

PLASMA GRANULOCYTE ELASTASE DURING HAEMODIALYSIS: EFFECTS OF DIFFERENT DIALYSER MEMBRANES AND STERILIZATION PROCEDURES

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Summary

Plasma granulocyte elastase in complex with α_1 -proteinase inhibitor (E- α_1 PI) during haemodialysis was investigated in 15 patients (37.4 ± 3.2 years) undergoing maintenance haemodialysis (47.0 ± 12.9 months) with different hollow fibre dialysers. Cellulose hydrate membrane caused a maximal increase of E- α_1 PI ($1,659 \pm 257$ ng/ml). Patients dialysed with polyacrylonitrile dialysers failed to exhibit comparable increases in plasma E- α_1 PI (238 ± 23 ng/ml). During haemodialysis plasma E- α_1 PI values rose to a peak 643 ± 175 ng/ml in patients on polymethylmethacrylate dialysers, to 557 ± 120 ng/ml on cuprophan dialysers, but to only 382 ± 54 ng/ml on ethylene-vinyl alcohol copolymer dialysers. E- α_1 PI was not influenced by the method of dialyser sterilization. The degree of polymorphonuclear leucocyte stimulation depends on the nature of the dialyser membrane material and granulocyte activation is independent of the sterilization procedure of dialysers and blood lines.

Introduction

Transient granulocytopenia occurs in patients during the initial phases of haemodialysis with cellulosic membranes [1] due to pulmonary sequestration provoked by complement derived fragments [2-4]. The intensity of complement activation is determined by the type of dialysis membrane. Non-cellulosic membranes have been reported to be more compatible with blood than cellulosic membranes [5]. Significant complement activation and anaphylatoxin formation were observed in patients dialysed with cuprophan hollow fibre membranes [6]. In contrast, haemodialysers containing polyacrylonitrile or polymethylmethacrylate membranes promoted only mild granulocytopenia and very little complement activation [6-8]. We have, therefore, attempted to characterize changes in plasma granulocyte elastase in patients undergoing maintenance haemodialysis with particular reference to the effects of cellulosic membranes and non-cellulosic membrane formations which have been reported to be more blood compatible [5-8].

Methods

Fifteen chronically uraemic patients (7 males and 8 females), aged 57.4 ± 3.2 years (mean \pm SEM, range 26–79) undergoing regular haemodialysis for 47.0 ± 12.9 months (range 6–132) were studied. Haemodialysis was performed 11.3 ± 0.3 hours weekly using five different dialysers in 10 patients and three different dialysers in five patients. Each patient served as his or her own control. The primary kidney disease was chronic glomerulonephritis in seven cases, polycystic kidney disease in two cases, diabetic glomerulosclerosis in three cases, interstitial nephritis in two cases and tumour nephrectomy in one case. Pre-dialysis plasma creatinine was 11.6 ± 0.98 mg/dl and urea 158.4 ± 12.4 mg/dl. Patients were each dialysed with hollow fibre dialysers made from cellulose hydrate (Secon 133, Secon, Göttingen, FRG), cuprophane (Hemoflow D₂, Fresenius, Oberursel, FRG), polymethylmethacrylate (Filtrizer, Toray, Tokyo, Japan), ethylene-vinyl alcohol copolymer (KF 101, Salvia, Homburg, FRG) and polyacrylonitrile (Biospal 2400 S, Hospal, Lyon, France).

Whole blood samples were drawn from the patient's arteriovenous fistula prior to dialysis and immediately after completion of dialysis. During the haemodialysis procedure blood samples were obtained at 30–120 minutes. All blood samples were immediately anticoagulated with sodium citrate.

Plasma was separated from the sample within 30 minutes after its collection to prevent leakage of leucocyte constituents. The plasma specimens were stored at -30° until assayed. The measurement of plasma granulocyte elastase in complex with α_1 -proteinase inhibitor ($E-\alpha_1$ PI) was performed as previously described [9,10].

