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COMPUTER MODELLING OF HAEMODIALYSIS/ ULTRAFILTRATION EXPLAINING THE PATHOGENESIS OF THE DISEQUILIBRIUM SYNDROME

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Summary

Based on the hypothesis that rapid corrections of pH, Na^+ and osmolality give rise to disequilibrium (DES) during efficient haemodialysis (HD), a 14 compartment model has been designed for dynamic analysis of the induced fluid shifts and the resulting haemodynamic reactions. Simulated HD and ultrafiltration (UF) on the model were based on data from 11 steady state dialysis (RDT) patients (diffusion coefficients for urea, body fluid compartments, haemodynamic monitoring by Swan-Ganz® catheters).

The model reactions correlated remarkably with clinical findings and indicate how far a patient's haemodynamic compensation can prevent circulatory collapse and hypovolaemia, mainly through lowering the mean pressure in a major portion of the capillaries.

Steady weight dialysis causes reduction of blood volume up to 65 per cent before circulatory collapse occurs.

Introduction

Efficient haemodialysis often leads to headache, nausea with vomiting, brief episodes of circulatory collapse and painful muscle cramps. These symptoms, called the Disequilibrium Syndrome (DES), are generally related to osmotically induced shifts in the fluid compartments leading to brain oedema and a tendency to hypovolaemia. Possible prevention of these serious side effects has prompted this study of the mechanisms of reactions to haemodialysis and ultrafiltration.

A 14 pool patient-dialyser system has been created on a hybrid simulation computer (MOSES = Modular Symbolic Electronic Simulator) as a tool for the analysis.

Compartmental description

The patient-dialyser system can be described as five spaces each containing the following simplified osmotically active variables: fluid volume, protein concentration, sodium concentration (except in ICS and CNS) and urea concentration. Diffusion of these variables (substances) takes place between the spaces according to their permeabilities (defined as their time constants).

During dialysis, the concentrations will decline as shown in Figure 1.

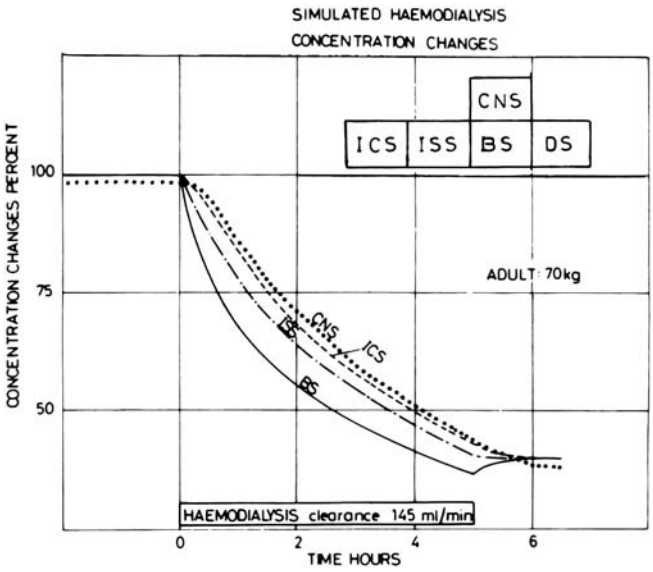

Figure 1. Schematic representation of spaces in a patient-dialyser system and simulated concentration changes in haemodialysis. BS: blood space; ISS: interstitial space; ICS: intracellular space; CNS: brain space; DS: dialyser space

Haemodynamic description

The circulation of blood through the organism provides an exchange between the blood space (BS), the interstitial space (ISS) and the brain space (CNS), where cardiac output has a proportional influence.

The blood space is subdivided into four haemodynamic sections with classical distribution of surface areas, volumes and resistances.

Differences in the areas of the sections determine the diffusion constants between the surrounding spaces and the section. The mass exchanges are determined by the diffusion constants.

Fluid balances in the spaces depend on osmotic and haemostatic pressure gradients. In BS the volume is dynamically regulated by the capillary pressure which in turn is controlled by arteriole contraction, cardiac output and central

venous pressure.

Individual data for the simulation were necessary for each patient. Clinical measurements were therefore carried out on 11 dialysis patients in steady state during separate ultrafiltration or steady weight dialysis.

Volume measurements

Volume measurements were carried out with isotope tagged tracers: *total fluid volume,* urea space, was determined with ^{14}C urea; *extracellular fluid volume,* inulin space, was determined simultaneously with inulin and ^{3}H-inulin, and *blood space volume* by ^{51}Cr tagged erythrocytes.

