PLATELET MICROAGGREGATES AND RELEASE OF ENDogenous PROSTACYCLIN DURING THE INITIAL PHASE OF HAEMODIALYSIS

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Summary

In six patients arterial blood samples were withdrawn during haemodialysis (HD) for the measurement of platelet microaggregates, platelet and leucocyte counts, pO2 and 6-oxo-PGF1α (the stable metabolite of prostacyclin). During the initial phase of HD the plasma concentrations of 6-oxo-PGF1α increased, indicating an increased release of endogenous prostacyclin. Coincidentally to this phenomenon, hypoxaemia, reduction in platelet and leucocyte counts, and an increase in number of platelet microaggregates could be observed. Since prostacyclin is able to resolve platelet aggregates, we interpret the increased prostacyclin release to be in part a self protection mechanism against embolisation of microaggregates released from the dialysate into lung and peripheral vascular systems.

Introduction

During the initial phase of haemodialysis (HD) the interaction between blood constituents and the dialyser membrane results in several phenomena; formation of platelet microaggregates, mild decrease of platelet count, leucopenia and decrease of arterial oxygen tension (paO2) [1,2]. The formation of platelet aggregates seems to be a sequela of platelet activation by the dialyser membrane. Leucopenia and hypoxaemia are probably associated with a complement-mediated pulmonary leucostasis evoking mild pulmonary oedema with impaired oxygen diffusion [3]. Exogenous prostacyclin inhibits platelet activation during HD [4], but seems to be unable to prevent leucopenia and hypoxaemia. On the other hand the release of endogenous prostacyclin by lung and peripheral arterial endothelium may be enhanced by two of the described alterations, namely hypoxaemia and circulating platelet microaggregates [5]. To study the release of endogenous prostacyclin we measured the arterial plasma levels of 6-oxo-PGF1α, the stable hydrolytic metabolite of prostacyclin.

122
Material and methods

Six patients (three males, three females), aged 16–58 years, were studied. They had terminal renal insufficiency due to chronic glomerulonephritis, and were dialysed for 6 hours thrice weekly using capillary kidneys (C-DAK).

Arterial blood samples were taken before HD and initial heparin dose, and at 10, 20, 30, 60, 180 and 360 minutes after starting HD. Arterial blood for measurement of 6-oxo-PGF\textsubscript{1α} was withdrawn into syringes containing aspirin, and Na-EDTA (final concentration 1mg/ml and 2mg/ml respectively). The plasma 6-oxo-PGF\textsubscript{1α} was estimated by a specific RIA using a double antibody method. In this assay the cross-reactivity with other prostanooids is below 1%, the lower level of sensitivity is 70pg/ml. Other tests performed at the same time intervals were platelet and leucocyte counts (Coulter Counter) and \textit{paO}_2 (AVL gas check). The platelet microaggregates were estimated according to Wu and Hoak [6]. The result of this assay is given by the so-called platelet count ratio (PCR) which is indirectly proportional to the number of platelet aggregates. Since the heparin treatment during HD may influence the test system we repeated the examinations without HD but using the usual heparinisation.

Student’s \textit{t}-test was used for statistical analyses. The data were expressed in \( \bar{X} \pm \text{SEM} \).

Informed consent was given by the patients according to the declaration of Helsinki before this study.

Results

The initial phase of HD is characterised by a reduction of PCR (indicating an increase in number of platelet microaggregates), mild decrease in platelet count, marked fall in leucocyte count as well as by an arterial hypoxaemia (Figure 1). During the same time period the concentration of 6-oxo-PGF\textsubscript{1α}, the prostacyclin metabolite, increased and reached the highest values 10 min after HD began in five of six patients. Then the values decreased again and reached approximately initial concentrations in the second half of HD. In the experiment with heparin but without HD we could not detect significant changes by the test systems applied.

Discussion

The demonstrated increased release of endogenous prostacyclin during the initial phase of HD might be caused by two mechanisms (Figure 2). The first seems to be the formation of platelet microaggregates in the dialyser, which may embolise to the small vessels, particularly in the lung. It is well known that the lung plays a an important role in the release of prostacyclin [5]. This pulmonary prostacyclin release could be enhanced non-specifically by a second mechanism, leucostasis-induced hypoxaemia. Our findings support the concept that the release of endogenous prostacyclin can be stimulated temporarily by several harmful conditions such as platelet microaggregate formation and hypoxia, as well as by mechanisms
Figure 1. Increased concentrations of 6-oxo-PGF₁₀, the stable prostacyclin metabolite, during the initial phase of haemodialysis, coincidentally with increase of platelet microaggregates (indicated by a decrease of platelet count ratio), decrease of platelet and leucocyte count and hypoxaemia.

Figure 2. Hypothetical concept on pathogenesis of increased prostacyclin release
previously described in hypertension, acute transplant rejection and initial phase of atherosclerosis [7–9]. In HD this mechanism is by no means able to prevent platelet microaggregate formation completely, but could be of importance in the limitation of membrane-platelet-interaction, as well as in the mitigation of rather harmful effects of another prostanoid formed during the initial phase of HD, namely thromboxane A₂.

Acknowledgment

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References

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Open Discussion

PARSONS (London) What were you using in your dialyser, bicarbonate or acetate, have you looked at the effects of bicarbonate on this disturbance?

LEITHNER We used acetate in our dialysis systems.

PARSONS Have you looked at the effect of changing to bicarbonate?

LEITHNER No we have not measured this.

LEVY (Israel) Have you looked at your measurement with the re-use of coils?

LEITHNER No, we do not re-use our dialysers.