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In lab studies, hydroxyethyl starch has direct harmful effects on kidney cells

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The increased risk of kidney injury related to the use of hydroxyethyl starch (HES) in resuscitation fluids reflects the mass of HES molecules, according to a report in *Anesthesia & Analgesia*, official journal of the International Anesthesia Research Society (IARS).

The "total mass of HES molecules" explains the harmful effect of HES on cultured human renal proximal tubule cells (PTCs), concludes the laboratory study by Dr Christian Wunder and colleagues of University Hospital Würzburg, Austria. Other factors—such as differences in the origin or molecular weight of HES solutions—appear to play little or no role in cellular-level toxicity of HES.

What Factors Affect Toxic Effects of HES on Kidney Cells?

Hydroxyethyl starch is a starch derivative that has been widely used for fluid resuscitation with volume expansion for critically ill or injured patients in shock. A growing body of evidence suggests that HES solutions may have harmful effects, including an increased risk of kidney injury and death.

In previous studies, Dr Wunder and colleagues found that HES caused impaired kidney function in animals with sepsis (severe infection). Those studies showed that HES was localized mainly in the kidney PTCs. The researchers performed a series of in-depth follow-up

experiments to look at factors influencing the toxic effects of HES on cultured human PTCs.

Most of the factors assessed had no major influence on reductions in cell viability caused by HES. Cellular toxicity was unrelated to the type of "carrier" solution used in the cell cultures, the use of HES made from different origins (potato versus corn starch), or the time cells spent in culture with HES.

The toxic effects were also similar for HES solutions of different molecular weights. That's an important finding, as newer low-molecular weight HES solutions were thought to be safer than previous products. There was also no evidence that the toxic effects of HES were related to the presence of inflammation.

Instead, the only significant factor was the total mass of HES molecules. The effect was dose-dependent: the greater the molecular mass, the greater the evidence of cell toxicity. The toxic effects started very soon after PTCs were exposed to HEC, and further increased at higher doses.

There is a long history of debate and confusion over potential harmful effects of HES solutions used for resuscitation. Recent studies have linked HES to reduced kidney function in patients with sepsis. Last year, both the US Food and Drug Administration and the European Medicines Agency issued statements that HES solutions should not be used in critically ill patients.

The new study suggests that the molecular mass of HES is the major factor responsible for damage to kidney cells. Other factors have no significant influence—even with new low-molecular weight HES solutions, cellular-level toxic effects appear just as likely, once the total mass of HES molecules is taken into account.

Although the study was performed in the laboratory on cultured kidney cells, the PTC toxicity caused by HES appears consistent with the risks of kidney damage and death observed in critically ill patients. Dr Wunder and coauthors conclude, "Our data show that HES itself has a negative impact on renal PTC, which should be considered when used clinically."

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