EFFECTS OF BLOOD–DIALYSER INTERACTION (SHAM-DIALYSIS) ON HAEMODYNAMICS AND OXYGEN TENSION IN HEALTHY MAN

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Summary

To evaluate the normal haemodynamic and respiratory responses to blood-membrane contact sham-dialysis, i.e. with blood flowing through a dialyser but without dialysate and ultrafiltration, was performed on healthy young men during 150 minutes. Heart rate, cardiac output, arterial blood pressure and pulmonary arterial blood pressure (continuously recorded during the initial 30 minutes) did not change significantly. The white blood cell count fell markedly to a minimum after 20 minutes of blood-membrane contact, then returning to above the baseline values, but PaO₂ did not change significantly.

Introduction

Increased interest has been focused on dialyser biocompatibility and its contribution to respiratory and haemodynamic responses during haemodialysis. Research so far has been performed during standard haemodialysis which makes it difficult to separate the effects of blood-membrane contact from those of diffusion and ultrafiltration [1–4]. Some protocols have exclusively tried to study the blood-membrane interaction but procedures have differed a great deal from the haemodialysis procedures [5,6]. In order to evaluate the respiratory and haemodynamic responses to blood contact with a cuprophan dialyser membrane we have performed sham-dialysis (SHD), i.e. with blood flowing through the dialyser but without diffusion or ultrafiltration taking place. Healthy young men have been studied because one aim of the study was to assess the normal physiological responses to membrane interaction, i.e. not changed by the uraemic state.

Material and methods

Eleven healthy men (mean age 27 ± 1 years) gave their informed consent and volunteered for the study.
Blood access for SHD was obtained by introducing a catheter to a femoral vein and a needle into a brachial vein. SHD was performed with a dialysis monitor (Gambro AK 10 UDM) and a cuprophane hollow fibre dialyser (1.2m², Gambro 120 M). The blood pump speed was 200ml/min. The blood compartment was primed with isotonic saline. The dialysate compartment was first primed with dialysate followed by ultrafiltration of 2L saline from the blood compartment, thereby rinsing the dialysate compartment free from dialysate; the inlet and outlet dialysate ports were then closed. The closed dialysate compartment contained about 100ml isotonic sodium chloride. At start of SHD a loading dose of 5000IU heparin was given which occasionally was followed by an additional dose of 2500IU. Blood temperature was followed with a thermodilution catheter and was held constant by clothing the dialyser with a metal foil and placing the inlet blood tubing in a blood warmer bath.

Right heart catheterisation was performed with a Swan-Ganz thermodilution catheter which was introduced percutaneously into an antecubital vein and positioned in the pulmonary artery to measure cardiac index (CI), stroke index (SI), pulmonary arterial blood pressure (PAP) and pulmonary capillary wedge pressure (PCW). A short Teflon catheter was introduced percutaneously into a brachial artery for blood pressures (AP) and blood sampling. Pressures were measured with strain gauge transducers (EMT 34, Siemens, Elema, Sweden) and recorded together with ECG on a UV-recorder (SE 3006, DI, SE lab, EMI, Feltham, England). Mean arterial blood pressure was calculated by electronic damping. Systemic vascular resistance index (SVR) was calculated and calf vascular resistance (CVR) was assessed by venous occlusion plethysmography. SHD was performed during 150 minutes on eight subjects with blood pressure measurements every 30 minutes. On two of these eight and on three additional subjects blood pressures were recorded continuously during the first 30 minutes of SHD.

Arterial blood samples were analysed for PaO₂ and PaCO₂ every 10 minutes the first 30 minutes, and then every 30 minutes of SHD (conventional electrode technique, ABL2, Radiometer). White blood cell count (WBC) from the arterial side of the dialyser was sampled every 10 minutes the first 30 minutes and at the end of SHD (Coulter counter; if less than 3 x 10³/L verified manually.

Statistical methods: two-way analysis of variance was performed to test overall changes over time. Only if the analysis showed a significant result paired ‘t’ test was performed. Values are presented as mean ± SEM.

The investigation was approved by the Ethical Committee of the Karolinska Institute and Huddinge University Hospital.

Results

No severe side effects or complications were observed in any of the subjects.

