besylate (150 μg/kg). After preoxygenation with 100% oxygen, the patient was separately intubated with a Robert Shaw tube (No. 37). Pressure support ventilation (PSV) was set. Respiratory parameters (respiratory minute volume, respiratory volume, respiratory rate, peak inspiratory airway pressure (Ppeak), positive end expiratory pressure (PEEP), and gas exchange (FiO_2, concentration of inhaled anesthetic) in the respiratory circuit were measured using a Dräger Primus gas analyzer (Germany).

Anesthesia was maintained by intravenous injection of cisatracurium besylate (1.5 μg/kg/min) and fentanyl (100–150 μg/kg/min), as well as by inhalation anesthetic – desflurane (MAC 1.0–1.4). Depth of anesthesia was monitored using bispectral index (BIS). In an express diagnostics laboratory, analysis of oxygen status indicators (pO_2, pCO_2, ctO_2), arterial blood acid-base balance (PH, $cHCO_3$) and electrolyte blood composition (K, Na, Ca, Cl). Hemoglobin and hematocrit were also analyzed.

After anesthesia induction and at the stage of pneumonectomy on the right, hemodynamic parameters were determined to be stable (blood pressure 140–110/90–75 mm Hg). Pulmonary artery systolic pressure was

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102 mmHg. After pneumonectomy, there was a tendency to hypotension on the right (blood pressure 75–80/41–52 mmHg). In correcting the hypotension amidst higher concentration of dopamine (up to 12.78 mg/kg/min), dobutamine (5 μg/kg/min) and norepinephrine were included with gradual increase in dose to 400 ng/kg/min. With the progression of cardiotonic- and vasopressor-resistant hypotension, increase in lactate to 7 mmol/L, hypercapnia (increase in pCO_2 to 85 mmHg), central VA-ECMO was used, providing up to 3.8 L/min circulatory support on the Maquet Rotaflow pump.

The lung transplant surgery was successful. It lasted for 13 hours 20 minutes. Endoscopic examination showed that the condition of bronchial anastomoses was satisfactory. Intraoperative blood loss was 2000 mL. The patient was transferred to ICU under VA-ECMO, providing 4.0 L/min circulatory support.

In the intensive care unit, significant increase in cardiotonic and vasopressor doses was required in order to stabilize blood pressure. So, norepinephrine was used at 950 ng/kg/min, dobutamine – 14 μg/kg/min, and dopamine – 13 μg/kg/min. In addition, adrenaline was added to the therapy at 200 ng/kg/min. SvO_2 was recorded at 55–65 level during online monitoring on a Cardiohelp apparatus (Maquet). Blood pressure was 80–90/45–55 mmHg amid high levels of cardiotonic agent, ECMO flow rate increased to 4.5 L/min.

On the next day (second day of the postoperative period), continuous infusion of levosimendan at the rate of 0.1 μg/kg/min was added to drug therapy. Positive dynamics were noted already by the 12th hour after levosimendan administration had started. So, dobutamine and norepinephrine doses were reduced to 6 μg/kg/min and 150 ng/kg/min, respectively, dopamine and adrenaline were withdrawn. Blood pressure was 132–128/81–75 mmHg. After completion of 24-hour continuous infusion of levosimendan, blood pressure was in the normal range (134–123/67–73 mm Hg) without vasopressor and cardiotonic support.

On the third postoperative day in the operating room, vascular decannulation was performed as the patient was weaned off VA-ECMO. Further postoperative management of the patient was done with no significant complications. The patient was discharged on day 30.

