Stem Cell Therapy for Kidney Disease—Present and Future

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Use of stem cell-based strategies have been used for treatment of situations where kidneys have been injured. One sees them work in acute kidney injury and repair, condition where modulating of immune response leads to healing and acts as a compliment to kidney transplantation.

It has been proved that kidney by itself is a source of variety of stem cells, simplest example of these cells helping repair, following injury is seen with acute kidney injury (AKI) due to ischemic and toxic insult, where the renal tubular epithelial cells undergo regenerative response that leads to recovery of renal function. It has been proved that the extra-renal stem cells of bone marrow origin are home to the kidney and are responsible for this reparative process after ischaemia-reperfusion injury. This is proved to have been mediated through, insulin-like growth factor – 1. These are examples of autotherapies carried out in the human body with its renal cells, by its intake ability.

In clinical practice both human embryonic (HESC’s) and allogenic/autologous haemopoietic stem cells transplantation (HSCT), have been used for some of the chronic kidney diseases which include autoimmune diseases and CKD Stage 5 needing renal transplantations. One of the important diseases which affects the kidneys and leads to a chronic disorder is systemic lupus erythematosus (SLE) leading to lupus nephritis. When it fails to respond to regular advanced therapy with high dose chemotherapy, haemopoietic stem cell therapy has been used since the year 2000 as reported by Traynar. Vankar et al from India from Ahemadabad group of Dr. H.L. Trivedi of IKDRC have reported their experience on 27 cases of resistant SLE who received the therapy from their blood group matched relatives. Donor-recipient HLA matching was performed on the first day. Donors were administered GN-CSE (10 mgs) B.W/day sc on day 2 and 3. On day 4 bone marrow aspiration was performed under local anaesthesia from posterior superior iliac crest. First 10 ml of aspirate was concentrated and 2 ml kept for thymic inoculation finally, the CD4 cell count of this concentrated inoculation was done together with total and differentiated blood count. Subsequently out of 300 ml of ungra BM that was aspirated 80 ml was infused into the sternum and anterior superior iliac crest; 120 ml into portal and 200 ml into peripheral circulation. Recipient was also given thymic inoculation of stem cells under GA. A specific protocol was followed and the last PBSC infusion was performed on day 14.

Cumberson procedure through result were encourage. On the first 5 years follow up development of self-tolerance was the central theme in this study by using multiple site infusion technique these Indian workers have developed an integrated approach to reconstitute the disturbed central and peripheral arm of self-tolerance. The same workers have now developed directed differentiation of human embryonic stem cells with the advantage of better grafting and great poteney owing to weaker HHC markers. In clinical solid organ transplantation; alloreactivity leading to organ rejection is controlled by immuno suppressive drug which have their own severe side effects. One of the cellular therapies is mesenchymal stem cell (MSC). It has been suggested that here the inhibition of lymphocytes is independent of HLA setting. Several workers in the world including one a group in India have been working on tolerogenic strategies for achieving high grade donor specific tolerance after organ transplantation. Their main hope is that induction of such tolerance will help eliminate the need for chronic, almost lifelong use of immunosuppressive drug which are also toxic. This is the coveted holy goal of all transplanters. Trivedi et al from IKDRC Ahmadabad first reported their clinical experience in a prospective randomized controlled trial of 24 patients by introducing unfractitioned HSCs into the thymus and periphery to create toleration. They concluded that this method of inducing tolerance was safe and efficacious. They further observed that this therapy yielded better graft function; minimum acute rejection and no CMV disease with just more therapy. They reported this in 2003, thereafter up to 2011 they had performed more than 1000 kidney transplants with their model of tolerance development with several modifications. Elsewhere in the world too; starting under the director of well known name in transplantation Dr. Thomas Starzal at the university of Pittsburg-Pennsylvania who used novel protocol with host pre-treatment in 96 patients with rabbit antithymocytic globulin; in 33 donor bone marrow cells were offered after transplantation after early signs of rejection had set in without responses. According to Dr. Stazl this strategy was “Counterintuitive”. He hence encouraged Dr. Trivedi to go ahead with his protocol and even helped him prove that tolerance is possible under the right circumstances. Besides mesenchymal stem cells from bone marrow and umbilical cord blood; adipose tissue too is a good source and have the potential to differentiate along differentia’s lineages and have been put to clinical use; as this source gives adequate single source for cell as reported by Trivedi et al from IKDRC-ITC. They transplanted these cells in portal circulation using their own technique of omental cannulation. In 2006-2007 subsequent to this not more experience has been gained over the years. Graft-versus host disease is yet another condition where immunomodulatory effect of mesenchymal stem cells therapy has been successfully utilized which have been resistant to steroid refractory state. In this situation too donor cell source adipose tissue has been used. Over 15 years lots of progress has taken place both in experimental bioengineering and in clinical usage. It’s visualized that solution to the problem of rejection and chronic allograft nephropathy is almost nearer the horizon and rapid scientific advances will help us to get a solution. This will be a boon in a country like India where we need cost-effective treatment; which will help us reach all needy patients of end stage kidney disease stage 5, who need kidney transplantation and are suitable, but

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are dying today for want of adequate financial support for their very costly therapy.

References
3. AV Vanikar, PR Modi, RD Patel, support from Transplantation proceedings. The Immune System protects the body against invading pathogens by recognizing them as "Non Self" 2007;39:703-708
7. According to Dr. Starzl, this strategy is “Counterintuitive” because instead of giving patients high doses of immunosuppression beginning at the time the organ is transplanted.
8. RH Lee, B Kim, H Kim......Human Mesenchymal Stem Cells (MSC), that have been reported to be present in bone Marrow, adipose tissue, dermis, muscles and peripheral blood, have the potential to differentiate along different lineages including those forming bone, cartilage, fat, muscle. Stated “Cellular physiology in 2004”.
9. S Bobis, D Jarocha.....There is an increasing number of reports describing their presence in “Adipose Tissue” [43]. Mesenchymal “Stem Cells”: characteristics and clinical.....Department of Transplantation, polish-American Institute of Pediatrics jagiellonian University Medical College. Folia Histochemical et Cytobiological stated in 2007.
10. Austism cerebral palsy, MR Diabeyes paraplegia +91 9011 111222 low cost. This invention essentially deals with a novel method of obtaining mesenchymal stem cell (MSC) from adipose tissue. Transplantation has become an acceptable therapeutic modality for patients dyinf of organ failure. There for embarked on our “Tolerance” seriously since August 1998.
11. M Von Bonin, F Stolzel, A Goedecke......marrow transplantation, therapy- resistant acute graft-versus-host disease with human adipose tissue derived, mesenchymal...calf serum antibodies, after transplantation in allogeneic hematopoietic stem cells. Recipients... support from the Deutsche Forschungsgemeinschaft[SFB 655]from cell to tissues]....stated on 2008.