Administration of Nebulized Saliva from Healthy Volunteers To Prevent Chronic Infection in Lung Transplant Patients

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ABSTRACT

Lung transplantation has poor long-term survival relative to other solid organ transplants. This can be largely attributed to higher rates of chronic lung allograft dysfunction and infection following transplant. The lungs are non-sterile and a lung microbiome is present primarily through microaspiration of upper respiratory tract microbiota. Patients who have undergone lung transplantation exhibit a dysbiotic lung microbiome relative to healthy patients. It is proposed that the saliva from the upper respiratory tract of healthy volunteers can be nebulized to produce aerosolized microbe-containing saliva droplets. Lung transplant patients can inhale nebulized saliva from healthy volunteers to help establish a healthy lung microbiome and prevent chronic infection following their transplant. This concept is analogous to the well-established use of a fecal transplant from healthy volunteers in patients with a dysbiotic colon.

INTRODUCTION

Lung transplantation has the lowest long-term survival relative to all other solid organ transplants.[1] A key barrier to long-term patient survival is chronic lung allograft dysfunction, which leads to significantly reduced forced expiratory volume and graft rejection.[2] It has been shown that multiple lung infections increase the risk of chronic lung allograft dysfunction[3] while the administration of azithromycin slows its progression.[4] This suggests that aberrant microbiota within the lungs are a driver of graft rejection in lung transplantation.

Unlike most solid organs, the lungs are non-sterile and continually exposed to our outside environment. It has been shown that a microbiome exists within the lungs.[5] The lung microbiome greatly overlaps with the biota of the upper respiratory tract,[5] and it has been reported that microaspirations of organisms in the upper respiratory tract are a primary route for establishing the lung microbiome.[6] Key bacterial taxa in the healthy lung microbiome include Firmicutes and Bacteroidetes phyla, while Prevotella, Streptococcus, and Veillonella are common genera.[7] Viral and fungal niches are also present in the lung microbiome, notably Anelloviridae and Ascomycota.[8-9]

The lung microbiota in patients with or without suppurative lung disease following lung transplantation is significantly disrupted relative to healthy lungs, where local growth of a pathogenic organism can represent a large portion of the lung microbiota and contribute to dysbiosis.[10] The microbiome in the lungs post-transplant has increased microbial biomass, lower alpha diversity, and frequent appearance of dominant organisms.[10] Dominant organisms in the microbiome in the lungs of patients post-transplant can include Pseudomonas aeruginosa, Achromobacter, and Staphylococcus aureus,[10] which can leave these patients susceptible to pneumonia.

HYPOTHESIS

If a healthy lung microbiome is established in transplanted lungs following surgery, then chronic infection in lung transplant patients can be reduced. To establish a healthy lung microbiome in post-transplant lungs, it is proposed that microbe-rich saliva from the upper respiratory tract of a healthy

volunteer can be collected and placed into a nebulizer (Figure 1). A nebulizer can apply a mechanical force with pressurized air onto the pooled saliva to produce aerosolized droplets of the saliva that contain microbes from the upper respiratory tract of a healthy volunteer (Figure 1). These microbe-containing droplets can be inhaled by the lung transplant patient (Figure 1). If the lung microbiome is established primarily through microaspiration of microbiota from the upper respiratory tract,[6] then this method will allow for the establishment of a healthy lung microbiome in patients following lung transplant.

