Results of Antithrombin III Treatment in Patients after Kidney Transplantation

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Dear Sir,

Acute local intravascular coagulation is common in kidney transplant rejection [1–3]. Mostly in hyperacute rejection the pathogenetic importance of intravascular coagulation in kidney damage could be demonstrated [4, 5]. It has also been shown that antithrombin III (AT III) levels rose during the rejection process before clinical signs were noticed [6]. The raised levels of AT III during transplant rejection might reflect an acute phase response to the rejection process. Also, as the role of this protein is to protect against intravascular thrombosis, the raised levels early in and throughout the rejection period might reflect a response by the body to supply an enhanced antithrombotic potential to protect the blood supply of the transplanted organ by diminishing glomerular fibrin deposits [6]. According to this a therapy with AT III could imitate the natural defense reaction and could have a protective effect on kidney function. Therefore, the effect of AT III treatment had been studied in 51 patients undergoing kidney transplantation. In 14 patients the vascular system of the transplanted kidney was perfused with 2,000 U AT III (Kybernin; Behring, Marburg) before implantation. In 15 patients additionally to the AT III perfusion a daily intravenous AT III treatment of 1,000 U was performed until the onset of an urine flow above 500 ml/day, while the remaining 22 patients served as a control group. The shortest duration of intravenous treatment was 3 days, the maximum was 28 days. The mean duration of AT III therapy was 10.3 ± 8.1 days. The three patient groups did not differ in age, sex, underlying renal diseases, warm and cold ischemia times and in the number of mismatches. In table 1 the duration of oligoanuria, the number of necessary hemofiltrations after transplantation and the number of detected transplant rejections are shown. The duration of oligoanuria and the Table I. Number of days of oligoanuria, of necessary hemofiltrations and of rejection episodes after kidney transplantation in the 3 groups; in the lower part mean values of AT III during the first 28 days after transplantation are shown (* $p < 0.05$).

Control	AT III	AT III
group	perfusion	perfusion
(n = 22)	(n = 14)	and i.v.
treatment		
(n = 15)		

Oligoanuria, days

12.3 10.6

11.4 6.3

10.3 8.1

Hemofiltration, n

5.5 4.4

5.0

2.8

4.3

3.5

Rejections, n

12

5

3*

pre-OP

115 ± 23

101 ± 18

100 ± 17

Post-OP

93 ± 18*

87 ± 18*

87 ± 18

Days post 1

86 ± 20*

81 ± 13*

89 ± 17

2

91 ± 22*

81 ± 8*

92 ± 22

5

103 ± 18

91 ± 11

116 ± 17

7

113 ± 21

107 ± 16

121 ± 16

12

123 ± 24

120 ± 21

130 ± 21

15

125 ± 24

118 ± 16

127 ± 24

18
 119 ± 23
 117 ± 12
 124 ± 25
 21
 119 ± 15
 120 ± 20
 121 ± 18
 28
 119 ± 19
 121 ± 24
 108 ± 20

number of performed hemofiltrations after kidney transplantation did not differ in the 3 groups. Therefore, the acute renal failure after transplantation could not be influenced by the both therapy regimens. But the number of rejections was significantly lower in the group with intravenous AT III treatment as compared to the control group ($p = 0.047$, according to Fisher's exact test). In the control group, rejection occurred in 12 of 22 patients, in the AT III perfusion group in 5 of 14 patients and in the AT III perfusion and intravenous treatment group in 3 of 15 patients.

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The AT III levels (measured with the chromogenic substrate S-2238; KabiVitrum, Stockholm) in the 3 groups are shown in table 1. The intravenous AT III treatment prevented the significant decrease of AT III found in the two other groups during the first 2 days after transplantation. (After testing for normality (W test, Shapiro and Wilk) the t test was used.) A reason for the failing in shortening the acute renal failure after transplantation might be the late start of therapy because ischemic kidney damage occurs during explantation. Therefore, AT III perfusion should be done immediately after explantation. In our study, AT III perfusion was performed before implantation. In contrast, in animal models of acute renal failure an early AT III treatment led to a protective effect of kidney function [7, 8]. An AT III perfusion was successfully performed in the transplantation of microvascular anastomized forearm cutane laps [9]. The authors explained the positive effect by a diminished number of thromboses in the transplant. But in this study the intravenous AT III treatment lead to a reduction of rejection episodes. The intravenous AT III treatment after transplantation might have diminished kidney damage by intravascular coagulation and therefore might have avoided the manifestation of kidney rejection in some patients. These results need to be confirmed in more patients and further studies are in progress.

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