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Perspective of clinical application of pumpless extracorporeal lung assist (ECMO) in newborn

Perspectiva de aplicação clínica da oxigenação extracorpórea por membrana (ECMO) sem auxílio circulatório em recém-nascidos

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Abstract

Extracorporeal lung assist (ECLA) has been proposed as an invasive alternative to conventional treatment when oxygenation is not possible by rigorous mechanical ventilation alone. Usually, ECLA is carried out by establishing a venovenous or venoarterial shunt consisting of a roller or centrifugal pump, a membrane oxygenator, and a heat exchanger. However, the extracorporeal membrane oxygenation (ECMO) with circulatory support lead hemolysis, coagulation disorders, inflammatory response, and specific technical complications inherent to a procedure of high risk and cost. To reduce the drawbacks of mechanical blood trauma during prolonged ECLA, the patient´s arteriovenous pressure gradient as the driving force for the blood flow through for the extracorporeal circuit can be used. In this article are analysed the main contributions of pumpless ECMO, used experimentally and in children and adults with respiratory failure, with perspective of clinical application in newborn.

***Descriptors*: Extracorporeal membrane oxygenation. Membrane oxygenators. Oxygenators. Infant, newborn.**

Resumo

A assistência pulmonar extracorpórea tem sido proposta como uma alternativa invasiva ao tratamento convencional, quando a oxigenação adequada torna-se impossível pelo uso de ventilação mecânica. Usualmente, a ventilação extracorpórea é realizada por meio de *shunt* veno-venoso ou

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veno-arterial, com bomba de rolete ou centrífuga, oxigenador de membrana e permutador de calor. Entretanto, a oxigenação extracorpórea por membrana (ECMO) realizada com auxílio circulatório produz hemólise, distúrbios da coagulação, resposta inflamatória e complicações técnicas inerentes a um procedimento de alto risco e elevado custo. Para reduzir os inconvenientes do trauma sangüíneo, durante a assistência extracorpórea prolongada, pode-se utilizar o gradiente de pressão artério-venoso para impulsionar o sangue através do sistema. Neste artigo são analisadas as principais contribuições da oxigenação extracorpórea por membrana (ECMO) sem auxílio circulatório utilizada experimentalmente e em crianças e adultos portadores de insuficiência respiratória, com a perspectiva de aplicação clínica em recém-nascidos.

Descritores: **Oxigenação da membrana extracorpórea. Oxigenadores de membrana. Oxigenadores. Recém-nascido.**

INTRODUCTION

The main functions of the lungs are to maintain oxygenation, remove carbon dioxide from the blood and maintain the sanguineous pH at physiological levels.

With the impossibility of performing heart surgery when the heart is beating, several machines were developed with the aim of substituting the functions of the heart and lungs whilst the heart is operated on.

The first model of a heart-lung machine was developed in 1936 by John Gibbon, who developed the first works about extracorporeal circulation in animals [1]. At that time a pump with rollers which played the role of the heart was utilized; oxygenation was performed by a series of wire meshes through which the blood circulated and received a flow of oxygen.

After many alterations, Gibbon in 1953 performed the first heart surgery for the correction of an interatrial connection, with extracorporeal circulation utilizing an oxygenator with rotating vertical cylinders [2].

In the 1950s, the experiments made using extracorporeal circulation presented with complications, mainly owing to the direct contact of the blood with oxygen and the non-endothelial surfaces. For the oxygenation of the blood, principles such as the following were used:

1) bubbling oxygen through the blood and subsequently removing the bubbles before introducing it into patients;

2) running the blood over large areas of plastic sheets (polyethylene, polyvinyl) in the presence of oxygen;

3) forming pedicles of blood on surfaces of rotating disks and

4) passing the blood through thin membranes or through thin tubes which were porous for oxygen and for carbon dioxide.

