Hydroxyethyl starch (HES/HAES),

sold under the brand name Voluven among others, is a nonionic starch derivative, used as a volume expander in intravenous therapy. The use of HES on critically ill patients is associated with an increased risk of death and kidney problems.[1]

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.[2] The European Medicines Agency commenced in June 2013 the process of agreeing to reduced indications which was completed in October 2013.[3] The process of full withdrawal in the EU was expected to complete in 2018.

An intravenous solution of hydroxyethyl starch is used to prevent shock following severe blood loss caused by trauma, surgery, or other problem. It however appears to have greater risk of a poor outcome compared to other intravenous solutions[1] and may increase the risk of death.[4]

Adverse effects

HES can cause anaphylactoid reactions: hypersensitivity, mild influenza-like symptoms, slow heart rate, fast heart rate, spasms of the airways, and non-cardiogenic pulmonary edema. It is also linked to a decrease in hematocrit and disturbances in blood clotting. One liter of 6% solution (Hespan) reduces factor VIII level by 50% and will prolong the aPTT and will also decrease vWF.[5] A coagulation effect of hetastarch administration is direct movement into fibrin clots and a dilutional effect on serum. Hetastarch may lead to platelet dysfunction by causing a reduction in the availability of glycoprotein IIb-IIIa on platelets.

HES derivatives have been demonstrated to have increased rates of acute kidney failure and need for renal replacement therapy and to decrease long-term survival when used alone in cases of severe sepsis compared with Ringer lactate solution.[6] The effects were tested on HES 130kDa/0.42 in people with severe sepsis; analysis showed increased rates of kidney failure and increased mortality when compared to LR.[7] It has been recommended that, since medium-MW HES solutions may be associated with harm, these solutions should not be used routinely for patients with septic shock.[8]

During 2010/11 a large number of research papers associated with a single author were retracted for ethical reasons, and this may affect clinical guidelines referring to HES preparations prepared before this date.[9]

Contraindications

Prescribing information contains the following contraindications:

This product should not be used in people who are hypersensitive or allergic to hydroxyethyl starch.

Patients with kidney failure not related to low blood volume and patients on dialysis should avoid this product in high doses which are used for volume expansion.

Use of hydroxyethyl starch with normal saline in its preparation is contraindicated in people with severe increases in blood levels of sodium or chloride.

Patients with intracranial bleeds should not use this product.

On November 25, 2013, following a public workshop to discuss new information on the risks and benefits of HES solution,[10] the USFDA announced the addition of a black box warning to the prescribing information which includes the following recommendations to health professionals:[11]

Do not use HES solutions in critically ill adult patients, including those with sepsis.

Avoid use in patients with pre-existing renal dysfunction.

Discontinue use of HES at the first sign of renal injury.

Need for renal replacement therapy has been reported up to 90 days after HES administration. Continue to monitor renal function for at least 90 days in all patients.

Avoid use in patients undergoing open heart surgery in association with cardiopulmonary bypass due to excess bleeding.

Discontinue use of HES at the first sign of coagulopathy.

Do not use HES products in patients with severe liver disease

Monitor liver function in patients receiving HES products.