TDM and stabilization of pediatric patients in liver and kidney transplantation

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Introduction

Immunosuppressants therapy must be guided by therapeutic drug monitoring (TDM) to prevent rejection. Understanding and prevention of blood levels variability is essential to the success of liver and kidney transplantation. Our purpose was to evaluate TDM practices and factors associated with stabilization in pediatric hepatic and renal transplantation.

Material & Methods

Retrospective study of pediatric patients with liver (LT; since 2007) or kidney transplant (KT; since 2002) in two university hospitals.
Main outcome: first-month percentage of tacrolimus (FK) and cyclosporin (CyA) therapeutic trough levels (FK LT 10-15 ng/ml; KT 8-12 ng/ml / CyA KT 250-350 mcg/L).
Statistical analysis: 30-days survival analysis (median survival in days (d) [CI95%]) of stabilization (defined as discharge from intensive care or hospital, or three-consecutive therapeutic trough levels) and univariate analysis of associated factors in LT with stabilization (log-rank test).

Results

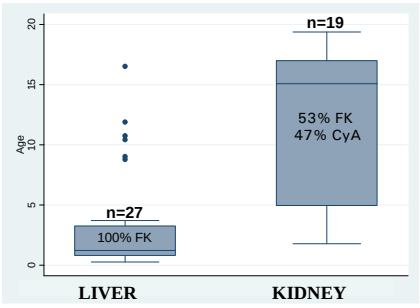

Figure 1. Age (year) distribution of transplanted children

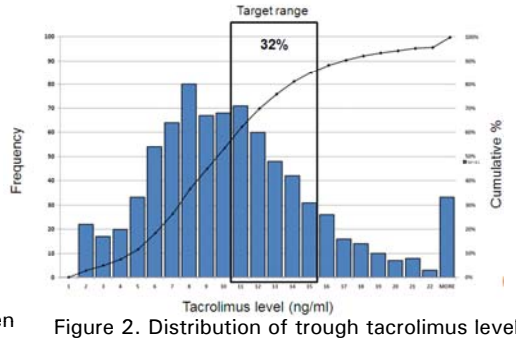

Figure 2. Distribution of trough tacrolimus levels for patients (n = 27) one month after liver transplantation

✓ 46 patients were included (figure 1)

✓ Only 32% (LT; figure 2) and 41% (KT) of FK trough levels, and 22% (KT) of CyA trough levels were in the range one month after tranplantation.

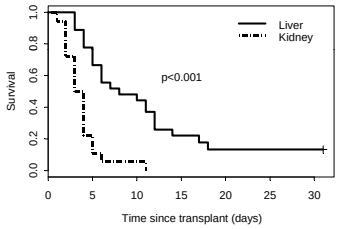

Figure 3. Discharge from intensive care

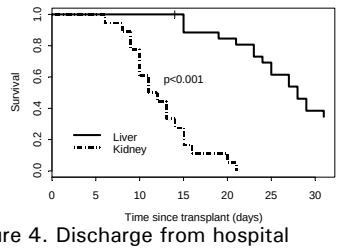

Figure 4. Discharge from hospital

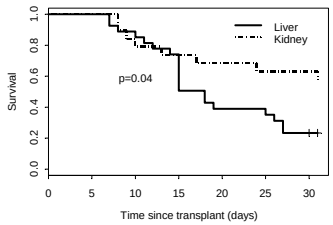

Figure 5. Trough levels stabilization

30-days survival analysis

✓ Discharge from intensive care and hospital occurred significantly later for LT month (8d (6;12) vs 3d (3;5) / 28d (25; no data) vs 11.5d (10;15), p < 0.001) (figures 3,4) but stabilization in terms of three-consecutive trough levels earlier) compared to KT (18d (15;27) vs not reached, p = 0.04 (figure 5).

✓ Compared to FK levels, CyA levels were not stabilized in KT patients after one month (not reached vs 20.5d [10; not available], p = 0.02), but no difference was seen on discharge.

Univariate analysis of associated factors with stabilization in LT

✓ Living donor transplant was significantly associated with an earlier discharge from intensive care (p = 0.02). Age < 30 years and transplant weight ≥ 291g were associated with a trend to earlier discharge from hospital (p = 0.048;resp. p = 0.06). Metabolic disease and weight-ratio transplant/patient ≥ 0.03 were associated with an earlier stabilization of FK levels (p = 0.01 resp. p = 0.05).

Conclusion

Immunosuppressant trough level variability was high in the first month after liver transplantation and in kidney patients receiving cyclosporin A. Associated factors with an earlier stabilization in liver transplantation have to be confirmed in a larger study.

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