The first observation of gas exchange through a synthetic membrane was made by KOLFF et al. in 1944 [3], performing the oxygenation of venous blood which flowed through cellophane tubes in the first artificial kidney created.

At that time, the utilization of hydrophilic membranes separating two aqueous mediums prejudiced gas exchange, the acid-base balance and solute and electrolyte exchanges. This led to an increase in research aiming at obtaining plastic membranes with a greater potential of hydrophobia.

The first successful clinical applications of a membrane oxygenator in approximately 100 heart operations were reported by CLOWES & NEVILLE [4] in 1958. In this phase, direct contact between blood and gas was eliminated.

In 1960, MARX et al. [5] reported that the capacity of transference of oxygen of a membrane oxygenator was directly associated with the denseness of the laminar blood flow in contact with the membrane.

Technological improvements of the biomaterials employed enabled more rapid gas exchanges and, thus, it was possible to reduce the membrane surface necessary to oxygenate patients.

In 1972, hill presented with the first successful case of the use of extracorporeal membrane circulation in an adult [6]. This consisted of a technique of prolonged cardiopulmonary support which aimed at assisting the lung and/or the heart, when one or other was insufficient and not responsive to conventional non-invasive treatment.

Using extracorporeal membrane circulation, Bartlett in 1975 was successful with a newborn baby suffering from acute respiratory failure [7]. Studies performed by this author between 1975 and 1981 demonstrated the efficiency and safety of this technique in children whose conventional therapy failed. Investigating 50 children treated using this method, BARTLETT et al. [8] had a survival rate of 54% and

3 years after, the survival rate had increased to 90%.

extracorporeal pulmonary assistance has been proposed as an invasive alternative to conventional treatment, when adequate oxygenation using mechanical ventilation becomes impossible. Generally, extracorporeal ventilation is performed by means of a veno-venous or veno-arterial shunt, with a roller or centrifuge pump, membrane oxygenator and heat exchanger. After the introduction of circuits coated with heparin and better technology of the membrane oxygenators, the mortality rate after extracorporeal pulmonary assistance in adult patients, initially high (90%) dropped to from 49 to 53%.

The main limiting factor of extracorporeal membrane circulation is the significant sanguineous trauma that produces hemolysis and coagulation disorders [9]. Hemolysis continues to be one of the most serious problems during cardiopulmonary bypass, extracorporeal membrane oxygenation and percutaneous cardiopulmonary support [10]. The coagulation disorders are mainly caused by an increase in the amount of degradation products of fibrin and in the presence of blood clots in the circuit, as well as the reduction of the fibrinogen levels.

Other limiting aspects include the inflammatory response and technical complications inherent in a high-risk high-cost procedure. Extracorporeal membrane oxygenation induces leukocyte activation and the liberation of cytokines. This reaction can, as it is an additional trauma, worsen the situation of the patient even further. The most common technical complications include oxygenator failure, problems with the cannulae, tubes, pump and heat exchanger.

To reduce the drawbacks of sanguineous trauma during prolonged extracorporeal assistance, the arterial-venous pressure gradient can be utilized to impulse the blood through the system.

The first experiments using this technique were made in 1951 by POTTS et al. [11], who performed pulmonary support in dogs induced to acute respiratory failure. The maintenance of this function was made using a homologous lung, placed in an arterio-venous position inserted between the aorta and the superior vena cava.

In the middle of the following century, RASHKIND et al. [12] utilized a disposable bubble oxygenator in dogs submitted to respiratory failure by asphyxia and inserted the oxygenator between the femoral artery and vein, improving considerably the gasometric parameters of these animals during the entire experiment. From these results, the authors employed this method in children with respiratory insufficiency due to varying etiologies, with some satisfactory results.

In 1971, WILDEVUUR et al. [13], using 250 and 750 Travenol oxygenators in a arterio-venous position in 15 animals induced to acute respiratory failure observed a considerable improvement in the oxygen saturation levels of 57% to 77%.

