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Clinical Investigation

CLINICAL INVESTIGATION

Volume kinetics of Ringer's lactate solution in acute inflammatory disease

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Abstract

Background: Little is known about the turnover of crystalloid fluids infused in patients with acute systemic inflammation. We hypothesised that systemic inflammation would be associated with altered distribution and elimination of Ringer's lactate solution (volume kinetics).

Methods: Ringer's lactate solution (15 ml kg^{-1}) was infused intravenously over 35 min in patients undergoing cholecystectomy (n=20) or appendectomy (n=20) starting before induction of general anaesthesia. Blood samples and urine were collected over the following 2 h. Plasma concentrations of inflammatory (tumour necrosis factor-α, interleukin-10, and C-reactive protein) and endothelial damage (syndecan-1) biomarkers were quantified by enzyme-linked immunosorbent assay. The volume kinetics was studied using mixed-effect modelling.

Results: Ongoing surgery (duration: 30–45 min) increased the rate constant for fluid transfer from the plasma to the extravascular space (k_{12}; from 32 to 57×10^{-3} min^{-1}; P<0.001), and decreased the elimination rate constant (k_{10}; from 5.3 to 0.6×10^{-3} min^{-1}; P<0.001). A lower mean arterial pressure was associated with reduced elimination, independent of conscious/anaesthetised state. The redistribution of fluid back to the plasma occurred more slowly in the group with appendicitis (P<0.02), in whom higher plasma concentrations of C-reactive protein were measured [median: 38.1 (range 1.8–143.6) *vs* 1.3 (0.1–159.0) μg ml^{-1}; P<0.001]. However, no biomarkers for inflammation or endothelial damage were significantly associated covariates in the kinetic model.

Conclusions: No association was found between the volume kinetics of Ringer's lactate solution and the degree of inflammation as indicated by established biomarkers in patients with cholecystitis or appendicitis. However, the rate of elimination was greatly retarded by general anaesthesia in both groups.

Clinical trial registration: ChiCTR-IOR-15006063.

Keywords: crystalloid solutions; humans; inflammation; kinetics; Ringer's lactate

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Editor's key points

- Damage to the endothelial glycocalyx layer may alter the kinetics of fluid distribution.
- There is lack of controlled studies in patients examining whether the kinetics of fluid infusions are altered in systemic inflammatory states.
- The distribution and elimination of Ringer's lactate solution (15 ml kg^{-1} i.v.), commenced before elective cholecystectomy and emergent appendectomy, were assessed.
- The degree of elimination of Ringer's lactate solution was chiefly influenced by general anaesthesia, and not associated with markers of inflammation (tumour necrosis factor-α, interleukin-10, and C-reactive protein) or endothelial injury (syndecan-1).

The distribution and elimination of crystalloid infusion fluids vary depending on age, arterial pressure[1] and state of hydration.[2] In recent years, much attention has been focused on inflammation and the role of the endothelial glycocalyx layer on fluid distribution.[3] This glycocalyx is damaged (shed) in the presence of inflammation, ischaemia,[4] and plasma volume expansion,[5] and this shedding is likely to shorten the intravascular persistence of infused fluid. The degree of inflammation can be assessed in most hospital laboratories by measuring the plasma concentration of C-reactive protein, whereas plasma biomarkers of endothelium shedding, such as syndecan-1, require a research laboratory. The relationships between inflammation and fluid distribution have mainly been investigated in microcirculatory models[3]; so little is known about the turnover of infusion fluids in the presence of inflammation and inflammation-induced shedding in an integrative human model.

The primary aim of the present study was to explore the covariance between biomarkers of inflammation and the distribution and elimination of Ringer's lactate solution as determined by volume kinetic analysis. The secondary aim was to compare the fluid kinetics between the conscious and anaesthetised state in the same subjects. For this purpose, we chose to study patients who presented with two common acute systemic inflammatory diseases: cholecystitis and appendicitis. We tested the hypothesis that high plasma concentrations of biomarkers would be associated with altered kinetics. In particular, we expected to find that a systemic inflammatory response would be followed by a speedier distribution of infused fluid.

