Tacrolimus is an immunosuppressant drug, calcineurin inhibitor, used after transplant organ as preventive and curative treatment. Therapeutic drug monitoring (TDM) is strongly recommended for this drug, because of its narrow therapeutic range, interpatient variability, drug interactions and toxicity depending on plasmatic concentration.

**Purpose**

We report the case of a transplant patient who did not achieve the target residual concentration (Cres) of tacrolimus.

**Background**

**Materials and Methods**

**Pharmaceutical analysis**

Despite tacrolimus dose adjustment, Cres was not reached.

**Results**

**Evolution of tacrolimus dosage and Cres**

Uncompliance and inappropriate samplings

Drug interactions in literature

- Tacrolimus + Ertapenem (same class as meropenem): increase of tacrolimus Cres\(^1\) excluded.
- Tacrolimus + Caspofungin: decrease of tacrolimus Cres during a 10-days co-administration\(^2\) insufficient to explain the very important decrease of the Cres

Pharmacogenetics: CYP3A5*3 allele

<table>
<thead>
<tr>
<th>Caucasian genotype</th>
<th>*3/*3</th>
<th>*3/*1</th>
<th>*1/*1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caucasian population</td>
<td>90%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dose of tacrolimus to introduce (mg/kg/day)(^3)</td>
<td>0.15</td>
<td>0.20</td>
<td>0.25</td>
</tr>
</tbody>
</table>

26th July: Mutation *3/*1 g.6986A>G

**Medical decision**

Replacement of tacrolimus by ciclosporin

**Conclusion**

Pharmacogenetics may explain some resistance to treatment occurrence. Characterization of the cytochrome 3A5 genotype can be a predictive means in tacrolimus dosage optimization allowing the achievement of effective Cres while avoiding toxic effects. Unfortunately, it is not always possible to wait for results because of their risk of transplant rejection.

It is important to raise awareness in the medical teams about pharmacogenetics.

References:

1. Drug interaction between tacrolimus and ertapenem in renal transplantation recipients, F.Bora, I. Aliosmanoglu, G. Suleymanlar et al, Department of General Surgery, Dicle University Medical Facility, Diyarbakir, Turkey, Available online 26 November 2012.


3. Pharmacogenetics may explain some resistance to treatment occurrence. Characterization of the cytochrome 3A5 genotype can be a predictive means in tacrolimus dosage optimization allowing the achievement of effective Cres while avoiding toxic effects. Unfortunately, it is not always possible to wait for results because of their risk of transplant rejection.

It is important to raise awareness in the medical teams about pharmacogenetics.