Haemodynamics

There were no significant changes of heart rate, CI, and SVR. CVR seemed to decrease between 30 and 150 minutes, but analysis of variance did not show a
significant change over time. Systolic, diastolic and mean AP were constant as were systolic, diastolic and mean PAP. AP and PAP measured continuously in five subjects and PCW recorded intermittently in three subjects between 0–30 minutes of blood-membrane contact did not change. Values in three subjects are shown in Figure 1.

**Blood gases and white blood cell count (Figure 2)**

WBC decreased by 59 per cent at 20 minutes, thereafter increasing to 35 per cent above baseline at 150 minutes. PaCO₂ increased slightly during the first 20 minutes but PaO₂ did not change significantly.

**Discussion**

It is known that blood-membrane contact activates the complement system [7,8] which may be the reason for granulocyte sequestration in the pulmonary
vascular system resulting in neutropenia early during dialysis. There is a great controversy concerning the possible relationship between the above mentioned phenomenon and the fall in $\text{PaO}_2$ during haemodialysis [1–4]. One reason for this is that in standard haemodialysis it is not possible to separate the influence
of diffusion across the membrane from the effects of blood-membrane interaction. Sham-dialysis as presented in this paper offers a unique way to study dialyser biocompatibility uninfluenced by the dialytic procedure.

Graf et al [9] suggested that pulmonary leucostasis during haemodialysis evokes a mild pulmonary oedema resulting in hypoxaemia. However, we were unable to record any change in PaO₂ in our normal subjects in spite of WBC decreasing to the same extent as observed in uraemic patients. It is conceivable that patients who are in an overhydrated state before haemodialysis are more vulnerable to pulmonary leucostasis, resulting in a defect in oxygen diffusion than young healthy men. Walker et al [5] found in the sheep an increase in pulmonary arterial pressure after injection of plasma incubated with cuprophan. However, we were unable to record any significant changes in PAP and PCW in spite of a marked fall in WBC. This indicates that pulmonary vasoconstriction is not a physiological response in normal man to WBC sequestration as a result of blood-membrane interaction in a dialyser.

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References

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Open Discussion

KOCH (Chairman) I expect some comments from London, Ontario because there seems to be a difference in results which may be caused, of course, by a species difference.

LINDSAY (London, Ontario) I am fascinated by your work and may I first of all congratulate you because I do not think that we would be able to do those experiments in North America. It seems to me that you have to do the same study in patients with end-stage renal failure requiring dialysis. I really cannot understand why the difference is not there because Dr Walker said earlier this morning we have seen changes in pulmonary vascular tone, occurring in patients with acute renal failure during monitoring, from a slight increase in pulmonary vascular resistance index*. It is either something that is different

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in the healthy person from the uraemic patients, not just the species difference as Dr Koch was suggesting, or I suppose that Gambro have a very good dialyser and you should be looking at a different manufacturer’s cuprophan.

GOTCH (Chairman) May I ask a question of both of you? Is there any possibility that there is a different amount of membrane contact, your sheep are 25–50kg and there is a stagnant time of 10 minutes in the system. Have you ever done your experiments with single pass flow through the dialyser and do you obtain the same effects? The other question is, do people have to become sensitised to the membrane? If you study a dialysis patient on his very first single dialysis would you expect to have the same results or do you become sensitised?

LINDSAY Frankly I don’t know the answer to the latter part of the question. Certainly with sheep you will see the same phenomenon with single pass, but obviously not to the same extent. Whatever is turned on causes an end-organ response which obviously is dependent upon the amount of factor or factors, let’s assume it is CS a or something else, that gets into the circulation on a unit time basis. I was talking just last week to Lee Henderson discussing this particular issue and he brought up some very interesting observations. He told me that with some material he has been looking at, the sheep is more sensitive than the pig, which is more sensitive than the dog, which is probably more sensitive than the humans, so there is a clear species difference there. Thus if one is looking at this phenomena it may well be that the sheep is the best animal model to use, but I can’t really say any more than that.

DANIELSON We only investigated the surface once.

DI GIULIO (Rome) Blood vascular access was different in Dr Walker’s study since he used arteriovenous while you used a veno-venous access. Do you think that this may account for the discrepancy of results between yours and Dr Walker’s study?

DANIELSON I think this is possible.

KOCH (Chairman) In your abstract you mentioned the measurement of catecholamines.

DANIELSON Yes, we unfortunately have not analysed this yet.