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Original Research Article

Influences of red blood cell and platelet counts on the distribution and elimination of crystalloid fluid

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ABSTRACT

Background and objective: A high number of blood cells increases the viscosity of the blood. The present study explored whether variations in blood cell counts are relevant to the distribution and elimination of infused crystalloid fluid.

Materials and methods: On three different occasions, 10 healthy male volunteers received an intravenous infusion of 25 mL/kg of Ringer's acetate, Ringer's lactate, and isotonic saline over 30 min. Blood hemoglobin and urinary excretion were monitored for 4 h and used as input in a two-volume kinetic model, using nonlinear mixed effects software. The covariates used in the kinetic model were red blood cell and platelet counts, the total leukocyte count, the use of isotonic saline, and the arterial pressure.

Results: Red blood cell and platelet counts in the upper end of the normal range were associated with a decreased rate of distribution and redistribution of crystalloid fluid. Simulations showed that high counts were correlated with volume expansion of the peripheral (interstitial) fluid space, while the plasma volume was less affected. In contrast, the total leukocyte count had no influence on the distribution, redistribution, or elimination. The use of isotonic saline caused a transient reduction in the systolic arterial pressure ($P < 0.05$) and doubled the half-life of infused fluid in the body when compared to the two Ringer solutions. Isotonic saline did not decrease the serum potassium concentration, despite the fact that saline is potassium-free.

Conclusions: High red blood cell and platelet counts are associated with peripheral accumulation of infused crystalloid fluid.

1. Introduction

This viscosity is a key parameter in the assessment of blood flow and tissue perfusion in microcirculatory studies. In the isolated hind-limbs of dogs, the blood viscosity increases exponentially when the hematocrit is raised, and the blood flow then requires a higher driving pressure [1]. However, the effects of variations in the red blood cell (RBC), platelet (Trc), and leukocyte counts within the normal range on the macrocirculation in healthy humans are poorly studied.

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Volume kinetics is a macroscopic method that is applicable to the study of these effects, if any [2]. The volume kinetic method is based on repeated measurement of the blood hemoglobin (Hb) concentration, which is the inverse of the blood water concentration [3]. Infusion fluids contain almost exclusively water; therefore, Hb changes are a useful index of the water volume that equilibrates with the circulating blood. This type of analysis can also be used for the simulation of the influences of combined differences in distribution and elimination of infused fluid on plasma volume expansion, peripheral edema, and urinary excretion [4].

The aim of the present study was to investigate the kinetics of a rapid fluid load of three different crystalloid fluids (Ringer's acetate, Ringer's lactate, and isotonic saline) in a randomized cross-over fashion in volunteers. The influence of variations in the RBC, Trc, and leukocyte counts on fluid kinetics was studied by applying these parameters as time-varying covariates in a population kinetic model for nonlinear mixed effects. The arterial blood pressure and the heart rate were also monitored because the hemodynamics may have competitive effects on the kinetics.

2. Materials and methods

The study was based on 30 strictly controlled infusion experiments performed in 10 male volunteers aged between 24 and 44 (mean, 32) years and with a body weight ranging between 72 and 95 (mean, 81) kg. All volunteers received an intravenous infusion of 25 mL/kg of Ringer's acetate, Ringer's lactate, and isotonic saline over 30 min, administered in a crossover fashion and in random order. The subjects gave their approval for participation after being informed of the study's purpose, which had been approved by the Ethics Committee of Huddinge University Hospital (Dnr 222/98, chairperson Lennart Kaijser). The project originally contained five infusions, and a two-step analysis of the hemodilution has been published [5]. Here, three of the infusions are studied in more detail.

The experiments were limited to only one experiment in one volunteer per day throughout the duration of the study. The wash-out period between the infusions was one week. On each occasion, the volunteer arrived at the Research Center at Söder Hospital in Stockholm at 8:30 AM. He had been allowed to ingest one glass (250 mL) of fluid and one sandwich 2 h before arrival. The volunteer rested for 30 min on a bed to reach a hemodynamic steady state. A cannula was placed in the cubital vein of each arm: one for blood sampling and the other for infusion of crystalloid fluid. Volunteers were covered in blankets to ensure good thermal comfort. The arm used for blood sampling was placed on a body-temperature heating pad.

The rate of infusion of crystalloid fluid was controlled using infusion pumps. During and after the infusions, venous blood (2–3 mL) was withdrawn to measure the Hb concentration, the hematocrit (Hct), RBC, Trc, and total leukocyte count on the Technicon H2 (Bayer, Tarrytown, NY, USA) instrument used for routine measurements in the Clinical Chemistry Laboratory of the Hospital. The samples were withdrawn in a standardized manner, using a discard sample to prevent admixture of rinsing solution (isotonic saline), to ensure a coefficient of variation (CV) of approximately 1%. A volume of saline was then injected that corresponded to the sampled plasma volume. Sampling was performed every 5 min for 2 h and then every 10 min during the following 2 h, for a total of 37 samples over 4 h. The baseline sample was drawn in duplicate, and the mean of the two measurements was used in the calculations. The subjects voided just before the experiments, and this urine was discarded. The volume of the urine excreted during the study was recorded.

The ionic contents in mmol/L of the three crystalloid fluids (all manufactured by Baxter Healthcare) were as follows:

Ringer's acetate Na^+ 130, K^+ 4, Ca^{2+} 2, Cl^- 110, acetate 130 (273 mosmol/kg)
Ringer's lactate Na^+ 130, K^+ 4, Ca^{2+} 2.7, Cl^- 109, lactate 28 (273 mosmol/kg)
Isotonic saline Na^+ 154, Cl^-154 (308 mosmol/kg)

The systolic and diastolic arterial pressures and the heart rate were measured on a noninvasive hemodynamic monitor (Propaq, Protocol Systems Inc., Beaverton, OR, USA) and the results were recorded for the same time points as the blood samples were taken. The mean arterial pressure (MAP) was calculated as the diastolic pressure plus one third of the difference between the systolic and diastolic pressures.

The serum sodium and potassium concentrations and the serum osmolality were measured every 15–30 min by a direct potentiometry technique using an IL BGE analyzer (Instrumentation Laboratory, Milan, Italy) with a coefficient of variation of 1%–2%.

2.1. *Kinetic model*

A two-volume kinetic model with two routes of elimination was simultaneously fitted to the dependent variables (frequently measured plasma dilution and total urinary excretion) in all 30 experiments. The reason why two elimination functions are used is that not all of the fluid that is eliminated from the kinetic system can be recovered as urine. The influence of various covariates on the model parameters was then tested sequentially, as guided by a reduction of the residual error (−2 LL = log likelihood).

This kinetic model has been used previously [4] and agrees well with physiological data showing the isotonic infusion fluids distribute between two compartments, the plasma and the interstitial fluid space.

Fluid infused into the plasma (V_c, volume) is eliminated by urinary excretion (k_{10}, rate constant) and residual elimination (k_b, rate constant; previously called "k_{10} residual" [4]), as well as being distributed (k_{12}, rate constant) and re-distributed (k_{21}, rate constant) to the interstitial fluid space (V_t, volume). All flow rates are proportional to the volume expansion of the respective body fluid space. Several other models have been tested, including one- and two-compartment models and zero-order k_b, but the present one has found to be most appropriate [6].

A schematic drawing of the kinetic model is shown in Fig. 1A. In the model, fluid is infused at rate R_o and expands

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