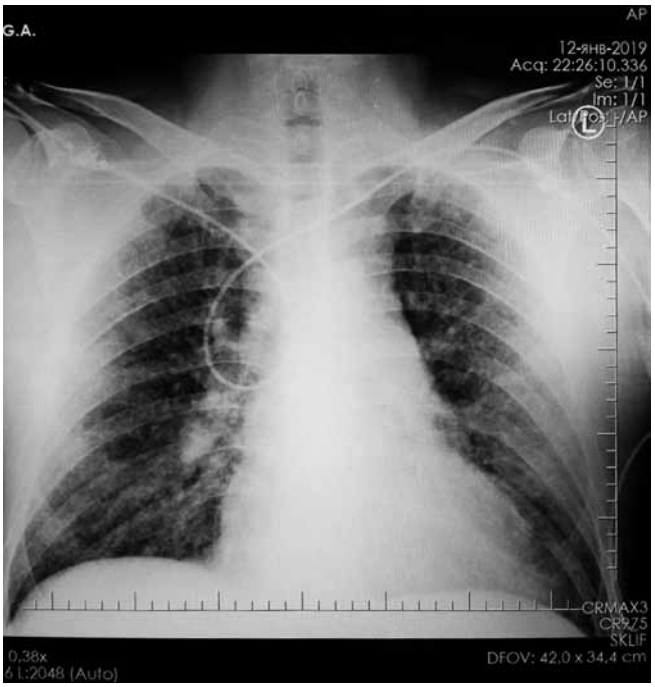

Fig. 1. X-ray picture before lung transplantation

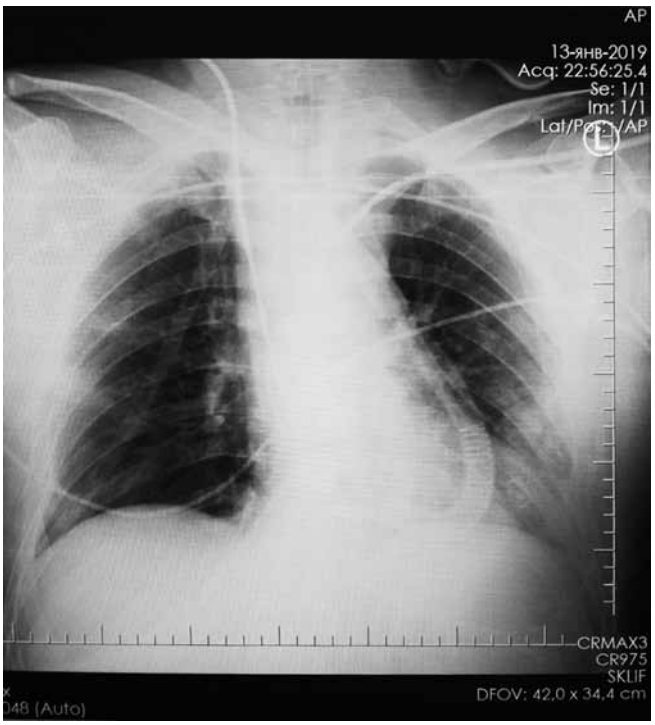

Fig. 2. X-ray picture after lung transplantation

DISCUSSION

Severe pulmonary hypertension is a risk factor for right ventricular failure in the early postoperative period after bilateral LT. Factors contributing to the development and persistence of pancreatic insufficiency are eliminated through a comprehensive approach – the use of maintenance therapy that increases cardiac output, corrects blood pressure correction, optimizes infusion therapy, reduces pancreatic afterload, prevents and treats arrhythmias and infectious complications, as well as the use of aggressive treatment methods, including continued VA-ECMO in the postoperative period [12, 13].

The mechanism of action of levosimendan is based on increased tropism for cardiomyocytes to calcium. The ability of myocyte to reduce begins with a change in cardiac troponin C configuration under the influence of calcium ions. At the beginning of systole, levosimendan is selectively bound by calcium-saturated cardiac

