Potential Protective Effect of Grape Seed Proanthocyanidine Extract in Cold Ischemia-Reperfusion Injury of the Transplanted Kidney

Dear Editor,

Kidney transplant is considered as the treatment of choice in selected patients with end stage renal diseases as it confers improved quality of life and survival over hemodialysis and peritoneal dialysis.[1,2] Rising incidence of organ failures in the ageing populations, the relaxation of recipient eligibility criteria, and advances in transplant technologies and immunosuppressant medications have all contributed towards the current situation where we have a persistent faster growing number of patients on the waiting lists compared with the available organs for transplantation. As a result, there has been an increasing shortage of organs available for transplantation. In the latest report from United Network for Organ Sharing / Organ Procurement and Transplantation Network on May, 2013, currently there are around 96 000 patients in the waiting list for a kidney transplant, a number that has exponentially grown from around 69 000 in the year 2005. However, the total number of kidney transplants since 2005 has remained stable, between 16 000 and 17 000 transplants per year (http://optn.transplant.hrsa.gov/latestdata/rptData.asp).

Transplantation is also a victim of its own success with increasing number of organ failure patients now demanding consideration for receiving a transplant and the demand for organs will increasingly exceed supply. Consideration of marginal donors and usage of organs from deceased brain death or cardio-circulatory death donors are some of the options used to expand the organ pool. Reduction in road traffic accidents and intracranial hemorrhage death rates have limited the availability of the organs from decreased brain death donors. The expansion of transplant programs and the success rate of transplanted organs from brain death and cardio-circulatory death donors very much depend on improvement of current equipment and preservation techniques to overcome the hurdles of "prolonged cold and warm ischemia.

After its initial introduction in 1970s, machine perfusion was very much replaced by the cold static storage system which is a cheaper, simpler and effective alternative.[3] In an attempt to increase the success rate of the renal transplants from cardio-circulatory death donors, to reduce the reperfusion injury and to expand such transplant options, machine perfusion has regained attention in the recent years.[4]

Solutions with different chemical and biologic characteristics have been used for the cold static storage system and the machine perfusion. The Food and Drug Administration workshop in 2011 reviewed the published clinical trials and studies, which were suggesting administration of various drugs/chemicals into the current preservation fluids for improving the cold static storage and machine perfusion systems. They acknowledged that although a few preservatives have demonstrated early improvements in delayed graft function, none have showed an improved long term graft function.[5] We are still lacking an ideal preservation fluid for the cold storage and machine perfusion systems.

Proanthocyanidine are poly-phenol extracts commonly found in vegetables, fruits and flowers with cytomodulating, antioxidant, antibacterial, antiviral, anti-apoptotic, and anti-inflammatory properties.[6] They are reported to have a wide spectrum of pharmacological properties against oxidative stress as well as a strong oxygen free radial scavenging ability.[7-9] They enhance the viability of the normal cells against the environmental damaging factors including the cancer chemotherapeutic chemicals, and drug induced cytotoxicity.[7,10] They exhibit these effects by modulating cell apoptotic, lipoxygenase, cycloxygenase pathways and inducing intracellular and epithelial nitric oxide production.[7,11,12] Grape seed proanthocyanidine extract (GSPE) is derived from grape seed during a complex preservation and pharmaceutical processes. In a few animal studies GSPE has been shown to reduce hepatic and renal ischemia-reperfusion injuries.[8,9,12,13]

Reperfusion injury is a biphasic process which causes cell damage in its ischemia and reperfusion phase. While the tissue damage in the ischemia phase is mainly caused by the energy deprivation and the subsequent disruption of the cellular hemostasis, the reperfusion phase damage (more severe damage) is secondary to the inflammatory reactions involving the oxygen free radicals, endothelial cells as well as the leukocytes.[3] This process is an early inflammatory response which follows the perfusion of warm blood into the previously ischemic and cold organ following transplantation. Reperfusion injury has detrimental effects on the tissue hemostasis of the ischemic organs, and may have a pivotal short and long-term impact on the renal allograft function.[14]

As GSPE seems to antagonize a number of steps in the ischemia-reperfusion process, and due to its anti-inflammatory properties, we hypothesize that GPSE could have a potential protective effect on the transplanted kidney when added to the machine Perfusion Fluid and Cold Static Storage System.

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Re: Hyperglycemia After Kidney Transplantation: Frequency and Risk Factors

Dear Editor,

In the past issue of the *Iranian Journal of Kidney Disease*, Khalili and colleagues have reported the association of hyperglycemia posttransplantation with higher doses of cyclosporine, cytomegalovirus infection, higher serum creatinine levels, and dyslipidemia in 22.5% of the Iranian patients.[1] As expected this association was compatible as of other reports. As mentioned in the limitations of the study, a history of pretransplant diabete