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Risk Assesment of Adverse Effects of Immunosuppressive Drugs on Kidney Transplants: Experience of Pharmaco-Toxicology Service of University Hospital Center Hassan II Fes-Morocco

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Main Objective: Highlight the benefits of therapeutic monitoring of immunosuppresive treatment on kidney transplants in order to prevent on avoiding the risk of rejection, guarrantee efficiency and prevent toxicity.

Method: It is about a retroprospective study concerning pharmacologic therapeutic monitoring of immunosupressive drugs on kidney transplants followed in the Service of Nephrology of University Hospital Hassan II Fes, Morocco (January 2001-December 2018). The data was seized in Excel and treated by SPSS and R.

Results: It concerns 1000 samples in 35 kidney transplanted patients from mostly living donators with at least 50% compatibility, aged in average between 45 years ± 15,22 (18:75 years). The sex ratio was 2:5 (H=25, F=10).

The patients are mostly treated by Tacrolimus 58% against 40% under ciclosporine and 2% under Everolimus. The main side effects are infertility and gingival hypertrophy in 4 patients treated by ciclosporine. For Tacrolimus, we observed some side effects of induced diabetes (2 cases), one erectile dysfunction (1case), one gingival hypertrophy (2 cases) and shaking (2 cases) associated with hypomagnesimy. One patient showed a neoplasic side effect of Sarcom de Kaposi type, which we will talk about in detail in a clinical case. Three transplant rejection cases were noticed, one of which of medication origin (nephrotoxicity induced by the tacrolimus).

Some high immuno depression therapeutic concentrations were observed with 53% over dose and 43% under dose for Tacrolimus and 51% and 49% respectively for the ciclosporine. Some are related to pharmacocinethic interactions due to intake of other medication types such as antifongic, antagonist calcic and marcolid. In a patient under colchicine and ciclosporine, neuromuscular side effects were increased by pharmacodynamic interaction due to immunodepressor.

The analysis shows that there is no linear relation between the dosage and the residual concentration of the two immunosupressors. The calculation of the correlation coefficient of tacrolimus is very weak (r=0,27) and not significant (p=0,08). As for the ciclosporine, the coefficient of correlation was weak (r=0;4) and significant (p=0,001) and the coefficient of determination was r2=0.16, so 84% of the dosage variation is not explained by its relation to the residual concentration.

Conclusion: The implementation of a rigorous therapeutic pharmacologic monitoring is necessary for the assesment of the risk and the toxicity of high concentratations of immunosuppressive medication.