Acute Changes of Endothelin 1 in Children on Hemodialysis

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Dear Sir,

In uremic patients, hemodialysis (HD) may change plasma endothelin 1 (ET-1) levels [1, 2], but, at present, little is known about its causes and consequences. The aims of this study were to estimate the effect of volume depletion and blood depuration on plasma ET-1 concentration during HD and to evaluate the potential importance of ET-1 as the modulating cardiovascular hormone in blood pressure control and myocardial hypertrophy.

Plasma levels of ET-1 were measured in 10 children with terminal renal failure (mean age 14.7 ± 5.1 years) studied 1-157 months (mean 40.6 ± 52.6), undergoing chronic HD with acetate or bicarbonate dialysis fluid and cuprophane suitable hollow disposable dialyzers. The clinical characteristics of the patients are summarized in table 1. Six patients were treated with nifedi-pine and captopril due to arterial hypertension. Blood samples were taken during a single dialysis session: before ultrafiltration, after ultrafiltration and after HD without fluid removal. Initially, the patients were only on ultrafiltration without dialysis until they achieved ‘dry weight’ or until symptoms of hypotension appeared. After that they continued dialysis without ultrafiltration for at least 2 h.

For ET-1 measurements, blood samples were collected in tubes containing aprotinin (Bayer, Leverkusen, Germany; Trasylol, 500 KIU/ml of blood) and EDTA (7.5 mmoy/ml of blood) and immediately centrifuged at +4°C. The plasma samples were stored at -80°C until assayed. Plasma ET-1 concentrations were measured by radioimmunoassay (RIA) using a commercially available kit (Biomedica, Vienna, Austria), after extraction with Ample C 18 columns that were preequilibrated with methanol and water. Plasma renin activity was measured by an angiotensin I RIA kit (SB REN 2, Cis bio international). M mode echocardiography was used to determine left ventricle dimensions. Left ventricle mass was calculated according to the Penn convention [3]. The left ventricular mass index was obtained by normalization of left ventricle mass to body surface.
Ultrafiltration decreased body weight and mean blood pressure but did not cause significant changes in ET-1 plasma concentrations and serum creatinine. Plasma renin activity increased with fluid removal during ultrafiltration and further rose during dialysis. During HD without fluid removal, mean plasma ET-1 increased, plasma creatinine and mean blood pressure decreased, while body weight did not change (table 1).

As yet, we can only speculate what effect the uremic state might have on ET biosynthesis. Like many other authors [4-6], we did not find a close correlation of plasma ET with plasma urea and creatinine. Depuration after HD may remove uremic toxins that, like those reported by Koyama et al. [7], suppress ET synthesis, but it also decreases other humoral factors that might have an influence on the ET-converting enzyme activity and improve ET synthesis. We found that during dialysis the mean plasma ET did not change significantly with central hypovolemia. It cannot be determined from the present study whether the observed results are due to a delayed release of ET-1 and/or an impaired baroreceptor reflex due to autonomic failure in the uremic state.

The patients with myocardial hypertrophy had lower plasma ET-1 before HD in comparison to patients without it (0.94 ± 0.28 vs. 1.85 ± 0.35; p < 0.05), while post-dialysis plasma ET-1 was almost identical in the patients with and without myocardial hypertrophy (2.95 ± 2.55 vs. 2.97 ± 2.10; p > 0.05).

Our results, like those reported by others [4, 8], do not shown any correlation either between plasma ET and arterial pressure or between plasma ET and myocardial hypertrophy [5, 6]. These observations raise the question whether circulating ET has any cardiovascular effects in chronic renal failure. That remains to be fully explored when specific ET receptor antagonists or ET-converting enzyme inhibitors become available for further clinical research.

Table 1. Clinical and laboratory data of 10 patients

<table>
<thead>
<tr>
<th>Primary renal disorder</th>
<th>Congenital malformation or dysfunction of the urinary tract</th>
<th>Glomerular disease</th>
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Data expressed as means, with standard deviations in parentheses.

T1 = Before ultrafiltration; T2 = after ultrafiltration; T3 = after dialysis without fluid removal; CHD = chronic hemodialysis; PRA = plasma renin activity.

*p < 0.05, **p < 0.01; n.s. = not significant.

References


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