Thrombocyte Alpha-2-Adrenoceptors and Hypotension in Hemodialyzed Patients

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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 α_1 -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] α_1 -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 ± 18 mm Hg prior to and 66 ± 13 mm Hg (mean $\pm$ SD) after hemodialysis, we determined an α_2 -adrenoceptor density of 192 ± 75 versus 246 ± 110 fmol/mg protein in hemodynamically stable patients ($n = 6$). Receptor density was assayed by 3H -rauwolscine 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 α_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

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Table 2. α_1 -Adrenoceptor densities and radioligand equilibrium dissociation constants (K_d) determined in human platelet membranes by using the antagonists 3H -

Bmas, fmol/mg protein

Radioligand Reference

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 hypo-tensive state as suggested by our own studies on symptomatic hypotensive hemodialyzed patients [14]. fmo/mg protein for the hemodynamically stable patients represents, as far as we know, the lowest standard mean value of thrombo-cyte α_2 -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 α_2 -adrenoceptor density should be repeated by assaying intact cells or using additional membrane preparation procedures.

221

148

144

180

114

188 yohimbine (Yoh) and , 7^

³/₄-rauwolscine 239

(Rau) 191

507 157

Brodde et al. [4] Cheung et al. [5] Cheung et al. [5] Daiguji et al. [6] Daul et al. [2] Garcia-Sevilla et al. [7] Limbird et al. [8] Lübbecke et al. [9] Mukherjee et al. [10] Neubig et al. [11] Sakaguchi et al. [12]

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