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PP11
ORAL TACROLIMUS TO INDUCE CLINICAL AND ENDOSCOPIC IMPROVEMENT IN STEROID-REFRACTORY ULCERATIVE COLITIS (UC)

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Background. Calcineurin inhibitors (cyclosporine and tacrolimus) are used in the treatment of solid organ transplantation and in the prophylaxis of organ rejection in allogenic liver or kidney transplantation. Bousvaros et al. [1] reported the results obtained in a multi-centre trial with oral tacrolimus in severe paediatric UC and Crohn's Disease not responding to conventional therapy.

Aim. To evaluate the efficacy of oral tacrolimus in steroid-refractory severe colitis. We defined as steroid-refractory, patients who initially responded to steroids but later relapsed during tapering and required the reintroduction of steroids to maintain symptom control.

Patients and methods. We enrolled four patients (pts, 6–8 years old) with a new onset of severe UC (PUCAI score at admission 72 ± 11.9). Each pt had failed induction-therapy with steroids. Diagnosis of UC was confirmed in all pts using clinical, endoscopic and histologic criteria. Modified Endoscopic Baron Score was about 3–4 point scale at start with a pancolitis extension of the disease. Pts received tacrolimus 0.1 mg/kg/dose twice daily with goal plasma levels of 7–10 ng/ml. All pts received prophylaxis for pneumocystis carinii pneumonia with trimethoprim-sulfamethoxazole. A positive response was defined after 2 weeks because of improvement of the PUCAI score. Patients who responded continued to receive tacrolimus for 3 months and if clinical remission was obtained, they were shifted to azathioprine for maintaining remission.

Results. A significant improvement of the PUCAI score was obtained in all pts (PUCAI score 11 ± 10) after 2 weeks. The modified baron endoscopic score was 0–1 point scale in all patients after 3 weeks. No significative adverse effects were reported.

Conclusions. Our findings demonstrate that low-dose oral tacrolimus can be considered as an alternative therapy to infliximab or intravenous cyclosporine in moderate steroid refractory CU. It could be considered a bridge-therapy for inducing remission and to begin AZA. No long-term benefit was shown in this study but only short-medium remission. Randomized and controlled trials are still necessary to confirm these results.

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PP12
IMPACT OF AGE IN PHENOTYPE OF THIOPURINE METHYLTRANSFERASE

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In subjects with Chron's disease and autoimmune hepatitis, remission is often maintained by the use of thiopurine drugs, in patients of all age. They are catabolized by cytosolic thiopurine methyltransferase (TPMT), which is subject to a genetic polymorphism. For many other drug-metabolizing enzymes is demonstrated the impact of age on enzyme activity. These phenomena influence the correct dosage of related therapy and the induction of well-known side effects. Few publications studying the impact of age on TPMT activity are available and are on limited samples, with discordant conclusions.

The aim of this study was, therefore, to evaluate whether age influenced the TMPT activity. After informed consent, the TPMT genotype and phenotype were determined in an unrelated population of 373 healthy young Caucasian children and 571 healthy adults (blood donors). The cohort was evaluated for the presence of the four most common defective alleles (TPMT*2, TPMT*3A, TPMT*3B and TPMT*3C). The adults had a 21.4 U/gHb median TPMT activity, which ranged from 0.0 to 72.0 U/gHb. Average activity was 22.6 U/gHb without a significant difference between gender. The children had a 23.5 median TPMT activity, which ranged from 8.8 to 75.2. The frequency distribution, both in adults and children, was compatible to a polymorphic distribution. All the subjects with a variant TMPT allele showed a reduced enzymatic activity.

A wild genotype was found in a total of the 534 adults and in 358 of the children. Therefore, these subjects made up our study population.

The TPMT activity in the children had a median value of 23.8 U/gHb, ranging from 8.8 U/gHb to 75.2 U/gHb. The average activity was 26.1 U/gHb, without a significant difference between gender.

The median of the adult subjects was 21.9 U/gHb min 8.3 max 72.0 with an average of 23.1 U/gHb.

