LATE ABSTRACTS

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Extravascular lung water and lung aeration after oleic acid in sheep

Kurkov V, Kirov M, Waerhaug K, Mortensen R, Kuklin V, Johnsen S, Nordhus K, Bjørnaes L

Medical Faculty, University of Tromsø, Tromsø, Norway

Aims: We compared extravascular lung water (EVLW) content, determined by transpulmonary single thermodilution (EVLWThr) and thermal-dye dilution (EVLWTrd) techniques, with lung aeration, as assessed by lung computed tomography (CT), before and after oleic acid (OA) induced acute lung injury (ALI) in sheep.

Methods: Nine yearling sheep were enrolled in a prospective study. Animals served as their own controls, and underwent CT before and after OA-induced ALI. OA was infused intravenously over 30 min (0.08 ml/kg). The overall duration of the study was 2 hrs. EVLWThr and EVLWTrd were determined by PICCO plus and COLD-2021, respectively (Pulsion Medical Systems, Germany). We used linear regression analysis to evaluate the relationships between EVLWThr and EVLWTrd and volumes of well, poorly and non-aerated lung tissue, respectively, as determined by Pulmo CT program (Siemens, Germany). P < 0.05 was regarded statistically significant.

Results: EVLWThr and EVLWTrd demonstrated a close agreement (r = 0.93, P < 0.05). After OA these variables increased by 85% and 155%, respectively (P < 0.05). In parallel, well-aerated lung volume declined by 48% whereas poorly-aerated and non-aerated volumes increased 3- and 5-fold, respectively (P < 0.05). Both EVLWThr and EVLWTrd correlated significantly with absolute volumes of well (r = -0.64 and r = -0.60), poorly (r = 0.54 and r = 0.58), and non-aerated (r = 0.56 and r = 0.62) lung volumes.

Conclusions: In OA-induced ALI, the rise in EVLW is associated with reduced well-aerated and increased poorly- and non-aerated lung volumes. Thus, during ALI, accumulation of EVLW might contribute to lung congestion and atelectasis.

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Artificial Blood, Current Perspectives

Drozin D, MD PhD

Department of Anesthesiology, Karolinska Institute at Soder Hospital, Stockholm, Sweden

To begin with, the terms "artificial blood" and "blood substitute" are both misnomers because current products intend to enhance the oxygen carrying capacity of blood or the platelets. This presentation will deal with products that increase the oxygen carrying capacity, because they offer a potentially greater market situation. An alternative term for these materials is oxygen therapeutics.

The desired properties of oxygen therapeutics are: oxygen carrying capacity, sufficient plasma retention time, uniform donor type, no vasoconstriction, no renal toxicity, no immunomodulation, and long shelf time. Moreover, it is important that the ingredients are rich in supply, and that the production cost is competitive.

Two main driving forces have led to the initiation of blood substitute programs: the military, which requires large volumes of blood at the site of casualties, and the medical community, which need products that are free for infectious agents. The public perception of the need for viral free materials escalated in 1982 with the first report of AIDS. However, the risk of an infection from blood transfusion is currently very low. The risk of transfusion-transmitted infection have been estimated to: for human Immune-deficiency virus, 1 in 493,000; for human T-cell lymphotropic virus, 1 in 641,000; for hepatitis C virus, 1 in 103,000; for hepatitis B virus 1 in 63,000 (1). One sterility check showed bacterial contamination in 0.6% of the packed red blood cell units (2). The risk of transferring miscellaneous infectious agents is very low, but the consequences are difficult to evaluate. A potential risk of transfused blood is blood type incompatibility, as a result of clerical error. Another major concern is the impending shortage of bank-blood. In the USA the number of transferred units increases at a rate far greater than donor collection.

There are two major classes of oxygen therapeutics, the hemoglobin based products and the perfluorocarbon emulsions. Perfluorocarbons are synthetic halogenated hydrocarbons originally designed to handle reactive uranium compounds. Perfluorocarbons have a limited oxygen carrying capacity because the need of a detergent markedly reduces their efficiency. Side effects include: hepatosplenomegaly, flue like symptoms, and a slight thrombocytopenia. Because of unfavorable outcome, no perfluorocarbon is currently in clinical trials.

Many of the candidate solutions have been based on hemoglobin. Hemoglobin has increased potential to load and unload significant amounts of oxygen within a small range of oxygen partial pressure due to the sigmoidal oxygen binding curve. However, several hemoglobin-based programs have been suspended because of adverse events in the treatment groups. The first large failure appeared in 1999, when an internal crosslinked ox-Hb showed increased mortality rates in a clinical trial on trauma victims. The protocol of this study has been criticized because the outcome could have been predicted by the pre clinical studies. These showed a marked vasoconstriction and by that, a reduced oxygen delivery (3).

The first testing of a crude hemoglobin solution to treat anemia was reported in 1916 (4), and in 1949 a desperate attempt to treat a severe post partum hemorrhage with cell a free hemoglobin solution was undertaken (5). The blood pressure returned promptly, but the patient died a few days later of renal failure. Cell free hemoglobin exerts a toxic effect when it is infused in the plasma. Side effects include systemic and pulmonary hypertension (due to vasoconstriction), bradycardia, renal failure, pancreatitis, abdominal pain, gastrointestinal dysfunction and jaundice. Residual red cell stroma contributes significantly to the side effects.

However, new purification methods are capable of eliminating cellular debris, which alleviates many of the toxic side effects. Molecular modification is still needed to prevent hemoglobin from degradation. Vasoconstriction remains as a hallmark pattern of the hemoglobin solutions. Therefore, the modifications are specifically designed in attempt to avoid vasoconstriction. However, the results vary and with few exceptions, mild to moderate vasoconstriction remains. The problem with vasoconstriction is that although the oxygen carrying capacity is increased with the hemoglobin content, the drop in cardiac output causes a reduction in oxygen delivery.