Dear Sir,

The clinical problem of hemodialysis-associated hypotension has partially been resolved by lowering ultrafiltration rates in hypotension-prone patients. However, the mechanisms leading to hypotensive circulatory states during hemodialysis or in the inter-dialytic phase in a subgroup of chronic hemodialyzed patients remain unclear. Caretta et al. [1] found in 10 hypotensive patients an extraordinarily increased number of thrombocyte \( \alpha_2 \)-adrenoceptors, a moderate elevation of plasma noradrenaline levels as well as a diminished lymphocyte cAMP production in response to isoproterenol. The authors suggested an adrenoceptor adenylate cyclase uncoupling as a mechanism of low blood pressure in these patients.

The results of Caretta’s [1] \( \alpha_2 \)-adrenoceptor determination are completely at variance to those observed by Daul et al. [2]. Moreover, in a very limited number of patients (\( n = 10 \)) with hemodialysis-induced hypotension with a mean arterial blood pressure of \( 102 \pm 18 \) mm Hg prior to and \( 66 \pm 13 \) mm Hg (mean \( \pm \) SD) after hemodialysis, we determined an \( \alpha_2 \)-adrenoceptor density of \( 192 \pm 75 \) versus \( 246 \pm 110 \) fmol/mg protein in hemodynamically stable patients (\( n = 6 \)). Receptor density was assayed by \( \frac{\text{B} }{\text{R}} \text{auwolscine} \) as receptor label. The differences failed to reach statistical significance, but are generally comparable to those of Daul et al. [2]. As shown in table 1, we assayed adenylate cyclase activity in 2 patients of the hypotensive and the normotensive group, prior to and after 2 h of hemodialysis. Adenylate cyclase activity showed a wide variation, the \( \alpha_2 \)-mediated (via inhibitory G proteins) inhibition of basal and stimulated enzyme activity was maintained. Thus, the basic receptor mechanism seems to be unchanged in these patients.

The experiments of Caretta et al. [1] appear to be carefully performed. However, as demonstrated in table 2, a mean value of \( 77.21 \)

Table 1. Adenylate cyclase activity of 2 normotensive and hypotensive male patients prior to (P) and after (A) of hemodialysis

<table>
<thead>
<tr>
<th>Patient</th>
<th>Before Hemodialysis</th>
<th>After Hemodialysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normotensive</td>
<td>120 ± 15</td>
<td>110 ± 10</td>
</tr>
<tr>
<td>Hypotensive</td>
<td>90 ± 10</td>
<td>80 ± 5</td>
</tr>
</tbody>
</table>

Table 2. \( \alpha_2 \)-Adrenoceptor densities and radioligand equilibrium dissociation constants (Kd) determined in human platelet membranes by using the antagonists \( \frac{\text{B} }{\text{R}} \text{mas} \), fmol/Kd, nM/mg protein

<table>
<thead>
<tr>
<th>Radioligand Reference</th>
<th>Kd (nM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \frac{\text{B} }{\text{R}} \text{mas} )</td>
<td>100</td>
</tr>
</tbody>
</table>

D-35392 Giessen (Germany)
Moreover, since in contrast to our patients [3, 14] plasma noradrenaline was elevated in Caretta’s [1] group, volume depletion as a frequent cause of this phenomenon should be excluded [15]. The circulating noradrenaline level, however, does not necessarily prove an adequate sympathetic response to the hypotensive state as suggested by our own studies on symptomatic hypotensive hemodialyzed patients [14]. fmol/mg protein for the hemodynamically stable patients represents, as far as we know, the lowest standard mean value of thrombo-cyte α2-adrenoceptor density ever reported in the literature. From our experimental experience, treatment of intact thrombocytes with hypotonic buffer alone is insufficient to obtain complete lysis and, thus, a homogeneous membrane preparation. Additional more vigorous methods (i.e., shock-freezing) should be employed and the results checked by light microscopy [13]. An incomplete disruption and staining of cell fragments by the Lowry reagent could have influenced the results of both groups to a different extent. The relatively high nonspecific binding (20% at 5 nM) could also be a consequence of incomplete cell lysis. Therefore, these interesting, unique results concerning α2-adrenoceptor density should be repeated by assaying intact cells or using additional membrane preparation procedures.

References


269