Editorial

RENAL TRANSPLANTATION IN INDIA : A FRESH LOOK

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End stage renal disease is defined as irreversible renal disease with creatinine clearance persistently less than 5 ml/min [1,2] where survival is not possible without dialysis or renal transplantation. It is a global problem. There are about 70,000 fresh cases of end stage renal disease every year in India. More than 10,000 renal transplants have been carried out in our country compared to more than 100,000 in the world.

Majority of centres report patient survival rates of over 90% at one year and mean graft survival rate of 80-90% over the same period [3-5]. Survival is longer in family related grafts with greater compatibility of cross match, HLA-B and DR match. HLA-A and C are of lesser importance. The most redeeming feature is defining the criteria of brain death and cadaveric renal transplant by our parliament (1993). This would provide more donors and would go a long way to prevent illegal sale of organ from unrelated donors.

Major advances and recent trends in renal transplantation have occurred in all the fields of Nephrology (except in the surgical techniques). These include immunosuppression, immunopathology and transplantation in children. The concept of immunological monitoring has died its own death. Specific immunosuppression is the ultimate goal of therapy. Immune regulation, genes and antigens of major histocompatibility complex, FC receptor system and T cell circuitry are being analyzed. Role of monoclonal antibodies, T

cell receptors and significance of alloreactivity are being looked into.

Greater emphasis is on the concept of "tolerance and unresponsiveness". Specific unresponsiveness selectively for the major transplant donor antigens remains the ideal goal of successful renal transplantation. Classic neonatal tolerance involves nonreactivity to all the determinants of a given haplotype. Experimentally in neonatal tolerance of chimeric animal models, the distinction between deletion of clones and inactivation by concurrently suppressor cells is an important one. One approach is to test for acute suppression by adoptive transfer of cells from neonatally tolerant mice to test recipients. Second one is to use cloning techniques to examine the number and acuity of precursors present in tolerant animals. It has been observed that neonatal animals have larger quantity of natural suppressor cells which decline in number after birth parallel to the acquisition of resistance to tolerance induction [6].

Immunosuppression regimens [2-4] could be variable and strategy would be based on the specific clinical situation. The most conventional therapy had been azathioprine and prednisolone. It was followed by the concept of induction by cyclosporine (6 months to one year) with prednisolone and switch over to prednisolone and azathioprine. Most of the renal centres also practice triple regimen comprising of cyclosporine, azathioprine and

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prednisolone in lower dosage. In difficult cases of cadaveric or second renal transplant, combination of azathioprine, cyclosporine, prednisolone with prophylactic ALG or OKT3 is administered. All these drugs have side effects on liver, kidney, bone marrow etc. and their modes of actions are nonspecific. Some agents act on dividing cells other than lymphocytes and consequently interfere normal repair, regeneration and growth in pediatric age group. Steroids can aggravate diabetes mellitus and diabetic end stage renal disease. Long term immunosuppression may lead to malignancies. Wider use of cyclosporine has led to plethora of literature about its undesirable side effects namely delayed graft reaction (DGR), nephrotoxicity (ARF), hypertension in 40% cases due to afferent vasoconstriction and haemodynamic effect of renal ischaemia. Current data suggest that low dosage therapy with 8-12 mg/kg/day instead of 25 mg/kg/day and maintenance dose of 4 mg/kg/day adjusted to maintain cyclosporine trough level within a relatively narrow therapeutic range minimise the risk of graft loss due to rejection and are associated with stable renal function. Individual adjustment of dosage should be done to yield cyclosporine trough levels between 100 and 300 mg/ml (whole blood, HPLC) or 150-400 mg/ml (whole blood radioimmunoassay). This must be interpreted with the concurrent estimation of creatinine clearance. It is also important to remember that blood concentration achieved with a specific dose of cyclosporine may vary over time and from patient to patient.

Movement is from multiple drug protocols to searching field of selective immunosuppression [2]. Should it be polyclonal immunoglobulins or monoclonals (OKT3) antibodies? What would be the relevance of prophylactic therapy by polyclonal or monoclonal antibodies with the conventional immunosuppression? Polyclonal immunoglobulins result in rapid clearance of lymphocytes due to reticulo endothelial uptake, expansion of suppressor cell population and complement mediated lysis of lymphocytes. However,

suppression of bone marrow, antigen antibody mediated glomerulonephritis and increased susceptibility to infection can occur. Use of better version of monoclonal antibodies is not without adverse effects. Hypotension, increased infection and first or second dose influenza like symptoms occur at high frequency. Multicentre trials are underway to assess the prophylactic use of OKT3 to provide a window of immunosuppression until graft function is established. Future of immunosuppressive therapy perhaps is in T cell specific magic bullets of low toxicity by the genetic engineering techniques to fully humanized anti T cell monoclonal antibodies or IL-2 receptors with IL-2 toxin fusion proteins in the complex immunological orchestra.

Transplantation in children under one year of age has its own unique problems [4]. Results of renal transplantation are inferior to long term chronic ambulatory peritoneal dialysis (CAPD). Vascular thrombosis and technical problems of vascular anastomosis from donor to recipient are the major problems. The dosage of immunosuppression is akin to those of adults due to rapid clearance of cytotoxic therapy. However, in contrast to adults, cyclosporine has not improved the survival rate in children.

However, the future trends in renal transplantation will reflect miracles in modern medicine.

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