Blood substitutes

Donat R Spahn

Address: Institut für Anästhesiologie, UniversitätsSpital, Zürich, Switzerland

Correspondence: Donat R Spahn, Professor of Anesthesiology, Institut für Anästhesiologie, UniversitätsSpital, Rämistrasse 100, CH-8091 Zürich, Switzerland. Tel: (41) 1 255 26 96; fax: (41) 1 255 44 09; e-mail: donat.spahn@ifa.usz.ch

Received: 16 August 1999
Accepted: 6 September 1999
Published: 24 September 1999

Crit Care 1999, **3**:R91–R92

The original version of this paper is the electronic version which can be seen on the Internet (http://ccforum.com). The electronic version may contain additional information to that appearing in the paper version.

Print ISSN 1364-8535 Online ISSN 1466-609X

Blood substitutes have long been sought after, and artificial oxygen carriers may soon become a reality. Despite increased safety of allogeneic blood in terms of transmission of infectious diseases [1], avoiding allogeneic blood transfusions remains an important goal in perioperative and intensive care medicine. This is because allogeneic blood transfusions may cause immunosuppression with an increased incidence of postoperative infections [2,3] and may adversely affect outcome in intensive care [4], and thus they remain a public concern [5].

Artificial oxygen carriers are promising substances to avoid allogeneic blood transfusions and related side effects. In addition, artificial oxygen carriers may be effective antiischaemic agents in a variety of diseases and conditions that are characterized by compromised tissue oxygenation. Artificial oxygen carriers may be grouped into haemoglobin-based oxygen carriers (HBOCs) and perfluorocarbon emulsions. The biological efficacy of both groups has been documented in a variety of animal experiments [6,7], and phase III trials are ongoing at present to prove their clinical efficacy.

In HBOCs (see article by Baron J-F, this issue of *Critical Care*), the haemoglobin is either human (outdated human blood), bovine or from a genetically engineered source [7]. All haemoglobin solutions tested contain modified haemoglobin to improve oxygen off-loading, by decreasing oxygen affinity, and to reduce side effects. At present, haemoglobin solutions in clinical trials are aqueous solutions, but the production of micro-encapsulated haemoglobin particles (neo red cells) might be a future option [8,9]. Comparison between HBOCs is difficult because there are very few studies that directly compare different products. It appears though that larger haemoglobin molecules, in particular haemoglobin polymers with a small residual haemoglobin monomer fraction, are better tolerated; this is probably due to a reduced penetration of these relatively large molecules into the vessel wall [10].

In the group of perfluorocarbon emulsions, only perflubron emulsion is in phase III testing. It has been shown recently that treatment with perflubron emulsion in conjunction with pure oxygen ventilation was more effective than retransfusion of autologous blood in reversing physiologic transfusion triggers [11]. With perflubron emulsion patients thus may tolerate lower haemoglobin levels, and perflubron emulsion may be used to modify the acute normovolemic haemodilution (ANH) into 'augmented ANH' (see article by Spahn DR, this issue of *Critical Care*). In this way, the added oxygen unloading capacity of the perflubron emulsion is utilized to compensate very low intraoperative haemoglobin values. Because of retransfusion of the ANH blood at the end of the procedure, the patient's are supported by their own blood in the postoperative period.

Comparing HBOCs and perfluorocarbon emulsions is difficult. First, there are no studies that directly compare the two groups of artificial oxygen carriers. Second, the practical use of these substances will be relatively different once they are on the market. Haemoglobin solutions might be used relatively similar to a conventional blood transfusion and haemoglobin measurement may still be used to assess the oxygen transport capacity. When used to avoid allogeneic blood transfusions, perfluorocarbon emulsions will be used preferentially in the concept of 'augmented ANH', and physiologic transfusion triggers [12] will be used primarily to assess the adequacy of oxygen delivery.

Despite a longer than expected final development phase, HBOCs as well as perfluorocarbon emulsions will eventually be released for general clinical use and will substantially alter standard clinical practice.

References

1. Goodnough LT, Brecher ME, Kanter MH, AuBuchon JP: **Transfusion medicine. First of two parts – blood transfusion.** *N Engl J Med* 1999, **340**:438–447.
2. Spahn DR, Leone BJ, Reves JG, Pasch T: **Cardiovascular and coronary physiology of acute isovolemic hemodilution: a review of nonoxygen-carrying and oxygen-carrying solutions.** *Anesth Analg* 1994; **78**:1000–1021.
3. Spahn DR, Schmid ER: **Haemodilution in cardiac and vascular surgery.** *Curr Opin Anaesthesiol* 1996; **9**:54–61.

HBOC = haemoglobin-based oxygen carrier; ANH = acute normovolemic haemodilution.

4. Hebert PC, Wells G, Blajchman MA, *et al*, and the Transfusion Requirements in Critical Care Investigators for the Canadien Critical Care Trials Group: **A multicenter, randomized, controlled clinical trial of transfusion requirements in critical care.** *N Engl J Med* 1999; **340**:409–417.
5. Goodnough LT, Brecher ME, Kanter MH, AuBuchon JP: **Transfusion medicine. Second of two parts – blood conservation.** *N Engl J Med* 1999; **340**:525–533.
6. Keipert PE: **Perfluorochemical emulsions: future alternatives to transfusion.** *Blood Subst Princ Meth Prod Clin Trials* 1998; **2**: 127–156.
7. Frietsch T, Lenz C, Waschke KF: **Artificial oxygen carriers.** *Eur J Anaesth* 1998; **15**:571–584.
8. Chang TM: **Artificial cells with emphasis on cell encapsulation of genetically engineered cells.** *Artif Organs* 1998; **22**:958–965.
9. Chang TM: **Modified hemoglobin-based blood substitutes: crosslinked, recombinant and encapsulated hemoglobin.** Vox Sang 1998; **74 (suppl 2)**:233–241.
10. Gould SA, Moss GS: **Clinical development of human polymerized hemoglobin as a blood substitute.** *World J Surg* 1996; **20**: 1200–1207.
11. Spahn DR, van Bremt R, Theilmeier G, *et al*, Perflubron Emulsion Study Group: **Perflubron emulsion delays blood transfusion in orthopedic surgery.** *Anesthesiology* 1999, in press.
12. A Report by the American Society of Anesthesiologists Task Force on Blood Component Therapy: **Practice guidelines for blood component therapy.** *Anesthesiology* 1996; **84**:732–747.