

Is the interaction between ticlopidine and cyclosporin dose related? Report of three cases

Ticlopidine is an effective anti-platelet agent used for prevention of thrombosis (1–3). It was reported that treatment with ticlopidine at the dose of 250 mg daily in kidney transplant patients caused significant reduction of cyclosporin A (CsA) blood levels (4, 5). In heart transplant patients treated with higher doses of ticlopidine 500 mg daily, it was found to cause significant decrease of cyclosporin concentration but not in those treated with only 250 mg daily (1, 2). It was thought that ticlopidine interacts with cyclosporin metabolism at cytochrome P450 (1–3).

We report three living kidney donor recipients whose blood level of cyclosporin decreased significantly under treatment with a very low dose of ticlopidine of 100 mg daily.

The patients were on immunosuppressive treatment with steroids, CsA, and mycophenolate mofetil (MMF) or azathioprin. The total daily CsA dose was 125–150 mg. The patients developed severe hypertension 15 days to 4 months after kidney transplantation. Serum creatinine was normal except in patient number 2 (Table 1). Doppler ultrasonography confirmed significant stenosis of at least 70% degree in the artery of the transplanted kidney. Percutaneous transluminal angioplasty (PTA) with stent placement was performed. Anti-platelet treatment with aspirin (160 mg/day) and ticlopidine (100 mg/day) were given to prevent thrombosis. CsA blood levels were monitored by C_0 (before morning dose) (Fig. 1). Under ticlopidine treatment, CsA blood levels decreased in patient 1 from 137 to 112 ng/ml, in patient 2 it

Table 1. Characteristic of three patients with kidney transplantation and renal artery stenosis

Characteristics	Patient 1	Patient 2	Patient 3
Age (years)	18	26	20
Gender	F	M	F
HLA mismatch	3	3	3
Serum creatinine (mg/l)	8.5	15.4	7.1
Number of anti-hypertensive drugs	3	4	3
Diagnosis of stenosis after transplantation	2 months	15 days	4 months
Date of PTA	2 months after the diagnosis	14 months after diagnosis	2 months after the diagnosis

Note: PTA, percutaneous transluminal angioplasty.

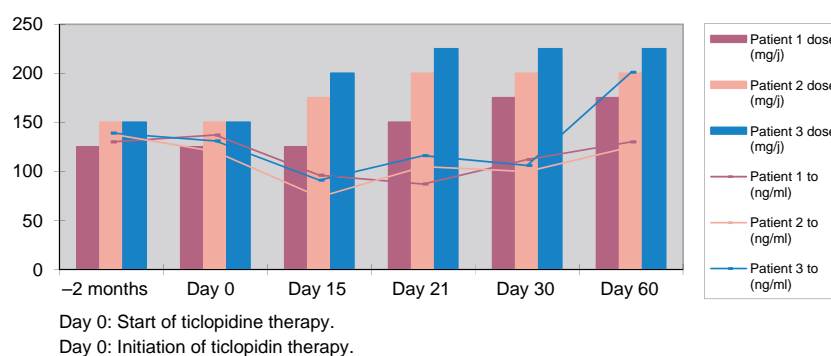


Fig. 1. Cyclosporin A blood levels (C_0) and doses during 60 days of ticlopidine therapy: follow of blood CsA levels and doses in the three patients.

decreased from 120 to 100 ng/ml, and in patient 3 it decreased from 131 to 106 ng/ml. Consequently CsA dose had been increased by 50–75 mg/day. No signs of acute kidney transplant rejection were observed.

In summary: In kidney transplant patients, ticlopidine can cause a significant decrease in CsA blood level even at a low dose of ticlopidine. The interaction of ticlopidine with CsA seems to be not related to the doses. We recommend careful monitoring of CsA blood level in patients treated with ticlopidine.

Tarik Sqalli Houssaini
Nephrology department
Ibn Sina University Hospital
Rabat, Morocco
Email: tariksqalli@hotmail.com

*Asmaâ Laboudi, Hakima Rhou, Fatima Ezzaïtouni,
Loubna Benamar, Naïma Ouzeddoun, Rabea Bayahia*
Nephrology department
Ibn Sina University Hospital
Rabat, Morocco

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