

Editorial

Food allergy in pediatric liver transplant recipients: Harmful or harmless?

We read with great interest the paper by Ozdemir et al. (1) on development of multiple food allergies in two children taking tacrolimus after heart and liver transplantation in the May issue of *Pediatric Transplantation*. The paper emphasized the association of transplantation and allergic disease as reported recently by several authors (2–6).

These authors reported liver transplant acquired food allergy. The etiology of this phenomenon is at present unclear; it has been ascribed, by some authors, particularly to tacrolimus (Tac) treatment (4, 5), and by others to cyclosporine (CsA) use as well (6).

Although the onset of allergic symptoms in transplanted children has been widely described, to our knowledge, there has not been any investigation of the influence that food allergy could exercise on management of the immunosuppressive therapy.

We presented a poster at the third Congress of the International Pediatric Transplant Association (Innsbruck, 6–9 August, 2005) to highlight this issue (7).

We retrospectively reviewed the clinical and laboratory data of 24 patients admitted to our Liver Disease Unit who underwent orthotopic liver transplantation for biliary atresia ($n = 18$), Byler disease ($n = 3$), diffuse angiomatosis ($n = 1$), tyrosinemia type I ($n = 1$), and hyperacute hepatic failure ($n = 1$).

The sample was divided into two groups: the first group (mean age 7.90 ± 4.44 yr, range 2.42–18.33 yr, five males) was composed of 12 patients who displayed food allergy before orthotopic liver transplantation (OLT). The second group (mean age 12.49 ± 5.49 yr, range 1.33–21.42 yr, six males) was composed of 12 patients whose clinical histories for food allergy and allergic tests before transplantation were negative.

The foods to which the children reacted included egg (three patients), cow's milk (eight

patients), and soy (one patient); all foods are known to cause allergic reactions. The symptoms were diarrhea (five patients), eczema (five patients), and failure to thrive (two patients). Reproducibility of the reaction was demonstrated by recurrence of clinical episodes in 10 of 12 children.

In the group of allergic children, a dietetic regime was prescribed in order to avoid the allergenic food. In all patients (allergic and non-allergic ones), the Tac and CsA serum blood levels were monitored at 6, 12, 18, and 24 months and their levels were maintained at 7–10 ng/mL and 200–400 ng/mL respectively.

Six allergic patients received Tac and six patients received CsA; four non-allergic patients received Tac and eight received CsA. In the allergic patient group, Tac and CsA were administered orally, with a mean dose of 0.12 ± 0.1 mg/kg/day and 10.7 ± 3.2 mg/kg/day, achieving a serum level of 5.06 ± 1.6 ng/mL of Tac and 239.1 ± 129.3 ng/mL of CsA respectively. In the non-allergic patient group, the mean dose of Tac and CsA for achieving serum levels of 5.1 ± 0.9 ng/mL and 268.2 ± 57.1 ng/mL were lower (0.08 ± 0.05 mg/kg/day for Tac and 8.1 ± 3.5 mg/kg/day for CsA).

At the end of the follow-up, in the allergic patient group, we noted that, following correct dietetic regime, Tac and CsA serum levels increased significantly, dictating the need to gradually taper the initial dose in order to maintain the above suggested levels.

We also observed that new onset of food allergy in the non-allergic group (four of whom were on Tac therapy and eight on CsA therapy) developed in only one patient during the two yr of follow-up. Therefore, the phenomenon of food allergy development after liver transplantation was uncommon in our series.

Previous reports in the literature suggests that food allergy should be screened for in pediatric

liver transplant patients in order to avoid adverse food reactions, but, to our knowledge, the possible role of the allergy in the management of the immunosuppressive therapy has not previously been detailed.

We assume that the alteration of gastrointestinal mucosal barrier may influence immunosuppressive blood levels. The intestinal mucosal barrier and mucosal immunity is impacted in food allergies (8). As the intestine plays an important role in the metabolism of immunosuppressive drugs, integrity of the intestinal membrane is essential to ensure correct absorption of immunosuppressive agents in order to avoid changes in drug bioavailability.

Our results show that allergic patients need higher doses of Tac and CsA compared with non-allergic patients to ensure that serum concentrations are in a safe therapeutic range. After an appropriate elimination diet, such patients need a lower drug dose to maintain the same drug level and doses and levels become similar to those of non-allergic patients.

Certainly, lower doses of immunosuppressive agents reduce adverse side effects (9); therefore, it is important that patients and their caregivers are educated about food allergen avoidance and recognition of allergic symptoms.

We think that dietetic treatment of transplanted allergic children is indicated not only to avoid allergic symptoms and life-threatening events, to positively affect the process of growth and development, but also to improve the immunosuppressive therapeutic management.

Immunosuppressive dosing in pediatric transplant recipients is complex, and the finding that food allergy impacts on drug dosing is an important observation. This association provides support for prospective studies of individualized immunosuppressant drug dosing in transplant patients based on the presence or absence of food allergy.

Our preliminary data indicate the need for longitudinal studies about the possible role of the allergy in the management of the immunosuppressive drug therapy in pediatric liver transplant recipients.

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