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 67Ga-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.

Subjective assessment of the peripheral circulation is still important in critically ill patients

The importance of clinical assessment of peripheral perfusion beyond the initial resuscitation phase in critically ill patients is unknown. Lima et al. enrolled 50 consecutive critically ill patients who had undergone initial resuscitation and stabilization within 24 hours of ICU admission.

Subjective peripheral perfusion was measured by capillary refill time and skin temperature. Objective central-to-peripheral temperature differences were also measured as was the peripheral flow index (PFI) derived from the pulse oxymetry signal. The authors specifically investigated whether subjective assessment of peripheral perfusion could predict an increase in SOFA score or subsequent hyperlactataemia.

After initial resuscitation a total of 23 patients (46%) had abnormal peripheral perfusion. Objective measures were congruent with subjective assessment. Haemodynamic variables were not different between patients with an abnormal or normal peripheral perfusion as was the dose of vasopressors.

Deterioration was more frequently seen in patients with abnormal peripheral perfusion both for an increase in SOFA score (odds 7.4, 95%CI 2 – 19) and for the existence hyperlactataemia (odds 4.6 (95% CI 1.4 – 15).

This study clearly suggests that the subjective assessment of the peripheral circulation predicts unfavourable evolution after initial resuscitation of the critically ill patient. Clinical assessment of the peripheral circulation therefore has the potential to optimize resuscitation procedures. Although this must be formally tested, it is nice to see that in an era of increasingly complex monitoring techniques, a simple bedside observation could still be useful. The authors should be congratulated for this.


The predictive value of blood lactate levels depends on the admission diagnosis

It is generally accepted that high lactate levels are bad and a decrease in lactate is good despite a multitude of underlying diseases. Jansen et al. investigated the prognostic value of repeated lactate levels in septic versus other patients with low-oxygen transport (e.g. haemorrhage), and in haemodynamically stable versus unstable patients.

Blood lactate levels were recorded on admission and after 12 and 24 hours. Differences between lactate levels on admission and 12 h, and between 12 h and 24 h were related to mortality. A total of 394 patients were included. In patients with sepsis (N = 140), there were no differences in admission levels of lactate between survivors and non-survivors, but levels after 12 and 24 hours were significantly higher in the non-survivors. In patients admitted with haemorrhage, non-survivors had higher lactate levels on admission and after 12 hours but not after 24 hours. These data were confirmed when haemodynamic status on admission (stable versus unstable) was taken into account.

The study shows that a decreasing lactate level in patients with sepsis is associated with improved survival but not, however, in patients with haemorrhage or other clinical conditions with low-oxygen transport. Apparently, the increased lactate levels at admission in non-septic patients were the result of profound tissue ischaemia resulting in irreversible tissue damage. In contrast, persistent lactate levels in patients with sepsis were not necessarily associated with a worse outcome. In these patients persistent hyperlactataemia could be explained by increased aerobic glycolysis, pyruvate dehydrogenase dysfunction or mitochondrial dysfunction. This study is helpful in understanding the prognostic value of serum lactate levels during the first 24 hours of admission.