REVIEW ARTICLE

A Mini-Review on the Implication of Bioartificial Lungs using Bioengineering Technologies

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ABSTRACT

Background: With the rising prevalence of acute and chronic lung diseases, the only way to compensate for the loss of organ function is to use an artificial organ or a transplant. Lung transplantation, on the other hand, is only available to a small percentage of patients due to the scarcity of transplantable organs. Despite the fact that the organ is artificially replaced for the kidney and heart, it has been a feasible option for many years, artificial pulmonary systems can only be replaced for a short period of time.

Aim: To discuss the implications of bio-engineering technologies in inventing the bio-artificial lungs.

Objectives: To discuss the current barriers to lung transplant in a country like India and discuss the current available treatment options.

Results: Longer-lasting wearable systems are now largely owing to advancements in the engineering of hollow fiber membrane gas exchangers, which can be used to help patients transition from lung failure to transplantation.

Conclusion: Advances in the conception of microchannel-based devices, which may even allow intracorporeal implantation, have given rise to the concept of biomimetic devices. Tissue engineering and cell-based technologies have been used to create bioartificial lungs with properties that are similar to those of the natural organs.

KEYWORDS

• Artificial lungs • Bioengineering • Innovation • Lung transplant

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INTRODUCTION

Lung diseases, both acute and chronic, are major health issues. When lung disease has progressed to the point where it is no longer treatable, lung transplantation is the only option. Dr. KM Cherian was the first person in India to perform a double-lung transplant (DLT) and a combined heart-lung transplant (HLT), in 1999, kicking off the era of lung transplantation in the country[1].Chennai was the site of India's first successful heart-lung transplant. The initial results were promising, as a result, thoracic organ transplantation in India has entered a new era. Since then, a few Indian centers have attempted to establish lung transplant programs, but they have faced numerous obstacles. For a successful lung transplant, it is critical to choose the right lung for transplant and the right recipient. In 2015, the International Society for Heart and Lung Transplantation (ISHLT) released a consensus document on lung transplant candidate selection as well as a statement on donor lung procurement (2020)[2].In India, the rate of organ donation was 0.52 per million people in 2019, equated to 36.07 donors per million in the United States (USA). One of the most difficult challenges the transplant program in India faces is doctors' sensitization to brain stem death declaration.

Barriers in India to Lung transplantation:

There is indeed a national passivity in association with the diseases due to the resource-intensive, limited, and expensive treatment options. Understandably, Organ replacement is still a ridiculous idea for a large number of these patients. The interpretations for the cadaveric program's failure are numerous and complicated. The most obvious are taboos and social and religious beliefs, as well as the bereaved family's lack of a decision-making process[3].Organ donation has been resisted for centuries due to multi-cultural, racial, religious beliefs, and diverse traditions. Organ donation, on the other hand, has recently increased in some parts of the country. Donor accessibility, late recommendations, health professionals' disinclination to refer cases due to a lack of optimism in clinical outcomes, graft rejection, infectious diseases both in the recipient and the donor, execution issues, value, and organisational issues are all issues that lung transplant units in India face.

Since the COVID pandemic swept the globe, India has seen a drop in the rate of organ donation. Lung transplantation in India has decreased due to a lack of available donors, the fact that lung retrieval rates are lower than other solid organs, and strained healthcare resources.

Current treatment options:

Assisted ventilation and extracorporeal membrane oxygenation are the only currently treatment choices available for acute end-stage lung failure sufferers. Airway overextension is a risk of mechanical ventilation and over-compression, as well as respiratory muscle eutrophication. Because the amount of blood that can be bypassed externally is limited, an ECMO device can only provide partial respiratory assistance[4]. Extracorporeal Membrane Oxygenation (ECMO) machines, during cardiac surgery, have been used to provide respiratory support since 1950s, which already have a form of artificial gas exchange interface. A bundle of porous hollow fibers is typically used as the membrane oxygenator in these devices. The fibres' outer surfaces are pumped with venous blood, while the lumens are pumped with oxygen-rich gas. In extracorporeal circulatory systems, unfractionated heparin is currently the standard anticoagulation therapy. Heparin, which is given intravenously and administered systemically, works by increasing antithrombin activity. Heparin is applied to the blood-exposed surfaces in addition to the systemic application to reduce coagulation activation. Recently, researchers have been working on an anticoagulation strategy that does not cause bleeding complications. The dimensions of the fibres that can be produced are limited by existing production technologies[5]. As a result, intramural diffusion rates and gas exchange surface area are substantially reduced compared to the native lung. Thus, increased gas exchange rates necessitate the use of pumps. ECMO devices, however, comes with a finite life due to clot formation on the fiber surface, which is caused by the artificial polymers used in the fibers.

