Prospective Effect of Norepinephrine Infusion in Acute Renal Insufficiency Induced by Interleukin 2 Therapy

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Dear Sir,

Adoptive immunotherapy using recombinant interleukin 2 (IL2) (Eurocetus) and $\alpha 2b$ recombinant inter-feron (IFN) (Unicet) with lymphokine-activated killer cells has recently been demonstrated to have an antitumor effect in humans [1]. Unfortunately, many side effects are observed, specially hypotension and prerenal azotemia [2, 3], which lead to compromising the dose of IL2 and patients' tolerance.

14 patients with metastatic renal carcinoma were treated with IL2 (4 MU/m²) and IFN (5 MU/m²) given as bolus injection every 8 h for 5 days. All the patients received ketoprofen and paracetamol to control fever, metoclopramide and atropine diphenoxylate as symptomatic treatment for vomiting and diarrhea, and systematic antibiotherapy to prevent infection. If necessary, albumin and dopamine were used. Furosemide was added in case of excessive weight gain.

The first 9 patients treated have developed severe side effects. Despite dopamine (mean 5 $\mu\text{g/kg/min}$) and a mean weight gain of 3.5%, systolic blood pressure (SBP) was measured at least once below 80 mm Hg during 20 days in 5 patients; 6 patients developed severe acute renal failure (plasma creatinine > 350 $\mu\text{mol/l}$) and 1 patient needed hemodialysis.

Norepinephrine is used to treat hemodynamic septic changes when vascular filling and dopamine have failed [4]. Because hemodynamic changes mimic septic shock [5] and, furthermore, hypotension and oliguria are poorly responsive to dopamine vasopressor support, we tried to minimize SBP drop and prerenal acute failure by norepinephrine perfusion. 5 successive patients were treated with the same protocol as described above but norepine-

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100 -i

Fig. 1. Daily creatinine clearance for 10 days in relationship to norepinephrine perfusion during IL2 + ITF infusion.

phrine (0.05–0.30 µg/kg/min) was infused when SBP decreased below 80 mm Hg or when an onset of acute renal failure occurred. The injected dosages of IL2 and IFN were comparable. However, SBP was measured below 80 mm Hg at least once during 10 days only in 3 patients. No patient had a serum creatinine level above 350 µmol/l. In Figure 1 daily creatinine clearance in these two groups of patients is shown during the days following initiation of therapy. Norepinephrine is able to treat hypotension and to increase renal function in patients receiving IL2 and IFN infusion for metastatic renal carcinoma and systemic addition of this drug will allow to administer higher dosages of the two lymphokines.

References

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