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F—I—4 Hemorrhagic Shock in Air Breathing Pigs Treated with Bubble-Forming Intravenous Dodecafluoropentane Emulsion.

C. E. G. Lundgren, G. W. Bergoe and I. M. Tyssebotn

Center for Research and Education in Special Environments and Department of Physiology and Biophysics, School of Medicine and Biomedical Sciences, University at Buffalo (SUNY), Buffalo, NY

In pigs, artificially ventilated with oxygen enriched (up to 26% O_2) air, potentially lethal hemorrhagic shock can be successfully treated by intravenous infusion of 0.3 ml/kg of a 2% dodecafluoropentane (DDFP) emulsion (DDFPe) forming oxygen transporting intravascular microbubbles (1). However in order to simulate a more field-realistic trauma situation the present study was undertaken on spontaneously air breathing pigs.

Pentobarbital anesthetized pigs were bled 36 ± 1 (SE) ml/kg (about 50% of the blood volume) over a 60 min period. The post-hemorrhage systolic blood pressure was 76 ± 2 mm Hg. In the course of 30 min, the control animals (Cs) (n = 6) then received preparation blank at 0.3 ml/kg i.v. Treatment animals (Ts) (n = 5) received 0.3 - 0.5 ml DDFPe/kg i.v. of a 2% DDFPe (i.e. 0.006 - 0.01 ml DDFP/kg). After the sham treatment, blood pressure and muscle Po_2 levels decreased in Cs and they died in 61 ± 8 min. Following DDFPe treatment, the muscle Po_2 in Ts stabilized at pre-hemorrhage levels, urine production continued and they retained systolic blood pressures above 100 mm Hg until euthanasia 5.5 hrs post hemorrhage.

Arterial blood DDFP concentrations of 0.45 - 1.0 μg/ml declined to trace amounts in about 1.5 hrs. The short lasting presence of DDFP suggests a corresponding bubble life span. This poses an interesting aspect on the pathophysiology in this shock model namely, while the direct effect on vital oxygen supply was relatively short, the treatment gave the organism time to activate effective innate defense mechanisms. Alternatively, the bubbles may have become volume stabilized by shells of organic blood-derived molecules.

It is noteworthy that this therapeutic effect was achieved with extremely small doses of DDFPe in combination with air breathing thus contrasting with the obligatory oxygen breathing when erythrocyte substitutes based on liquid fluorocarbons are used. Moreover, part of the beneficial effect of the DDFP emulsion can probably be ascribed to the volume replacement effect achieved when, at body temperature, the liquid DDFP (boiling point 29°C) undergoes phase transition and expands.

We conclude that the treatment modality described above holds considerable promise as a first line intervention in hemorrhagic shock.

1. Tyssebotn, I.M., Bergoe, G.W., Lundgren, C.E.G., Abstract, p. 41, Syllabus of Fourth International Symposium on Current Issues in Blood Substitute Research, June 5-8, 2002, Stockholm, Sweden.

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