Methods

Forty patients who underwent surgery for inflammatory disease at Shaoxing People's Hospital in South China between March 2015 and April 2017 were recruited for the study. The protocol was approved by the Ethics Committee of the Shaoxing People's Hospital (no. 2015013; official in charge: Yu Qian) and the study was registered at the Chinese Clinical Trial Registry (ChiCTR-IOR-15006063). Written informed consent was obtained from each study subject.

Procedure

Two groups of patients were studied. The first group consisted of 20 patients with cholecystitis who underwent elective laparoscopic cholecystectomy. The second group was composed of 20 patients who underwent acute surgery for appendicitis. The inclusion criteria were ASA Classes 1–2, age between 18 and 60 yr, and BMI between 18 and 25 kg m^{-2}. The exclusion criteria were severe mental, cardiac, hepatic, or renal disease; bleeding disorders; and pregnancy.

The patients with cholecystitis had fasted overnight, whereas the patients with appendicitis had fasted for at least 2 h before the surgery. No premedication was given. When the patients arrived in the operating theatre, a radial artery cannula was inserted after local anaesthesia infiltration; this cannula was used for blood sampling and for monitoring the arterial blood pressure.

An i.v. infusion of 15 ml kg^{-1} of Ringer's lactate solution (Pharmacia–Baxter, Shanghai, China) was given over 35 min via an infusion pump. The infusion was initiated before general anaesthesia was induced. The study extended throughout the surgery and into the postoperative period. No other fluid (except drug vehicles) was given during the study period of 120 min.

Anaesthesia was induced with midazolam 50 μg kg^{-1}, propofol 1.5 mg kg^{-1}, cisatracurium 0.15 mg kg^{-1}, and sufentanil 5 μg kg^{-1}, followed by tracheal intubation and mechanical ventilation. The anaesthesia was maintained with propofol 6 mg kg^{-1} h^{-1} and 1.5 minimum alveolar concentration of sevoflurane. Additional cisatracurium 0.05 mg kg^{-1} and sufentanil 2 μg kg^{-1} were given as required. All patients had an indwelling catheter placed into the bladder, and the excreted volume was measured during the experiment.

Monitoring included pulse oximetry, electrocardiography, heart rate, and invasive arterial pressure. Data were displayed on a multifunction monitor (Datex-Ohmeda, Hoevelaken, the Netherlands) and saved digitally. Blood loss was the sum of the volume of sanguinous fluid in suction bottles and the weight change of the sponges used to drain the operating field.

Blood analyses

Arterial blood samples, 2 ml each, were collected every 5 min during the first 60 min and every 10 min during the next 60 min. The blood haemoglobin (Hb) concentration was measured on a GEM Premier 3000 instrument (Instrumentation Laboratory, Lexington, IL, USA), which has a coefficient of variation (CV) of 2%.

At the beginning of the experiment (before the induction of anaesthesia), samples were drawn for analysis of the plasma concentration of C-reactive protein on an AU5400 (Beckman Coulter, Inc., Brea, CA, USA), with a CV of <5%, in the hospital's routine laboratory.

We quantified, by spectrophotometry (SpectraMax Plus, Molecular Devices, Sunnyvale, CA, USA), the following inflammatory biomarkers using enzyme-linked immunosorbent assays: tumour necrosis factor-α (TNF-α), interleukin-10 (IL-10) (Multisciences Biotech, Hangzhou, China) and syndecan-1 (Cloud-Clone Corp., Katy, TX, USA), TNF-α reflects the degree of systemic inflammation, IL-10 is an anti-inflammatory cytokine, and syndecan-1 is a shedding product that is used to quantify the severity of endothelial injury. According to the manufacturers of the kits, the intra- and inter-assay precision CV of these measurements were 4.1–7.0%, 3.2–8.2%, and <12% for TNF-α, IL-10, and syndecan-1, respectively.