The Cryopreservation of Red Blood Cells Using Hydroxyethyl Starch
A Cryogenic Technique to Increase the Safety and Sustainability of Blood Supply

The deep-freezing of red blood cells (RBC) is appropriate in cases of rare blood groups, problems due to multiple antibodies and possibly as an interim aid during temporary shortage, especially in cases of civil or military disasters. Additionally, RBC deep-freezing is useful to increase viral safety by quarantine and eliminates the growth of microorganisms during storage. For routine clinical practice, cryopreservation might help to overcome the outdating of autologous blood deposits for elective surgery, which is a problem if only liquid storage is applied.

In contrast to the established cryoprotectant glycerol, the colloid hydroxyethyl starch (HES) does not need to be removed after thawing (Knorpp et al., Science 157, 1312, 1967). Moreover, in the case of hypovolemia, it serves as a plasma substitute. After numerous in vitro (Cryobiology 27, 667, 1990) and animal experiments (Cryobiology 28, 546, 1991), autologous studies were carried out on 7 healthy volunteers (Cryobiology 30, 657, 1993; CryoLetters 16, 283-288, 1995).

The first clinical application was the case of a 16 year old female who was considered to be unable to donate sufficient blood within the limited liquid storage period for a completely autologous hemotherapy (Cryobiology 31, 584, 1994). The RBC from 3 donations were frozen according to the HES procedure. When the hemoglobin concentration dropped to 7.6 g/dl intraoperatively, 3 units of RBC were administered without post-thaw washing. No unfavorable effects or hemoglobinuria were observed. The patient was discharged after a normal postoperative period without complications.

A clinical study to determine the safety and tolerance of red blood cells cryopreserved with the HES procedure in accordance with the ethical standards of the Committee on Human Experimentation of the Medical Society of Hamburg has been performed. In this study the first RBC concentrate obtained from 36 patients undergoing preoperative autologous blood donation was randomly assigned to the conventional storage method (4°C, PAGGS-mannitol = group 1) or to cryopreservation with HES (MW = 200,000, MS = 0.5) at a final concentration of 11.5% (w/w) using liquid nitrogen (= groups 2,3). Prior to surgery, an additional 900 ml of blood were drawn and compensated by isovolemic hemodilution. Patients belonging to group 1 received the conventionally stored RBC, those in group 2 a cryopreserved and washed RBC. In group 3, however, no washing step prior to transfusion was performed. To balance the amount of HES administered, patients in groups 1 and 2 received an additional 500 ml HES (10%). Data were assessed after induction of anesthesia, hemodilution, transfusion of the RBC and at regular intervals intra- and postoperatively. No significant differences between the 3 groups could be detected regarding hemodynamic or blood gas parameters and tissue oxygenation. No adverse reactions after transfusion of washed and unwashed cryopreserved RBC were observed. Plasma hemoglobin levels increased 3-fold in group 3 after transfusion, compared to group 1 but always decreased to baseline levels within 24 hours. The data suggest that the transfusion of one unit of RBC after cryopreservation with HES is safe and well tolerated (Anaesthesia & Analgesia 85, 739-745, 1997).

Further investigations are deemed necessary to evaluate the effects of larger volumes of homologous HES cryopreserved RBC. Sponsors are needed.