Poster

[P26-5] P26-5: Immunosuppressive drugs (4): Individualized dosage adjustment

Chair: Kohshi Nishiguchi, Japan

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[P26-5-7] Sublingual tacrolimus administration: experience in pediatric liver transplant patients

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Background

Tacrolimus (FK) products include capsules and intravenous formulations. However, young children usually have difficulties in swallowing the capsules. Especially after surgery, oral route is contraindicated by gastrointestinal failure, digestive motility troubles or septic shock. Furthermore, post-transplant patients are under sedoanalgesia (SA) and with mechanical ventilation support(MV). FK suspension has low stability and intravenous FK is toxic and only useful for a few days. Therefore, sublingual (SL) administration was the chosen route to achieve therapeutic levels and to avoid early graft rejection in these patients. We aimed to describe our experience withSL FK administration in hospitalized pediatric patients who could not swallow due to age, MV and/or SA, during their stay in the intensive care unit (ICU).

Methods

A retrospective analysis including pediatric patients with biliary atresia transplanted in 2014-2015 immediately after post-transplantation was carried out during hospitalization at the ICU. Trough FK levels (C0), adverse events, clinical, biochemical parameters and drug-drug interactions were recorded. FKC0 normalized by dose were compared before and during concomitant administration of interacting drug (steroids, nifedipine and clarithromycin).Efficacy was evaluated by the occurrence of acute rejection (AR). Wilcoxon matched pairs test was used for statistical analysis.

Results

22 patients were included, with a median (range) follow-up and age of 22days(6-68) and 0.9years(0.6-6.3), respectively. Three AR and 3 adverse events (nephrotoxicity, hypomagnesemia and neurotoxicity) occurred during the study period. The median (range) daily dose and FK C0 was 0.11mg/kg(0.02-0.31) and 6.4ng/ml(2.0-23.2), respectively. During concomitant administration of clarithromycin, a significant increase was observed in dose normalized FKC0 ($p<0.05$).

Conclusions

We described safety and efficacy parameters of SL FK administration in hospitalized young pediatric liver transplant patients who had difficulties in swallowing the capsules due to sedoanalgesia and/or mechanical ventilation. According to FK C0 achieved, the present route of delivery was acceptable. The pharmacokinetic

behavior of FK after SL administration is currently being assessed prospectively in the described population. The results of this studycould be used in conjunction with therapeutic drug monitoringto optimize SL FKadministration and immunosuppressive treatment.