Anaphylactoid Reactions, Angiotensin-Converting Enzyme Inhibitors and Extracorporeal Hemotherapy

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Dear Sir,

Anaphylactoid reactions have been reported during the last years in patients undergoing hemodialysis [1,2]. The reactions, which occur within 10 min of initiating extracorporeal treatment, were mostly attributed to AN-69 high-flux membranes although other membranes and causes have been accused. The mechanism of origin remains quite unclear so far, membrane characteristics, residual ETO, endotoxin fragments and glucosaminoglycans were suspected as possible causes. The reactions are neither histamine dependent nor mediated by complement activation. They are presumed to develop from drastic rises in plasma bradykinin [6] which will not be degraded in ACE-inhibited patients. The generation of bradykinin is activated by contact of whole blood or plasma with negatively charged or strongly protein-adsorbing surfaces. Of 95 regular dialysis treatment patients treated in our unit, 23 were on ACE-inhibitor therapy in 1991. In 55 patients, high-flux membranes were used [cellulose acetate 16, po-lysulfon 18, polymethylmethacrylate (BK-series) 19, polyamide 2], 11 of these patients were on ACE-inhibitors as well. Six of them suffered from anaphylactoid reactions of different extension (bradycardia, hypotension, abdominal cramps) immediately after start of hemodialysis. In all cases, polymethylmethacrylate membranes (gamma-sterilized) were involved. After withdrawal of either dialyser or ACE-inhibitor, the reactions ceased.

Recently we observed similar reactions on 3 consecutive sessions of low-density lipoprotein apheresis (dextran sulfate adsorption) in a patient receiving ACE-inhibitors (enalapril 10 mg). The reaction started when about

100 ml of plasma returning from the adsorber column reentered the circuit. Slowing of the plasma pump ameliorated the seriousness of the reaction. Antihistaminics, H₁-antagonists, steroids, volume repletion and sympatho-mimetics were without effect.

Premedication with dextran 1 (probit 1.5 g) did not prevent the reaction on different occasion, IgE and C₁-esterase inhibitor were normal in quantity and function, ETO antibodies were absent and there was no eosinophilia. After withdrawal of enalapril, no further reactions were seen. Hypertension in this patient was controlled later by captopril medication twice daily which was omitted before apheresis treatment.

Contacting distributor (Kaneka, Bad Homburg FRG) and other centers, we became aware that adverse reactions in ACE-treated patients on extracorporeal hemotherapies were more common than expected, although the coincidence often remained unnoted. AN-69 high-flux dialysis [1, 2], polymethylmethacrylate high flux dialysis [own observation], membrane plasma separation [Dr.

Wagner, Essen] and reused polysulfone [7] have caused such effects as well as cascade filtration [Dr. Jontofson, Freiburg; Dr. Tschöpe Villingen-Schwenningen] dextran adsorption [3,4; Dr. Pfohl, Tübingen; Dr. Bahr, Bielefeld, Dr. Keller, München], heparin precipitation [Dr. Schuff-Werner, Göttingen] and immunoadsorption [Dr. Pfohl, Tübingen].

These reactions were different in severity but similar in symptomatology which fits with the individually different expression of the ACE-coding gene [5]. Since it is known that dextran sulfate and AN-69 are potent activa-

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tors of the contact-activating system [6], one would assume that all the anaphylactoid reactions which occur in ACE-inhibited patients during extracorporeal treatments have only two things in common: intake of ACE-inhibitors and contact activation. Because prescription of ACE-inhibitors is increasing rapidly, their coincidental application in patients undergoing extracorporeal hemotherapy will occur more frequently in the future. From the lesson taught by AN-69 dialysis reactions, we strongly recommend greater caution in all extracorporeal treatments where blood or plasma of ACE-inhibitor-treated patients contacts activating surfaces which may generate bradykinin.

References

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Book Review

Allen R. Nissenson Richard N. Fine

Dialysis Therapy

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This is a useful multiauthor soft book dealing with all the theoretical and practical aspects of dialysis therapy. It is up to date, concise, and each section has a few choice references for further reading. It is a must for fellows in Nephrology who need to know the theoretical aspects as well as the practical details of hemodialysis and peritoneal dialysis. The book covers dialysis in both adults and children and should be purchased by all nephrologists in training, as well as by those in charge of training programs.