

SHORT COMMUNICATION

Donors Declined for Islet Transplantation: Understanding the Primary Causes to Overcome this Challenge

Marluce da Cunha Mantovani^{1*}, Mari Cleide Sogayar^{1,2}

¹Department of Medicine, University of São Paulo Medical School, São Paulo, Brazil

²Department of Biochemistry, University of São Paulo, São Paulo, Brazil

DESCRIPTION

Islet transplantation based on pancreas obtained from heart-beating organ donors offers a hopeful avenue for Type 1 Diabetes Mellitus (T1D) treatment; however, its potential is hampered by the insufficient availability of pancreatic preserved under suitable conditions. Our Cell and Molecular Therapy NUCEL Group embodies a diverse team of researchers, including clinicians and surgeons from local hospitals. This team operates at the University of São Paulo [1], focusing fundamental research on the molecular mechanisms controlling cell proliferation and differentiation, and performed the first pancreatic islet transplantation in Brazil on a T1D patient, who suffered from metabolic instability and recurrent severe hypoglycemia [2]. As Brazil's pioneering center for human islet isolation and transplantation, a total of 11 islet infusions were applied to five patients, resulting in notable post-transplantation benefits, including reduced or no hypoglycemic episodes, decreased resistance to exogenous insulin, measurable C-peptide production and absence of hyperlability.

Our previous studies [3] revealed that only approximately 8% of the pancreas offered were accepted for islet transplantation, underscoring a significant gap between potential and actual donors. The primary causes of organ (pancreas) refusal were investigated aiming at enhancing the ratio of potential viable donors, leading to an increased acceptance rate.

The primary reasons for pancreas refusal in our NUCEL group were: 1) Hyperglycemia; 2) technical issues; 3) age; 4) positive serology and 5) hyperamylasemia [3].

During potential organ donor patients stays at

Intensive Care Unit (ICU), various factors can contribute to fluctuating glycemic levels. Certain medications, such as thiazide diuretics and corticosteroids, have been linked to elevated blood sugar levels [4]. Excessive insulin secretion can be associated with some compounds such as dopamine, potentially compromising β -cells function and viability [5]. Hyperglycemia can be associated with prolonged use of glycosylated serum without proper monitoring, particularly in donors with extended ICU stays, indicating the need for better management of donor glycemic levels at the ICU.

Technical issues, such as scarcity of qualified personnel and/or specific reagents and supplies and organ transportation problems, also significantly contributed to pancreas refusal. Due to the high costs of ICU care for organ donors in Brazil, there is a shortage of deceased organ donors, making it challenging to provide transplantation services to all in need. Increasing the number of organ (pancreas) procurement and processing teams in different regions of the country would improve the efficiency of organ procurement and reduce the travel distances for patients, potentially lowering costs and improving access to treatment. However, implementing these solutions would require significant investment in training, infrastructure and continuous funding for teams and facilities. The issue of supply availability is dependent upon the complex regulatory Brazilian importation system, but efforts were taken by the scientific community to address this issue [3].

As in other countries, islet transplantation in Brazil is considered as an experimental procedure, therefore, the pancreas offered to our group had already been previously declined by other teams procuring whole organ pancreases for pancreas transplantation. Despite data from the ABTO indicating that 38% of heart-beating donors were between 41 and 60 years old [6], in our previous study [3] it constituted a significant proportion, only 60% of the donors fell within this age range. This variation implies a scarcity of pancreas from younger donors, who are more favorably considered by whole organ pancreas transplantation teams. Given that the donor age appears to influence the quality of the isolated islets obtained, efforts to reduce the average donor

Received 11-Mar-2024 Manuscript No. IPP-24-19118 **Editor assigned** 15-Mar-2024 PreQC No. IPP-24-19118 (PQ) **Reviewed** 29-Mar-2024 QC No. IPP-24-19118 **Revised** 05-Apr-2024 Manuscript No. IPP-24-19118 (R) **Published** 02-Jan-2025 DOI: 10.51268/1590-8577-26.S11.1-2

Correspondence Marluce da Cunha Mantovani

Department of Medicine, University of São Paulo Medical School, São Paulo, Brazil

E-mail marluce@usp.br

Citation: Mantovani MC. Donors Declined for Islet Transplantation: Understanding the Primary Causes to Overcome this Challenge. JOP. J Pancreas. (2025) 26:1-2.

age could potentially enhance the outcome of the islet isolation process.

The fourth cause of pancreas refusal for islet transplantation was positive serology [3]. This seropositivity refers to Chagas disease, toxoplasmosis, rubella, syphilis, cytomegalovirus, hepatitis B and C and HIV. These donors are called marginal donors presenting additional risk factors, but nothing that can be done, since these organs can only be accepted in situations in which the risk of patient death due to heart disease is greater than that offered by the donor [7].

Hyperamylasemia is often elevated in cases of brain death due to violent death and trauma, representing most cases of brain death in Brazil [8]. However, it can also be caused by various factors, including acute pancreatitis, pancreatic tumors or abscesses, making it difficult to suggest actions to reduce hyperamylasemia in order to improve the pancreas status.

The high costs associated with isolating and transplanting islets presents a significant challenge in Brazil. This process requires a specialized team with a specific expertise, as well as specialized equipment and facilities. Presently, only three centers in Brazil offer this procedure: 1) NUCEL, our group, which conducted the inaugural islet transplantation in 2002 [2]; 2) a laboratory in Curitiba associated with PUC-Paraná University and the Pro-Kidney Foundation, which performed one islet transplant in 2005 [9]; and 3) a human islet isolation laboratory at the Endocrine Division of the Porto Alegre Clinical Hospital in Rio Grande do Sul [10], although this unit has yet to perform islet transplants in patients. This limited availability presents logistical hurdles and increased procurement costs, particularly for patients residing far away from these centers. Expanding organ procurement and transplantation services requires substantial investments in infrastructure, equipment, personnel and ongoing funding and support. Moreover, addressing ethical and cultural barriers to organ donation and transplantation is essential to fully realize the potential benefits of these services. Understanding the primary causes of pancreas refusal for islet transplantation is essential and should be encouraged to design new strategies to overcome these obstacles and improve the treatment outcome of T1D patients globally.

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