Review Report

Indian Journal of Hospital Administration
Volume 2 Issue 1, January - June 2018

Cadaveric Organ Transplantation and Tissue Harvesting: An Unexplored Domain

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Abstract

The Transplantation of Human Organs is used in treatment of patients who has irreversible damage to their organs. The demand of various organs for transplant patients far exceeds than the number of organs actually donated but transplantation is offered only to patients who have a prospect of achieving an acceptably good quality and duration of life after transplantation.Since the inception of organ transplantation, the huge gap between the demand and supply of organs has been widening exponentially. The growing need for transplantable organs necessitates finding sources other than heart beating donors (HBD), and living donors (LD). The other probable source of a transplantable organ from Non Heart Beating Cadaver (NHB) or a Donation after Cardiac Death (DCD) has not been explored extensively. An important aspect of organ donation is harvesting the selected organ within a stipulated time period, known as Warm Ischaemia Time (WIT). If an organ is retrieved by the organ retrieval team within the specific WIT attributed to different organs, then there are increased chances of their proper functioning post transplantation with reduced incidences of graft rejection. Thus, detecting the viability of an organ and its functionality within the accepted range of normal limits is of paramount importance for successful organ harvesting and its subsequent transplantation. The authors discuss about the various intricacies of harvesting organs from Non Heart Beating cadavers brought for autopsy, thereby utilizing a large pool of still inaccessible organs for the greater benefit of the entire society.

Keywords: Organ Retrieval; Therapeutic Transplantation; Non Heart Beating Cadaver; Warm Ischaemia Time.

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Received Date: 13 June 2018
Accepted Date: 22 June 2018

Introduction

The Transplantation of Human Organs is an important emerging concept in treatment of patients who has irreversible damage to their organs. Though Medical Science cannot replace God in making a human body but efforts can be made due to availability of latest technology to treat and allay the diseases of individuals and help the mankind as a whole. Transplantation of Human Organs and tissues is a noble cause which the Government of India is also taking very seriously with various National Donor programs and Registry [1]. The demand of various organs for transplant patients far exceeds than the number of organs actually donated but transplantation is offered only to patients who have a prospect of achieving an acceptably good quality and duration of life after transplantation [2].

Current Challenges for Organ Donation

Since the inception of organ transplantation, the huge gap between the demand and supply of organs has been widening exponentially. The reasons are manifold like:

1. Extremely meager amount of organ donation.

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2. Elaborate selection criteria for organ donation, rendering most organs unsuitable for transplantation both in dead and living.
3. A very small number of registered Transplantation centers.
4. Lack of an Expert Organ retrieval team in hospitals.
5. Poor infrastructure& logistic facilities for organ retrieval, transport and its transplantation within the stipulated time period.
6. Huge financial burden on the patient's relatives of an organ transplantation surgery and its long term maintenance.
7. Lack of co-ordination between the different Clinical Departments of a Hospital.
8. A dire lack of awareness about the necessity of organ donation in the general population.

All these reasons result in very low percentage of organ donation in Indian scenario, and even poorer success rate post transplantation.

Non-Heart Beating Donors- Anunexplored Domain

Heart Beating Donors (HBD) include organ donation from a living person or the patient who is brain dead but with a functioning heart. The growing need for transplantable organs necessitates finding sources other than heart beating donors (HBD) and living donors (LD).[3] The other probable source of a transplantable organ from Non-Heart Beating Cadaver (NHB) i.e. a Donation after Cardiac Death (DCD) has not been explored extensively. Maastricht (Netherlands), Japan and parts of the United States of America as well several units in the United Kingdom, have long standing programs to retrieve organs (principally kidneys) from non-heart beating donors [4]. A major limiting factor to the widespread adoption of a non-heart beating organ donation and transplantation is the uncertainty regarding the function of the graft once transplanted. Delayed function, rejection and extended hospital stay are all a concern with non-heart beating organ donation but primary non-function has more significant consequences.