The children were grouped according to age. Group 1: 74 subjects 0–2 years had a median TMPT activity of 26.7 (range 10.2–51.7) U/gHb with an average of 28.3. Group 2: 74 subjects 3–5 years had a median TMPT activity of 24.8 (range 11.1 to 49.1) U/gHb with an average of 25.8 U/gHb. Group 3: 95 subjects 6–9 years had a medium TMPT activity of 22.4 (range 11.6–75.2) U/gHb with a average of 25.8 U/gHb. Group 4: 84 subjects 10–13 years had a median TMPT activity of 23.1 (range 8.8 to 59.2) U/gHb with an average of 25.3 U/gHb. Group 5: 31 children 14–17 years had a median TMPT activity of 21.8 (range 12.7–61.2) U/gHb with a average of 24.5 U/gHb.

Although the difference in the TMPT activity between the adults and children was statistically significant, the ample enzymatic variability at all ages, also in subjects with a wild genotype, demonstrate that determining the TMPT activity is fundamental for the detection of subjects at risk of thiopurine toxicity.

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PP13
ROLE OF DESAMETHASONE 21P LOADED ON RED BLOOD CELLS IN THE THERAPY OF PAEDIATRIC ULCERATIVE COLITIS

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Introductions and aim. Some patients with ulcerative colitis (UC) unresponsive to standard therapy become dependent from oral corticosteroids. In spite of the efficacy, long-term use of steroids is limited by very important side effects, including failure to thrive and bone demineralisation, especially in children. Recent studies demonstrated that dexamethasone, the most used steroid in UC, can be loaded on reed blood cells (RBC) and used as successful therapy for Crohn's disease (CD) in children and in adult affected by CD and UC. Aim of this study is to demonstrate if autologous Red Blood Cells, loaded with Desamethasone 21P (dex 21P) and reinfused to the same patient, can be a safe and efficacious therapy to maintain remission also in paediatric mild-severe, steroid-dependent ulcerative colitis.

Materilas and methods. All paediatric patients with steroid dependent UC without concomitant pathologies, were admitted to the study. Infusions of RBC DEX 21P were performed about every four weeks. Seven patients performed MOC–DEXA at the beginning of therapy and 4 repeated the exam after about 12 months. Blood pressure, heart rate and CAI was periodically controlled.

Results. Ten patients (M = 4, F = 6) mean age 16.4 ± 4.7 years, mean interval from UC diagnosis and starting date of therapy with RBC loaded with Dex 21-P was 9.61 ± 4.44 years. Mean CAI before starting this therapy was 6.6 ± 3.4; while assuming a mean dose of oral steroids 9 ± 4,6 mg/die. All but two patients could taper and completely discontinue oral steroids therapy. CAI value decreased at 6, 12 and 18 months respectively to 3.5 ± 2.88; 3 ± 3.9 and 1 ± 2. Three patients (30%) required periodic treatment with oral or local steroids enemas and two of them, that could not discontinue steroid therapy, required surgery. Only three patients performed therapy with loaded RBC for a longer period than 18 months and their CAI at that time was 0. Mean infusions per patient were 16 ± 9. Mean Dex 21-P administered by RBC was 8.8 mg (range 2.4–14.7) for each infusion. Blood pressure and heart rate after RBC infusions resulted within the normal range in all patients. Only one patient referred head each after infusion, but it did not seem related to infusion. Eight, weight and BMI did not show significant deviations from the attended values. MOC- DEXA value at the start was 1.17 ± 1.9; in four (40%) patients MOC- DEXA was repeated after about 12 months after beginning and mean value was decreased to 1.4 ± 0.4. No side effects were registered during the whole period of therapy.

Conclusion. We can conclude that therapy with monthly infusions of autologous RBC Dex 21P can be considered an efficacious and safe therapy for maintenance of mild steroid dependent UC in paediatric patients.

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PP14
SELF-CONCEPT AND PSYCHOPATOLOGICAL RISK IN LIVER TRANSPLANTED CHILDREN

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Aims. Increased recipients' life expectancy in children undergoing orthotopic liver transplantation (OLT) has triggered several studies focussing not only on organic problems but also on neurological and psychological aspects.

Aim of the present study is to assess psychopatological risk and self-concept in liver transplanted children as