Employing a hollow polypropylene fiber membrane oxygenator, as partial respiratory support in dogs induced to respiratory insufficiency by hypoventilation over 7 hours, OHTAKE et al. [14] obtained an improvement in the gasometric results with stable hemodynamic patterns without obvious hemolysis.

CHAPMAN et al. [15] investigated the hemodynamic response to pump-less membrane extracorporeal oxygenation in 11 dogs induced to respiratory insufficiency by the intravenous use of oleic acid (0.01 mL/kg). The results demonstrated that there was an improvement in the gasometry, resulting in significant alterations in the peripheral vascular resistance, systemic arterial pressure and cardiac output. The authors demonstrated that an infusion of dopamine (5 ìg/kg/min) was more effective than an increase in the volume (15 mL/kg) in the maintenance of cardiac output, arterial blood pressure and gasometry.

At the start of the 1990s, some authors [16,17] confirmed that pump-less extracorporeal membrane oxygenation was efficient in solving acute respiratory insufficiency in dogs induced by hypoventilation for a period of 24 hours.

In Brazil, research utilizing artificial respiration with a pump-less extracorporeal membrane oxygenator in the arterio-venous position was restricted to experimental works performed by GOMEs et al. [18]. The authors, studying two groups of 6 dogs, one control and the other with respiratory insufficiency induced by oleic acid (0.035 mL/kg), confirmed that this method was capable o maintaining acceptable levels compatible with life.

The first clinical application of pump-less extracorporeal membrane oxygenator in the arterio-venous position in adult patients was performed by LIEBOLD et al. [9], who investigated 20 individuals suffering from acute respiratory failure and with hemodynamical stability. They concluded that this method is easily applied and maintained, with a significant improvement in the oxygenation and the removal of carbonic gas. Additionally, in 60% (n = 12) of the patients the results were satisfactory.

Recently, LIEBOLD et al. [19], using the same method with 70 patients with severe pulmonary failure and stable hemodynamic function with ages ranging from 8 to 72 years old, verified that pump-less extracorporeal membrane oxygenation was extremely effective in the oxygenation and removal of carbon dioxide.

Pump-less arterio-venous perfusion presents with several advantages such as:

- it is simple, easy to install and relatively safe, without the necessity of intensive care or very specialized technicians as well as a low cost.

- reduced risk of cerebral embolia
- it does not increase the heart overload when the flow is maintained constant
- preservation of the flow to several organs
- oxygenation of pulmonary blood has a vasodilator effect on the arteriolar sphincters reverting pulmonary spasm (vasoconstriction)
- it can also promote a cure of pulmonary parenchyma
- eliminates trauma to blood components produced by the pumping mechanism

Studies are being made in the Medical School of São José do Rio Preto (Famerp), São Paulo, aiming at in vitro and in vivo evaluation of artificial respiration with pumpless low-resistance extracorporeal membrane oxygenators in the arterio-venous position. Preliminary results have demonstrated a considerable efficiency of this type of extracorporeal pulmonary assistance in the exchange of oxygen and carbon dioxide and the low-pressure gradient of the oxygenator (5 mmHg).

Currently, with the development of new materials such as polymetylpentene (PMP) utilized for the manufacture of hollow fibers for the oxygenation membrane, there was an improvement in the distribution of the pores along the wall increasing the diffusion of oxygen and carbon dioxide. These improvements at the same time has promoted a more dense membrane thus totally eliminating the passage of plasma or water through the pores, evicting direct contact of the blood (outside the capillary) and the air or oxygen (inside the capillary) and reducing sanguineous trauma. This technological innovation might easily contribute to increasing the useful time of the membrane oxygenator in extracorporeal circulation.

Considering that the beneficial effects of this technique are evident, the same might be applied in situations whose conventional ventilatory support methods are not sufficient to maintain the life of hemodynamically stable newborn babies and sufferers of respiratory insufficiency.

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