Continuous Ambulatory Peritoneal Dialysis Improves Immunodeficiency in Uremic Patients

F.		Giacchino
F.		Quarello
M.		Pellerey
G.		Piccoli

Medical Nephrology Institute of the University, Nephrology and Dialysis Unit, San Giovanni Hospital, Turin, Italy

F. Giacchino, MD, Nephrology and Dialysis Unit, San Giovanni Hospital, Largo Gottardo 143, I-10154 Turin (Italy)

Dear Sir,

The high incidence of infections and malignancies in uremic patients [1, 2] is a clear indication of the immuno-suppressive effect of uremia [3–5].

Numerous hypotheses have been put forward, including protein-calorie malnutrition [6], vitamin deficiency [7], and lowered blood zinc levels [8], but so far none of them has proved satisfactory. A more recent suggestion is that serum factors (medium molecular weight) may be responsible for this phenomenon in vitro [9], and in experimental animals [10]. There is still considerable debate however, as to whether middle molecules play a toxic role in cell-mediated immunity in man [11].

In order to evaluate the effect of different degrees of removal of middle molecules by dialysis treatment on cellular immunodeficiency, we analyzed the immunological state of 60 uremic patients treated by continuous ambulatory peritoneal dialysis (CAPD) and hemodialysis (HD) during a follow-up of 12 months.

30 healthy people were also studied as controls. DNCB and PPD skin tests, E- and active E-rosettes, the E-rosette inhibition assay were investigated as markers of cellular immunity [12]. The results of our study are summarized in table I. CAPD patients showed an improvement in cellular immunity, with a significant increase in the E-rosette count ($p < 0.01$), and improved delayed hypersensitivity reactions 3 months after treatment was started, while no difference was observed in HD patients. The most compelling evidence for a role of middle molecules in cell-mediated deficiency has been provided by the E-rosette inhibition test. Serum from CAPD patients showed a significant reduction of the percentage of E-rosette inhibition ($p < 0.02$), even 1 month after treatment was started, and the results were confirmed at the following controls. In the HD patients the percentage of inhibition remained high throughout our study.

Our results are in agreement with previous findings in vitro and in animals [9, 10]. Since CAPD removes middle molecules more satisfactory than hemodialysis [13], and Table I. Cellular immunity in CAPD and HD patients

CAPD (25) a

b

c
 HD (35) a
 b
 c
 Controls (30)
 DNCB positive %
 24(6)
 36(9)
 48 (12)
 28.6 (10)
 28.6 (10)
 23(8)
 96
 DNCB negative %
 76 (19)
 64 (16)
 52 (13)
 71.4 (25)
 71.4 (25)
 77 (27)
 4
 PPD positive %
 40 (10)
 40 (10)
 52 (13)
 37 (13)
 37 (13)
 37 (13)
 78
 PPD negative %
 60 (15)
 60 (15)
 48 (12)
 63 (22)
 63 (22)
 63 (22)
 22
 E-rosettes %
 26 ± 12
 41 ± 7*
 45 ± 8*
 27 ± 9
 28 ± 6
 24 ± 4
 56 ± 10
 Percentage of inhibition

76 ± 11
33 ± 9**
34 ± 5**
77 ± 9
73 ± 12
74 ± 11
10 ± 5

*p < 0.01 vs. value before treatment; **p < 0.02 vs. value before treatment.

a = Before treatment was started; b = 3 months after treatment was started; c = 12 months after treatment was started.

Number of patients per group shown in parentheses.

210

Giacchino/Quarello/Pellerey/Piccoli

since cell-mediated immunity improves in subjects treated by CAPD, it seems extremely likely that middle molecules have an immunosuppressive effect. The significance of this in terms of resistance to infections and malignancy needs further study.

References

- Miach, P.J.; Dawborn, J.K.; Xippel, J.: Neoplasia in patients with chronic renal failure on long-term dialysis. *Clin. Nephrol.* 5: 101–104 (1976).
- Traeger, J.; Touraine, J.L.; Navarro, J.; Freyria, J.; Contreras, P.: Immunodeficiency in chronic renal insufficiency. *Proc. Eur. Dial. Transpl. Ass.* 17: 375–381 (1980).
- Boulton-Jones, J.M.; Vick, R.; Cameron, J.S.; Black, P.J.: Immune responses in uremia. *Clin. Nephrol.* 1: 30–35 (1973).
- Hoy, W.E.; Cestero, R.V. M.; Freeman, R.B.: Deficiency on T and B lymphocytes in uremic subjects and partial improvement with maintenance hemodialysis. *Nephron* 20: 182–187 (1978).
- Giacchino, F.; Alloatti, S.; Quarello, F.; Bosticardo, G. M.; Giraudo, G.; Piccoli, G.: The immunological state in chronic renal insufficiency. *Int. J. artif. Organs* 5: 237–242 (1982).
- Law, D.K.; Dudrick, S.J.; Abdou, N.I.: The effect of dietary protein depletion on immunocompetence: the importance of nutritional repletion prior to immunological induction. *Ann. Surg.* 179: 168–173 (1974).
- Dobbelstein, H.: Immune system in uremia. *Nephron* 17:409–415 (1976).
- Golden, M.H.N.; Golden, B.E.; Harland, P.S.E.G.; Jackson, A.A.: Zinc and immunocompetence in protein-energy malnutrition. *Lancet* i: 1226–1227 (1978).
- Touraine, J.L.; Touraine, F.; Revillard, J.P.; Brochier, J.; Traeger, J.: T lymphocytes and serum inhibitors of cell-mediated immunity in renal insufficiency. *Nephron* 14: 195–208 (1975).
- Navarro, J.; Touraine, J. L.; Corre, C.; Traeger, J.: Prolongation of skin allograft survival and inhibition of graft versus host reaction in rodents treated with middle molecules. *Cell. Immunol.* 31: 349–354 (1977).
- Bergström, J.; Furst, P.; Zimmerman, L.: Uremic middle molecules exist and are biologically active. *Clin. Nephrol.* 19: 229–238 (1979).
- Giacchino, F.; Belardi, P.; Coppo, R.; Quarello, F.; Picolic, G.: Effects of blood transfusion on cellular immunity. *Proc. Eur. Dial. Transpl. Ass.* 18: 465–468 (1981).