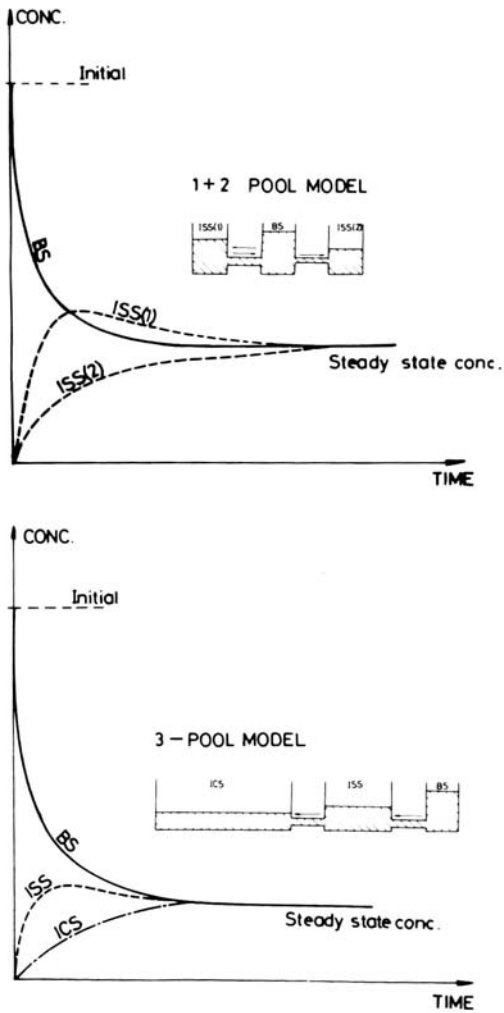

Figure 2. Pattern of concentrations in a 1 + 2-pool model and in a 3-pool model. BS: blood space; ISS: interstitial space; ICS: intracellular space; CNS: brain space; DS: dialyser space

Haemodynamic measurements

Haemodynamic monitoring was made with a Swan-Ganz® catheter and equipment, pressure and thermodilution determination of cardiac blood flow (Edwards Laboratories).

Blood sampling was at least every 15 minutes during treatment including relevant concentrations (urea, creatinine, protein, Na^+, K^+, oncotic pressure, osmolarity, etc.).

Determination of individual time constants

Repetitive transient analyses were used to determine the time constants in patients. Bolus injections of tracers (^{14}C-urea 0.8μci/kg, ^{3}H-inulin 0.4μci/kg) and frequent sampling of blood concentrations was made eight hours before dialysis until steady state conditions were reached.

Determination of inulin time constants required a repetitive division of the interstitial space into a slow and a rapid diffusion volume, see Figure 2.

The haemodynamic section of the model includes the following parameters: mean arterial pressure, central venous pressure, cardiac output, precapillary resistance, and mean capillary pressure.

Compartmental analysis

Comparison between simulated separate ultrafiltration and constant weight haemodialysis, excluding the haemodynamic compensating mechanism, shows that the osmotically induced fluid shifts from the BS are more pronounced in the dialysis situation causing severe reduction in BS. This condition is exaggerated if azotaemia is pronounced (Figure 3).

Haemodynamic analysis

The haemodynamic compensation mechanisms compensate for the reduction in BS. This is brought about primarily through reduction in capillary pressure. When BS is reduced it causes a lowering in CVP resulting in reduced cardiac output. Arteriole contraction is initiated and compensates the reduction in mean arterial pressure. Simultaneous venule/venous contraction hampers the reduction in cardiac output.

Clinical comparison

If relevant patient data are included, the model reacts like the patient. The osmotically induced reduction in BS is so severe that tissue ischaemia develops causing sudden reduction in the peripheral vascular resistance and low arterial pressure. This is accompanied by a reduction in BS because of an increase in capillary pressure leading to further circulatory collapse. The situation is reverted (as in the clinic) by brief interruption of dialysis and addition of fluid and sodium to BS (infusion of 200ml saline) (Figure 4).

