Hydroxyethyl starch

Hydroxyethyl starch (HES/HAES) is a nonionic starch derivative. It is one of the most frequently used volume expanders under the trade names Hespan by B. Braun Medical Inc. Voluven or Volulyte by Fresenius Kabi and Tetrahes or Hestar by Claris Lifesciences Ltd. HES is a general term and can be sub-classified according to average molecular weight, molar substitution, concentration, C2/C6 ratio and Maximum Daily Dose.

Its use in those who are very ill is associated with an increased risk of death and kidney problems.

Infusion of the colloid hydroxyethylstarch has been used for volume substitution to maintain hemodynamics and microcirculation after e.g., severe blood loss. In the last decade it was revealed that hydroxyethylstarch can aggravate acute kidney injury, especially in septic patients. Because of the serious risk for critically ill patients, the administration of hydroxyethylstarch was restricted for clinical use.

The European Medicines Agency commenced in June 2013 the process of agreeing reduced indications which was completed in October 2013.

Animal studies and recently published in vitro experiments showed that hydroxyethylstarch might exert protective effects on the blood-brain barrier. Since the prevention of blood-brain barrier disruption was shown to go along with the reduction of brain damage after several kinds of insults, Schick et al. revisited the topic hydroxyethylstarch and discuss a possible niche for the application of hydroxyethylstarch in acute brain injury treatment [1)].

In order to prevent cerebral vasospasm after a subarachnoid hemorrhage (SAH), the so-called triple H therapy (hypertension, hypervolemia, hemodilution) could be applied. In these cases, colloidal solutions containing Hydroxyethylstarch (HES) are used to induce hypervolemia. The administration of HES is very much under debate for the mentioned use because in general the application of HES for the treatment of critically ill patients has been reduced tremendously in the last years due to its nephrotoxic effects. In this context, there are limited data investigating the influence of HES on the blood-brain barrier. These data might help to assess if a transient administration of HES is possibly justifiable to prevent cerebral ischemia during vasospasm despite the risk of an acute kidney injury. To address this question, a mouse blood-brain barrier in vitro model based on cell line cerebEND was exposed to different HES concentrations and compared to NaCl-containing control solutions. In order to assess the effects of HES on blood-brain barrier properties, cell viability, transendothelial electrical resistance, permeability of carboxyfluorecein, mRNA and protein expression and localization of tight junction proteins were determined. In summary, 1.5-4% HES attenuated cell viability in a mild, concentration dependent manner compared to the NaCl control solution (0% HES). At the mRNA level 1% and 4% HES significantly increased the expression of tight junction associated proteins (ZO-1 and occludin) and the glucose transporter Glut-1 (Slc2a1). In correspondence to this, 4% HES inhibited breakdown of the paracellular barrier in comparison to the control NaCl group (0% HES) shown by transendothelial electrical resistance values and the permeability of the paracellular marker carboxyfluorescein. These effects at the functional level were confirmed by immunofluorescence microscopic images of junctional proteins. The obtained in vitro data showed a potential for HES to counteract blood-brain barrier damage. Future studies are needed to reveal the applicability of HES as a blood-brain barrier stabilizing agent [2)].

A retrospective study compared SAH patients who received HES with those who received crystalloids and found no significant difference in RRT [3].

Another retrospective study showed no positive correlation between the cumulative doses of HES and serum creatinine in SAH patients who had a normal renal function and concluded that the administration of HES 6% 130/0.4 is safe in SAH patients without pre-existing renal insufficiency. However, caution is warranted in the period of repetitive administration of contrast media [4]

HES has been sometimes used to maintain an optimal volume status to prevent delayed cerebral ischemia (DCI) due to cerebral vasospasm following a subarachnoid hemorrhage (SAH) as a component of the triple H-therapy. Compared to the standard therapy group, the goal-directed fluid therapy (GDFT) with a HES bolus group showed reduced frequencies of vasospasm and cardiopulmonary complications [5].

1)
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5)
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