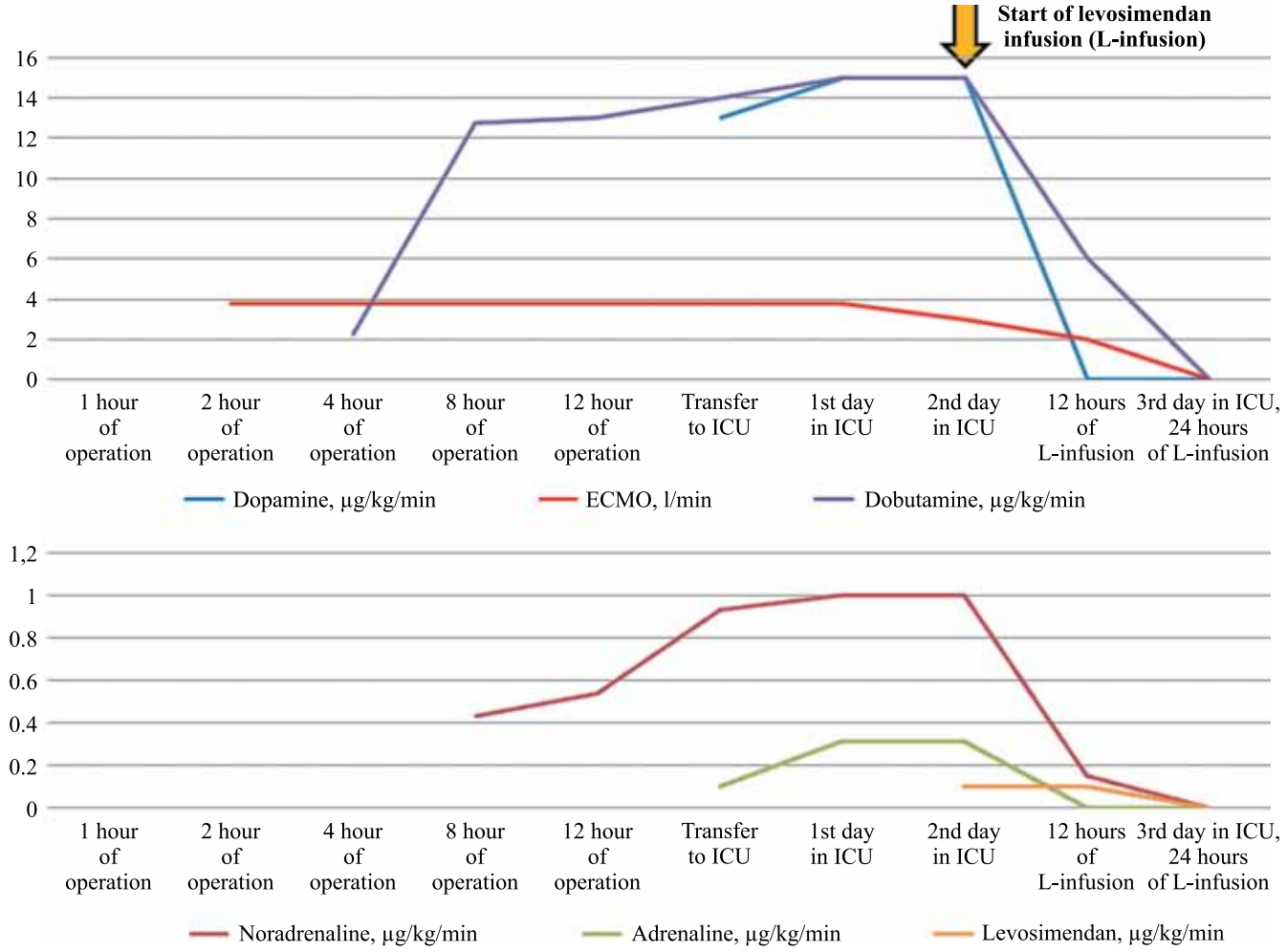

Fig. 3. Dosage of cardiotonic and inotropic agents in the early postoperative period

troponin C, which leads to stabilization of the conformation of this protein, triggering contraction of myofibrils. As a result of this interaction, connection of transverse myosin bridges with actin is lengthened, which leads to both increased strength of muscle contraction and increased number of bonds per unit time. It should be noted that the effect of levosimendan is reversible. So, in diastole at lower concentrations of calcium, the drug "frees" troponin C. This creates persistence of myocardial relaxation [14].

In an experiment on healthy animals, the ability of levosimendan to increase right ventricular contractility without significant effect on pulmonary vascular resistance was demonstrated [15]. One more mechanism of action of levosimendan by which ATP-sensitive potassium channels in the smooth muscles of the vascular wall and mitochondria can be opened should be noted. The clinical result is coronary artery dilation and reduced pulmonary blood pressure [16].

Thus, in our opinion, reduced afterload due to dilated pulmonary arteries in combination with adequate preload and cardiotonic effect of levosimendan promoted gradual cardiac output restoration and blood pressure normalization.

CONCLUSION

A 24-hour continuous infusion of levosimendan led to hemodynamic stabilization without arrhythmia induction. This agent can be used in liver transplant recipients with postoperative right ventricular failure and pulmonary arterial hypertension to significantly reduce pulmonary artery systolic pressure and increase the stroke volume.

The cardioprotective properties of levosimendan in combination with VA-ECMO, vasopressor support and optimized infusion therapy, made it possible to compensate for chronic heart failure and pulmonary hypertension in the early postoperative period.

The authors declare no conflict of interest.

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