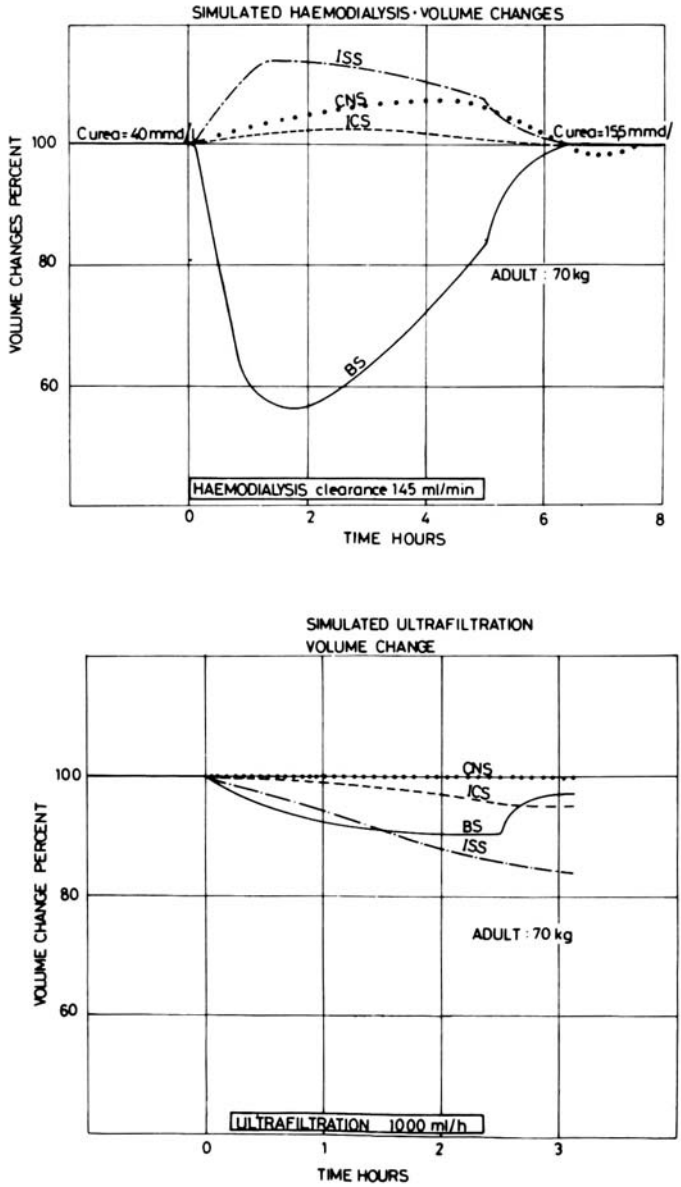

Figure 3. Simulated volume changes in haemodialysis and ultrafiltration. BS: blood space; ISS: interstitial space; ICS: intracellular space; CNS: brain space; DS: dialyser space

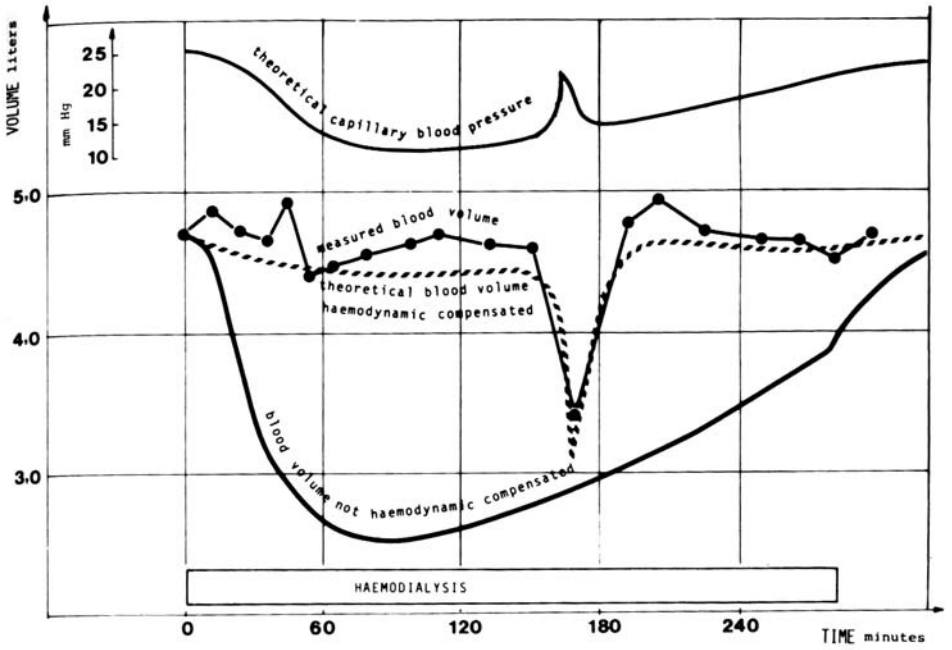

Figure 4. Comparison between simulated and clinical haemodialysis

Conclusions

1 The presented 14 compartment dynamic model has proved to be a useful tool in analysis of the dynamic changes caused by extracorporeal therapy.

2 Based on patient data prior to dialysis the model reacts to dialysis in a manner remarkably similar to the clinical situation.

3 According to the model the capillary pressure plays a central role in the dynamic defence of maintaining blood volume in the dialysis patient.

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