Results

Effect of different dialysers

Cellulose hydrate membrane caused a maximal increase of plasma $E-\alpha_1$ PI ($1,659 \pm 257$ ng/ml). Patients dialysed with polyacrylonitrile dialysers failed to exhibit comparable increases in plasma granulocyte elastase (238 ± 23 ng/ml). During haemodialysis plasma $E-\alpha_1$ PI values rose to peak 643 ± 175 ng/ml in patients on polymethylmethacrylate dialysers to 555 ± 120 ng/ml on ethylene-cuprophane dialysers, but to only 382 ± 54 ng/ml on ethylene-vinyl alcohol copolymer dialysers (Table I).

Effect of different sterilization of dialysers and blood lines

Sterilization of the different dialysers and blood lines with gamma radiation or ethylene oxide did not influence the increase in plasma $E-\alpha_1$ PI during haemodialysis (Table II).

TABLE I. Effect of different membrane materials on plasma levels of granulocyte elastase in complex with α_1 -proteinase inhibitor (E- α_1 PI)

Dialyser	n	Before dialysis	30 min	120 min	After dialysis
Cellulose hydrate	10	207 ±58	558*** ±216	1114** ±149	1659*** ±256
Cuprophan	15	128 ±13	271* ±116	517*** ±159	557*** ±120
Polymethylmethacrylate	10	174 ±34	291* ±54	422** ±113	643*** ±174
Ethylene-vinyl alcohol polymer	15	142 ±23	205** ±68	328 ±62	381*** ±54
Polyacrylonitrile	15	141 ±17	192** ±30	242*** ±33	237 ±22

Mean values ± SEM (ng/ml)

*p<0.05; **p<0.005; ***p<0.001 versus before dialysis

TABLE II. Effect of gamma radiation versus ethylene oxide sterilization of different membrane materials on plasma E- α_1 PI levels

	Polyacrylonitrile membrane		Cuprophane membrane	
	E- α_1 PI (ng/ml)	E- α_1 PI (ng/mg protein)	E- α_1 PI (ng/ml)	E- α_1 PI (ng/mg protein)
Before dialysis	100 ±9	2.0 ±0.2	131 ±13	2.5 ±0.3
30 minutes	182** ±21	3.0** ±0.3	198* ±36	3.3 ±0.6
120 minutes	266** ±26	4.5** ±0.5	421** ±61	6.8** ±1.0
End of dialysis	320** ±38	4.7** ±0.6	462** ±71	6.9** ±0.9

Mean values ± SEM from nine patients

*p<0.05; **p<0.01 versus before dialysis

Discussion

In the present study, the effect of different membrane materials (cellulose hydrate, cuprophan, polymethylmethacrylate, ethylene-vinyl alcohol copolymer,

polyacrylonitrile) on plasma granulocyte elastase during haemodialysis was investigated. Cellulose hydrate membrane caused a maximum level of E- α_1 PI of 1,659 \pm 257ng/ml. The lowest plasma E- α_1 PI values were observed using the polyacrylonitrile membrane. Similar results were obtained in patients dialysed with ethylene-vinyl alcohol copolymer dialysers. Cuprophan and polymethylmethacrylate membranes caused a significantly greater increase of plasma E- α_1 PI (Table I).

The mean plasma E- α_1 PI concentrations before haemodialysis were in a range between 127 \pm 14 (ethylene-vinyl alcohol copolymer) and 207 \pm 58ng/ml (cellulose hydrate). The highest E- α_1 PI values were found during haemodialysis with cellulose hydrate dialysers. Therefore, the E- α_1 PI values measured on the institution of haemodialysis are not the result of the previous haemodialyses and are not related to the sequence of the use of the different dialysers. Recent studies from our laboratory showed E- α_1 PI concentrations of 112 \pm 10, 151 \pm 13, 174 \pm 25ng/ml [10] and 188 \pm 20ng/ml [9] before dialysis. It is evident that daily differences exist in uraemic patients and their plasma E- α_1 PI is always significantly greater than those of healthy controls (70 \pm 4ng/ml).

In summary, the observations reported here are compatible with what is currently known about the biocompatibility of dialysis membranes. Polyacrylonitrile dialysers provoke minimal C₃a [6] and E- α_1 PI (Table I) formation and consistently fail to induce extensive leucopenia. The results of the comparison of the effects of five different hollow fibre dialysers on the plasma content of elastase complex with α_1 -proteinase inhibitor (E- α_1 PI) indicate that this parameter may be a further index of biocompatibility.

References

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