TRANSPLANTATION

HTK solution: should it replace UW solution for kidney preservation?

Histidine-tryptophan-ketoglutarate (HTK) solution is increasingly replacing University of Wisconsin (UW) solution for the preservation of abdominal organ allografts, especially kidneys. However, authors of two studies published recently in the *American Journal of Transplantation* caution that HTK solution might be associated with an increased risk of graft loss in deceased-donor renal transplantation, and urge that further studies of this solution are needed.

Although UW solution has been considered the gold standard solution for the preservation of abdominal organs since 1987, use of HTK solution in the US has nearly doubled since 2004. Perceived advantages of HTK solution include lower cost, decreased risk of hyperkalemia, and reduced viscosity, which results in improved perfusion of the microvasculature. Although single-center and some multicenter studies have found the outcomes of renal allografts preserved with HTK solution to be similar to those of allografts preserved with UW solution, other multicenter studies have found that preservation of organs with HTK solution might be associated with an increased risk of delayed graft function (DGF) and reduced graft survival.

HTK solution was introduced as an alternative to UW preservation solution in the division of transplantation at the University of Nebraska Medical Center in 2003. "Shortly after converting to HTK, we observed an unexpected increase in the rate of pancreatitis and thrombosis in pancreas recipients," says Brian Stevens, lead author of one of the recent papers. When his team analyzed the data, they found that graft loss due to thrombosis was significantly more common in cases where HTK solution had been used for preservation than in cases where UW solution had been used. These findings in pancreas transplantation prompted Stevens *et al.* to review the outcomes of kidney allografts flushed with HTK solution.

In an effort to get their results out to the transplant community as quickly as possible, Stevens *et al.* performed a retrospective analysis of the outcomes of 234 deceased-donor kidneys that had been flushed with HTK or UW solutions and given to adults with a minimum follow-up period of 1 year. Although patient survival, graft survival and graft rejection rates were similar in the two groups after 2 years of follow-up, a significantly increased rate of early graft loss (that is, graft loss occurring during the first 6 months) was observed in the HTK group. Cox proportional hazards analysis determined HTK solution to be the only predictor of early graft loss (hazard ratio 3.24 versus UW solution). The increased risk of early graft loss was largely a result of an increased rate of primary nonfunction in HTK-flushed allografts. Although overall a numerically (but not statistically significantly) lower rate of DGF was observed in HTK-flushed kidneys, in cases where DGF was present, the risk of primary nonfunction was much greater in HTK-flushed kidneys than in kidneys preserved with UW solution. Stevens and colleagues also found that marginal kidneys were more susceptible than high-quality kidneys to delayed graft function with HTK solution.

The study reported by Zoe Stewart and colleagues at the Johns Hopkins University School of Medicine involved analysis of data from the United Network for Organ Sharing (UNOS) of 21,626 patients undergoing kidney transplantation in the US. On multivariate analysis, the risk of graft loss was 20% higher in organs preserved with HTK than in organs preserved with UW solution. No difference in the rate of DGF was seen between groups. Of interest, the risk of graft loss associated with HTK solution was significantly increased in African American recipients, in allografts that survived for at least 1 year, and in patients who received allografts from extended criteria donors.

The need for further study of the effect of HTK solution on graft survival and function in different patient groups is clear. "The impact of HTK should be properly examined, first in large animal transplantation experiments and then with human subjects in an appropriately powered, blinded, multicenter, prospective, randomized trial," says Stevens. "Why such a trial was not completed prior to HTK's approval for use in organ recovery is troubling." Such a trial might actually identify recipient groups for which HTK preservation is ideal, and Stewart *et al.*'s next step will be to investigate why some centers have had favorable experiences with HTK, to identify particular center-specific practice patterns that might improve outcomes with HTK solution.

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Original articles Stevens, R. B. *et al.* Increased primary non-function in transplanted deceased-donor kidneys flushed with histidine-tryptophan-ketoglutarate solution. *Am. J. Transplant.* **9**, 1055–1062 (2009).
Stewart, Z. A. *et al.* Histidine-tryptophan-ketoglutarate (HTK) is associated with reduced graft survival of deceased donor kidney transplants. *Am. J. Transplant.* **9**, 1048–1054 (2009).