Type of fluid loading in septic and nonseptic patients does not affect pulmonary oedema

On theoretical grounds crystalloids result in more pulmonary oedema formation than colloids. The difference between crystalloids and colloids could decrease at high permeability.

Van der Heyden et al. studied 24 septic and 24 nonseptic mechanically-ventilated patients with clinically diagnosed hypovolaemia. Patients were assigned to NaCl 0.9%, gelatin 4%, hydroxyethyl starch 6% or albumin 5%. Cardiac output, intrathoracic blood volume and extravascular lung water (EVLW) were measured by transpulmonary thermal-dye dilution. Pulmonary vascular permeability was measured by the validated pulmonary leak index (PLI) for $^{67}$Ga-labelled transferrin.

Colloid fluid loading resulted in 13% and crystalloid fluid loading in 5% plasma volume expansion resulting in a greater increase in cardiac output with colloids. The PLI increased by 5% (median) during fluid loading independent of fluid type or underlying disease. EVLW did not change during fluid loading independent of fluid type or underlying disease. There was a positive correlation between CVP and EVLW for both crystalloids and colloids and a negative correlation between EVLW and Colloid Osmotic Pressure minus CVP. Changes in EVLW were not correlated with changes in PLI.

This study shows that provided fluid loading takes place on the steep part of the cardiac function curve, the type of fluid does not effect pulmonary oedema formation in hypovolaemic patients, even if complicated by increased pulmonary permeability. Several other groups also showed that fluid loading does not increase EVLW as long as cardiac output increases but this is the first time that different fluid regimens have been studied. The power of the study was insufficient to detect differences between colloids. This study may help the clinician in guiding fluid therapy in the face of increased vascular permeability.


Endotoxin tolerance in humans in-vivo

Animals pretreated with a low dose of endotoxin show a reduced mortality when rechallenged with a normally lethal dose of endotoxin. This is called endotoxin tolerance. Human in vivo data are extremely sparse. Draisma et al. studied the development of endotoxin tolerance in 14 healthy male volunteers challenged with an intravenous injection of 2 ng/kg E. Coli LPS for 5 consecutive days.

Symptom scores and vital signs were obtained before and up to 6 hours after LPS administration. Liver and renal function were measured daily for toxicity screening. Elastase, von Willebrand factor and several cytokines were measured at regular intervals both before and after LPS administration. The symptom score significantly decreased from 6.1 ± 3.1 (Day 1) to 0.3 ± 0.6 (Day 5). Temperature increase, heart rate increase and blood pressure decrease were also attenuated after 5 days of endotoxin administration. On comparison with Day 1 endothelial cell activation measured by circulating von Willebrand factor was attenuated on Day 5. Elastase levels decreased from 775 (481-950) ng/ml 4 hours after LPS administration on Day 1 to 384 (205-481) ng/ml on Day 5. All measured cytokines, both pro- and anti-inflammatory were significantly attenuated after 5 days of LPS administration. The reduction in the proinflammatory phase after 5 days of LPS administration was 95 ± 2% and 99 ± 1% in the anti-inflammatory phase.

This study clearly shows that endotoxin tolerance can be induced in humans after 5 consecutive days of LPS administration. The results point to a generalized attenuated innate immune response, as the production of both pro- and anti-inflammatory cytokines was decreased together with reduced endothelial cell and leucocyte activation. The importance of endotoxin tolerance stems from the potential of cross tolerance resulting in protection against other forms of tissue damage of which ischaemia-reperfusion injury may be the most significant. This needs to be confirmed in humans. Further studies are eagerly awaited.