Hydroxyethylstarch and renal function in kidney transplant recipients

SIR—Cittanova and colleagues (Dec 14, p 1620)[1] report the effect of hydroxyethylstarch in brain-dead kidney donors on renal function in kidney-transplant recipients. They suggest that hydroxyethylstarch impairs immediate renal function in kidney-transplant patients. Furthermore, they indicate that several other reports support this notion.[2,3] I have some comments.

First, they used Elohes, but do not tell us about its half-life and bioavailability. From other compounds, such as antibiotics, which are excreted by the kidney, we know that the half-life of a substance is important and dosage has to be adjusted according to kidney function.[4] Elohes has a plasma half-life of 24 h and a bioavailability of 6–8 h. Haes-Steril, another hydroxylethylstarch, is characterised by a half-life of 3–4 h and a bioavailability of 3–4 h. The figures for gelatine are 4–6 h and 2 h, respectively. Especially in intensive care, a longer half-life and bioavailability may have a striking effect on organ function, in particular when renal function is already impaired.

Second, for a general statement on the effect of hydroxyethylstarch one should compare results of studies with the same product in similar situations. I seriously doubt that comparing the effect of hydroxyethylstarch in pre-existing glomerular damage to an undamaged kidney in a donor, but not considering half-life and excretion of different compounds with respect to kidney damage is a sound scientific approach. Furthermore, information on the products used in cited work is missing.

Third, there are existing reports on beneficial effects of hydroxylethylstarch in intensive-care patients,[5] a situation in which kidney failure is imminent, and on donor organs, suggesting that the issue is more complex.

Last, several indices are regarded as physiological endpoints for organ donors: systolic blood pressure, central venous pressure, urine output, core temperature, packed cell volume, $Oxygen_2$-saturation, and pH. Have Cittanova and colleagues data for these indices? These workers also indicate a different fluid volume loading in the two groups. Maybe the described effects are caused by the differential fluid loading.

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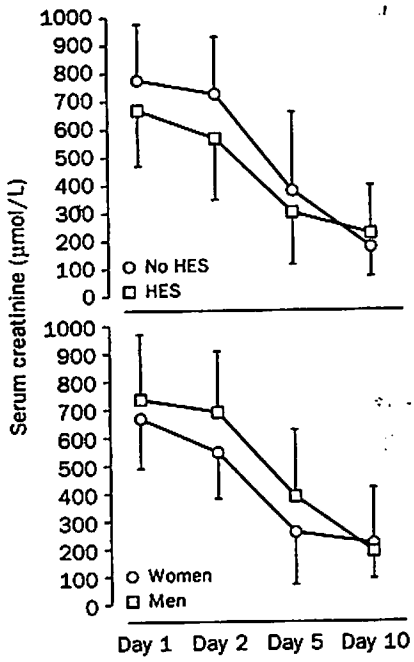
SIR—Cittanova and colleagues' report[1] has led us to review our data in 24 recipients of kidney grafts. We found no difference in the kidney-graft function at 1, 3, and 6 months post-transplantation, irrespective of hydroxyethylstarch use in brain-dead organ donors. The frequency of osmotic nephrotic-like lesions was also similar in those who had received hydroxyethylstarch and those who had not, and had no effect on kidney-graft function at these times after transplantation.[2] By contrast, Cittanova and colleagues recorded, during the first 10 days post-transplantation, reduced kidney-graft function with higher creatininaemia or more requirements for haemodialysis in recipients in the hydroxyethylstarch-gelatin group. In our study, creatininaemia in the first 10 days post-transplantation was lower in the hydroxyethlystarch group. This discrepancy between the two studies could be caused by the sex-ratio in Cittanova's hydroxyethylstarch-gelatin group which had more men than women. We therefore examined the sex ratio in our recipients, and there were 12 men and 12 women. Creatininaemia in the men was higher than in the women in the first 10 days post-transplantation and was equal thereafter (figure).



Creatininaemia in renal-graft recipients in first 10 days post-transplantation
Upper: hydroxyethylstarch (HES) compared with no HES (ANOVA test) for repeated measures, not significant.
Lower: men compared with women (ANOVA not significant).

Thus, the differences between the two studies could be attributable to the sex-ratio of the groups of recipients. In the longterm, would the evolution of creatininaemia be similar in men and women, as Legendre and colleagues' results have suggested[3]?

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Authors' reply

SIR—Elohes has a low molecular weight (220 000), with a molar substitution ratio of 0·62. Since it is a polydispersified solution, its induced-blood-volume expansion is related to the medium half-life. Iguchi et al[1] studied the increase in plasma volume after a 500 mL infusion of Elohes. 24 h later, a 240 mL plasma volume expansion was still observed. This rather long half-life may be of concern with respect to renal toxicity. We are fully in agreement with Holzheimer that the effect of hydroxyethylstarch should be evaluated in similar situations. This is exactly what we did. Only in our discussion did we allude to the study of Waldhausen et al.[2] In our first report,[3] as well as in those of Hannemann[4] and Coronel and their colleagues,[5] the methods used were inappropriate to assess precisely whether hydroexyethylstarch was nephrotoxic; this is why we initiated a correctly designed, randomised trial, to provide strong data to resolve this important issue. All relevant indices, apart from central venous pressure, were compared in the groups, and no significant difference was noted. With respect to fluid loading, the difference in the two groups was not statistically significant and was therefore unlikely to account for the difference in renal function.

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