Due to the complexity of the systems and concurrent biocompatibility issues, modern tech only enables the respiratory support usage for a short span of time, ranging from days to a few weeks. As a result, lung support systems

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are not currently an option for patients with terminal benign lung diseases who require long-term care.

DISCUSSION

The engineering of the bio-artificial lung's internal surfaces, where the crucial feature of blood-to-air gaseous exchange occurs is critical to its success. The alveolar and vessel walls of the human lung make up this surface, which is perfused with air and blood via the bronchiole tree and pulmonary vasculature's extensive branching networks. A healthy adult lung has about 100 m2 of surface area and 300–500 million alveoli. Furthermore, the alveolar wall is 0.5 m thick, and pulmonary vessels can be as small as 5 m across. Reproducing the complex multi-scaled architecture of the extra-cellular matrix of a human lung for the reasons of cell seeding appears to be an insurmountable challenge[6].

The type of scaffold material used to build the bioartificial lung, as well as its composition, are critical. Because of the hydrophobic character of the polymers most often used in ECMO devices to make hollow fibres are silicone, which limits cell adhesion, the development of a wearable bioartificial lung is hampered. To ensure consistent cell attachment and generate a monolayer of cells that is tolerant to extreme fluid shear stress caused by blood flow, surface modification such as a result of physical and chemical and/or chemical intervention is required[7].

To enable the circulation of dissolved gas throughout the interstitium, the scaffold must have the adequate pore size and interconnectivity. Circulating cells should be able to enter and migrate due to the material's porosity and substrate properties. The lung should be organised for the diaphragm to deform it with sufficient force, and the scaffold material must have the right density to ensure that now the bioartificial lung is of the correct weight. The material must also be able to withstand various large deformation cycles without losing its integrity or mechanical characteristics[8]. After implantation, providing these cells by using body's own tissue regeneration into the scaffold with their correct spatial organization could be a suitable option Bone marrow-derived cells circulate in the blood includes fibrocytes as well as endothelial and epithelial progenitor cells. One alternative for optimizing natural regeneration is to inoculate the scaffold using the patient'on with the bioartificial trachea. Since mononuclear cells (MNCs) are found, this might function by securing timely deliveries of the cell types which are necessary, improving host cell homing, and reducing inflammation after implantation. Computational modeling can be used to stimulate cell attachment during scaffold perfusion seeding, allowing experimental flow rates that provide optimal cell surface coverage to be predicted. The gas exchange of the bioartificial lung can also be predicted using mathematical modeling, which takes into account the characteristics of the ECM's architecture and permeability[9].

Commencing an idea of bioartificial lungs:

Recent advancements in tissue engineering and regenerative medicine have made a way for new treatment options. Successful transplantation procedures using tissue-engineered tracheas have been a watershed moment in the field. These are made with a scaffold, which is made up instead of a decellularized donor organ or an artificial material that serves as the trachea's extracellular matrix (ECM).The bioartificial trachea's resounding success has raised the possibility that, in the future, similar techniques could be used to create working pulmonary tissue for any patient. However, due to the lung's more complex architecture than the trachea, there is a lot of work to be done. It's challenging to seed a lung scaffold with the appropriate number of different cell types found in the native lung, particularly epithelial cells (EPCs) and endothelial cells (ECs)[10].

CONCLUSION:

Although lung transplantation is a last resort treatment for lung failure, limited donor organ availability necessitates alternative management, such as artificial lung technology. Bioengineered lungs, on the other hand, were implanted into four pigs and showed no signs of rejection. The bioengineered lungs also developed vascularization. The beginning of preclinical investigations, which ideally led to the potential of offering bioengineered lungs to transplant into patients in need in the future, has been a lengthy process[11]. For those suffering from severe lung infections, a transplant can be a long-term option.

Ethics declaration: The study is done within ethical standards.

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