Viability of an Organ: Concept of Warm Ischaemia Time

An important aspect of organ donation is harvesting the selected organ within a stipulated time, known as Warm Ischaemia Time (WIT). The onset of ischaemia immediately impairs oxidative metabolism, depletion of adenosine triphosphate (ATP), an increase in anaerobic glycolysis and the inhibition of Na+/K+ ATPase. Membrane transport mechanisms will slow down, causing intracellular accumulation of water and ions which results in cell oedema and disruption of the cytoskeleton. Impaired oxidative metabolism triggers the formation of reactive oxygen species (ROS) that have a direct detrimental effect on the cell [5]. If an organ is retrieved by the organ retrieval team within the specific WIT attributed to different organs, then there are increased chances of their proper functioning post transplantation with reduced incidences of graft rejection [6]. Thus, detecting the viability of an organ and its functionality within the accepted range of normal limits is of paramount importance for successful organ harvesting and its subsequent transplantation [7]. Several biological factors influence short-term outcome as well as long-term function of transplanted organs and most of the research till date is concentrated on this aspect only [8].

In 2002 Gamez et al. [9] performed 5 lung transplants from uncontrolled NHBD (Maastricht category I, dead on the arrival at OR): the maximum WIT was 120 min (90 min from cardiac arrest to arrival at the hospital Emergency Unit and 30 min to the start of preservation manoeuvres). Lung transplants from NHBD showed excellent gas exchange in the post-operative period and a post hospital evolution similar to recipients from HBD. Nguyen et al. [10] (Maastricht category III) got a biliary complication rate similar in NHBD and in HBD and suggested that for liver transplantation, the WIT should be less than 30 min and the CIT should be less than 9 hour. Regarding kidney transplantation, Sanni et al. [11](Maastricht categories II and III) showed that WIT should be 37 minutes and also highlighted that survival rates and graft quality at 1 year were not different between the two groups of HBD & NHBD donors. In 2009 Ali et al. [12] described cardiac resuscitation in a controlled NHBD after a WIT of 23 min.

Tissue Harvesting

Bio banking of stem cells from bone marrow, umbilical cord, and adipose tissue is increasingly used by pathologist to maintain cell lines and bioengineering. Newer applications of autologous banked tissues for future use are being regularly reported with use of blood vessels, testicular and ovarian tissues, sperm, cord blood, placenta etc [13]. Skin donation can be taken upto 12 hours and with precautions even upto 24 hours after death.

The donation is possible if the deceased person was more than 16 years of age and was not harboring transmissible infections such as Hepatitis B, Hepatitis C and HIV. Those suffering from skin cancer, septicemia and with damaged skin e.g. scleroderma, pemphigus are not suitabledonors [14]. Castagnoli C [15] in his study, investigated the viability of postmortem allografts (n=350) harvested from 35 different donors, using theMTT salt assay. The viability index (VI) of skin is expressed as the ratio between the optical density (O.D.) produced in the MTT assay by the skin sample and its weight in grams. The results indicated that samples tested within 12—30 hours from harvesting have an average viability index of about 75 with little variation. Samples tested within 60 hours have an average viability index of 40, showing a viability decrease of about 50%.

Viability Assay

A viability assay is an assay to determine the ability of organs, cells or tissues to maintain or recover viability. Viability can assay mechanical activity, motility (spermatozoa or granulocytes), contraction (muscle tissue or cells), mitotic activity, etc [16]. Different viability assay commonly employed include the ATP test, Calcein AM, Clonogenic assay, Ethidium homodimer assay, Evans blue, Fluorescein diacetate hydrolysis/ Propidium iodide staining (FDA/PI staining), Flow cytometry, Formazan based assays (MTT/XTT), Green fluorescent protein, Lactate dehydrogenase (LDH), Methyl violet, Propidium iodide, DNA stain that can differentiate necrotic, apoptotic and normal cells, Resazurin, Trypan Blue: a living cell exclusion dye (dye only crosses cell membranes of dead cells) and TUNEL assay [17].

Recommendation

Future research should be carried out to assess the viability of certain organs and tissues (lung, heart, liver, kidney, cornea, skin, bone) in a Non Heart Beating patient at different time interval which can easily be carried out in cases brought for autopsy, as only small amount of tissue needs to be collected for assessing the viability and the ethical part including the consent of the relatives of the deceased can be fulfilled easily. The viability may be tested for different time interval later on after having a baseline data and the research may be continued in the direction of new results obtained from further studies. A large pool of organs can be used for the greater benefit of the entire society.

Conflict of Interests: Nil.

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