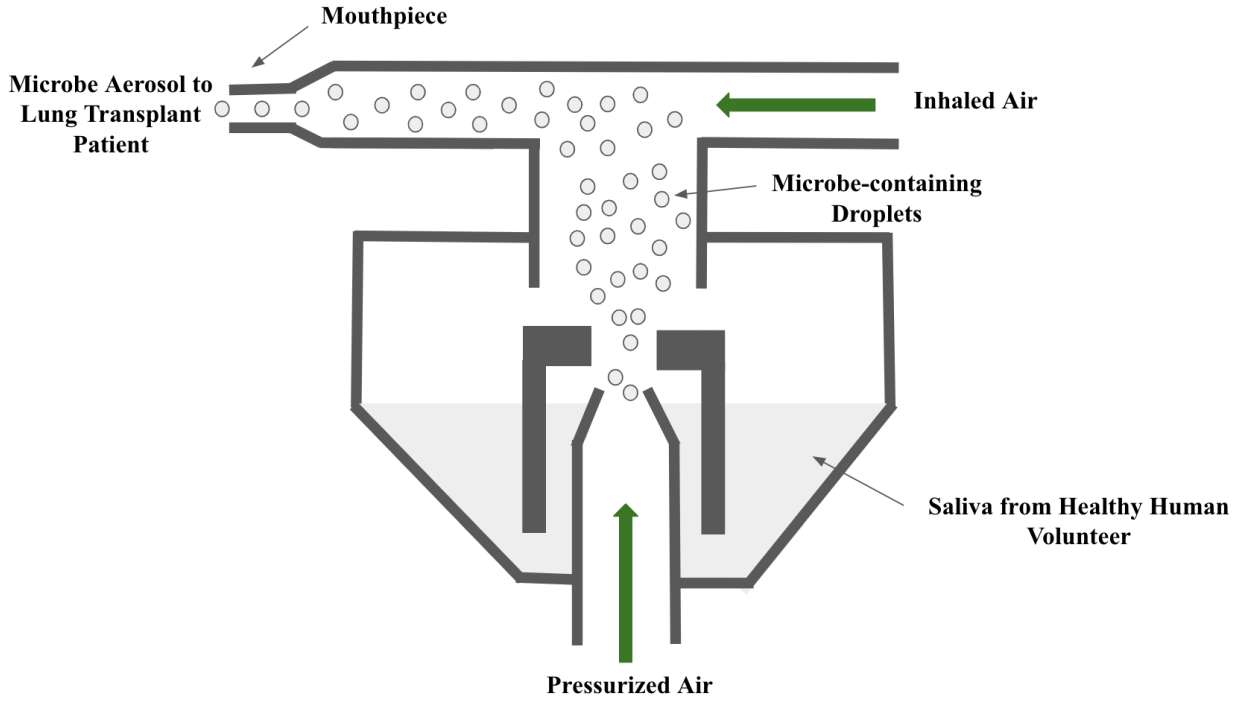

Figure 1. Nebulization of Saliva from a Healthy Human Volunteer to Establish a Healthy Lung Microbiome in Patients Following Lung Transplant.

DISCUSSION

This saliva nebulization method may be especially useful for patients who have a suppurative lung disease (e.g. cystic fibrosis) following lung transplant. Moreover, these patients otherwise have a persistently disrupted upper respiratory tract microbiome with frequent pathogen colonization despite a

lung (lower respiratory) transplant.[11] The aberrant microbiota in the upper respiratory tract of these patients is still capable of traveling into their newly transplanted lungs via microaspiration. However, the higher frequency of inhalation of microbe-containing droplets from the nebulized saliva of healthy volunteers into the lungs of these patients can likely outcompete the basal level of microaspiration of aberrant microbes. Thus, it is also worth exploring whether nebulized saliva from healthy volunteers can help treat patients with cystic fibrosis prior to a lung transplant. An analogous concept exists via the use of fecal transplantation from healthy volunteers to treat patients with Clostridium difficile infection in their colon.[12]

There are some factors to consider with this specific nebulization method. A dilution of the saliva may be necessary in order to prevent excessive microbe biomass in the lungs from accumulating, though the degree of dilution is likely dependent on the patient and their lung disease history (i.e. suppurative vs nonsuppurative). One must also be careful not to introduce too many nebulized droplets into the lungs of patients in order to prevent a counterproductive increased risk of infection through liquid accumulation in the lungs. Additionally, although human saliva is relatively easy to obtain, this nebulization method is also possible with liquid from a bronchoalveolar lavage from a healthy volunteer. However, a bronchoalveolar lavage in a healthy volunteer is much more invasive and impractical.

CONCLUSION

Lung transplantation offers poor long-term survival relative to other solid organ transplants. A microbiome exists within the lungs that is primarily derived from the microbiome of the upper respiratory tract through microaspiration. Patients who undergo lung transplant have a dysbiotic lung microbiome that can increase their susceptibility to infection. Saliva from healthy volunteers can be placed into a nebulizer to produce aerosolized microbe-containing droplets from their upper respiratory tract that lung transplant patients can inhale through a mouthpiece and establish a healthy lung microbiome. The establishment of a healthy microbiome can help to combat chronic infection in lung transplant patients, potentially improving postoperative outcomes.

CITATIONS

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