Increased Incidence of Cerebral Hemorrhage Mortality in Patients with Analgesic Nephropathy on Hemodialysis

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Dear Sir,

Analgesic nephropathy (A) is a serious problem in Belgium with an incidence of 18,4% of patients with end-stage renal failure [1]. We wish to report here a retrospective autopsic analysis of 75 hemodialyzed patients: 12 with A and 63 with nonanalgesic nephropathy (NA). The results of this study showed a significantly higher incidence of cerebral hemorrhage as a cause of death (table I) in the A group: 25% (3/12) as compared to 3% (2/63) in the NA group. (Yates corrected $\chi^2 = 4.43$, $p < 0.025$). The mean age at death of patients was comparable in both groups: 51 ± 12 years in the A and 56 ± 11 years in the NA group. Female preponderance, as already described [2], was observed in the A group with a female/male ratio of 75% as compared to 38% in the NA group ($\chi^2 = 5.57$, $p < 0.025$).

In order to explain the reasons of such a higher incidence of cerebral hemorrhage, various autopsic (left ventricular thickness, aortic and coronary atherosclerosis appreciated macroscopically – (score 0–5) -, presence of acute or healed myocardial and cerebral infarction) and clinical parameters (blood pressure before and during hemodialysis treatment and analysis of the clinical causes of death of patients with A on hemodialysis dying during the same period, but not autopsied) were compared in each group.

First, the analysis of the blood pressure levels prior to the start of hemodialysis treatment showed no difference between both groups in the relative number of patients presenting hypertension (74% in the A vs. 83% in the NA group), in the severity (17% of the A group patients presented a blood pressure $> 200/120$ mm Hg as compared to 18% in the NA group), and in the duration of hypertension (42% of the A group patients were known to have blood pressure levels $> 160/95$ mm Hg for at least 2 years as compared to 49%) in the NA group).

Second the thickness of the left ventricle of the A group patients, measured at autopsy, showed values similar to that of the NA patients (1.90 ± 0.18 vs. 1.94 ± 0.18 cm). The relative percentage of analgesic patients presenting severe aortic atherosclerosis (score 4–5)

Table I. Causes of death

Causes of death

NA

N

autopsied	
%	
N	
nonautopsied	
%	
autopsied	
%	
N	
nonautopsied	
N	
%	
85	
12	
17	
100	
100	
100	
100	
Cerebral	
Hemorrhage	
Other Cardiopulmonary Neoplasia	
Kidney, Bladder	
Other Suicide, dementia Other, unknown	
Total	

168
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was 25% and that of the patients presenting severe cerebral atherosclerosis was 17% as compared to 34 and 21%, respectively, in the control group. Moreover, the relative number of patients presenting at autopsy either an acute or healed myocardial infarction (25 vs. 24%, respectively) was not statistically different. However, a greater incidence of cerebral infarction was observed in the A group (43 vs. 25% in the NA group). This last observation, even though not reaching statistical significance, added to the female preponderance in the A group could be an argument in favor of a greater degree of atherosclerotic involvement in this group, as already shown [3].

Third, the analysis of mortality data (table I) in patients on hemodialysis with A (n = 17) and NA (n = 85, table I), dying during the same period of study but not autopsied, showed 5 deaths due to suicide and dementia: 17% (5/12 + 17) in the first group (autopsied and nonautopsied patients) and 2.7% (4/85 + 63) in the second (Yates' corrected $\chi^2 = 12.71$, $p < 0.0025$). This suggests a persistent toxicomania with persistent analgesic consumption in A patients even during hemodialysis treatment. Similar psychiatric disorders (introversion, neurosis, and denied continued analgesic ingestion) have been previously described by Murray [4] and Murray et al. [5].

In conclusion, one of the leading causes of death in patients with A on hemodialysis appears to be cerebral hemorrhage. Such a high incidence could be explained by a greater vascular fragility due to a more severe hemor-rhagic diathesis (persistent analgesic consumption and systemic heparinization during hemodialysis), added to a probably more severe atherosclerotic involvement.

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