The Effect of Fluosol-DA® on the Reticuloendothelial System in Surgical Patients

Chu Suzuki

The effect of Fluosol-DA® (Perfluorochemicals), an oxygen carrying blood substitute, on the function of the reticuloendothelial system (RES) was investigated by means of Ferrichondroitin sulfate in a series of patients undergoing gastrectomy for cancer of the stomach. In 20 patients, 500 ml of blood were replaced with the same amount of either Fluosol-DA® or hydroxyethylstarch (HES) prior to surgery. Changes of perioperative cellular immunity were studied by PHA-stimulated T-lymphocyte transformation. It was found that the RES functions were significantly depressed postoperatively and fairly recovered by the sixth postoperative day in the Fluosol-DA® group. A prolongation of the suppression of cellular immunity with sustained fever was noted in this gastrectomized series. In analyzing the decay of infused Perfluorochemicals in blood, the half life of Fluorodecalin (FDC) was 4.9±0.1 hr, for Perfluorotripropylamine (FTPA) it was 5.1±0.1 hr. The prolonged depression of the RES function might be caused by saturation of RES with particles of Perfluorochemicals. (Key words: ferrichondroitin sulfate, colloidal carbon, perfluorochemicals, PHA-P, phagocytic index)


The research for a blood substitute that would be capable to carry and deliver oxygen and to remove carbon dioxide in an emergency has been going on for many years. The clinical applicability of Fluosol-DA®, a mixture of Perfluorochemicals (PFCs), has been investigated in Japan by Mitsuno et al.1 as an oxygen transporting blood substitute.

Infused Fluosol-DA® is supposed to be expired into alveolar air. In vitro, the mean particular size of Fluosol-DA® is 0.1 micron and no particles are larger than 0.6 micron. As particles larger than 0.4 micron would cause microemboli and would be captured by monocytes, no Fluosol-DA® particles should be captured by them. However, this has not been confirmed in vivo clinical cases, as the effect of surfactants, pluronic F-69 and yolk phospholipid which are used to keep the particles in emulsion, may be altered in the blood stream resulting in larger particles by coadhesion. The possibility of depression of the reticuloendothelial system (RES) function remains if agglomerated particles of infused Fluosol-DA® are captured by the RES, resulting in RES saturation.

The RES plays important roles in phagocytosis, opsonification and antibody production. RES suppression due to shock or trauma is known to negatively affects survival rates. To ascertain the safety of Fluosol-DA® infusion in patients in hemorrhagic shock, its effect on the RES function must be studied. In the present study, the effect of Fluosol-DA® in surgical patients

Department of Anesthesiology, Gunma University School of Medicine, Maebashi, Japan
Address reprint requests to Dr. Suzuki: Department of Anesthesiology, Gunma University School of Medicine, 3-39-22 Showa-Machi, Maebashi, 371 Japan

J Anesth 1:8-14, 1987
who received Fluosol-DA® as a blood substitute to induce a mild autohemodilution was assessed.

**Methods**

(1) Experimental protocol

Twenty patients undergoing gastrectomy for cancer of the stomach were subjected to this study. Written, informed consent was obtained from all participants according to the Ethical Committee. All were younger than 60 years, their expected blood loss was less than 1,000 ml, their Hb values were over 11.5 g/dl and their ASA physical status was 1 or 2.

The patients were anesthetized with 2.5% thiopental and their trachea were intubated with succinyldicholine chloride. General anesthesia was maintained with 66% N₂O and 33% oxygen supplemented with 0.5-1% halothane. Optimum doses of pancuronium were used as muscle relaxant during surgery. Intraoperatively, normocapnic ventilation was maintained.

Before surgery, the 20 patients were randomly divided into two equal groups. In 10 patients, 500 ml of blood were replaced with the same amount of either 20% Fluosol-DA® or 6% HES (hydroxyethyl starch which degree of saturation by hydroxyethyl on starch, DS 0.55. Actually 3% HES with DS 0.65 has been used as the solvent for 20% Fluosol-DA®, however, 6% HES with DS 0.55 in clinical use has the same colloidal osmolarity). The drawn blood was kept at room temperature in Red Cross blood bank reservoir bags containing ACD-A anticoagulant and re-transfused either when intraoperative blood loss reached 500 ml or at the end of surgery.

Re-transfusion was performed within 3 hours of blood removal. None of the patients required supplemental intraoperative blood transfusions, however, there were 3 patients who received transfusion in 48 hours postoperatively.

The vital signs (BP and HR), Hb and Hct values were examined and blood gas analysis on hemodilution was carried out. Changes in serum transaminase, GOT and GPT levels (Karmen IU/1) were followed by UV method³ for two weeks postoperatively. The body temperature was recorded at six o'clock in the morning for two weeks postoperatively. The concentration of MFCs in blood and urine was determined by gas-chromatography⁴ for one week postoperatively.

The RES functions were assessed by phagocytic indices on iron⁵,⁶. Colloidal ferrichondroitin sulfate (Blutal®, Dainihon Pharmaceuticals Co.) 0.8 mg/kg was administered intravenously as an indicator, and 2 ml of plasma were obtained 10, 20 and 30 min thereafter. Deferrization of indicator in plasma was performed by adding 2 ml of 0.8 N HCl. Subsequently, the samples were deproteinized for 2 min in a water bath (80-95°C) and centrifuged with 2 ml of 16% TCA. To the resulting 3 ml of supernatant was added 1 ml of sodium bathophenanthroline sulfonate (40 ml/dl) for colorization.

The phagocytic index (K-value) was obtained spectrophotometrically at 535 nm according to the formula:

\[ K = \frac{\log C_1 - \log C_2}{t_2 - t_1} \]

values were determined before, and 1 hr, 2 and 5 days after surgery.

In two patients of each group, the cellular immunocapability was investigated by evaluating the rate of transformation of patient T-lymphocytes stimulated by purified phyto-hemagglutinin (PHA-P) in micromethod⁷. Peripheral venous blood (1 ml) was mixed with 10 unit of heparin, 0.1 ml of this mixture was suspended in 0.9 ml TC-medium 199 and incubated for 24 hr at 37°C in humidified air with 5% CO₂. After adding 1 μCi of ³H-thymidine, incubation was continued for an additional 24 hr. Cells were harvested, washed with RLB (red cell lysis buffer) solution to induce rapid lysis of the erythrocytes and 10 ml of 5% TCA was added. This was followed by filtration through a millipore filter (pore size 1.2 micron) and the radio-activity remaining in the filter was measured in a liquid scintillation counter (scintisol AL-I®; Wako).

(2) Reproducibility of the phagocytic index

The reproducibility of the technic applied in the present study regarding the RES function was confirmed using three healthy male volunteers. Four consecutive tests were run on each volunteer, employing the same experimental time schedule as in the clinical series.

(3) Accuracy of the colloidal ferrichondroi-