Objectives

- Potential interaction between tacrolimus and azole antifungals is often detected in the transplanted patients with fungal colonization or infection.
- To compare the influence of voriconazole and isavuconazole on the maintenance of plasma levels of tacrolimus and to analyze their safety.

Study Design

- A retrospective observational study that included all patients immunosuppressed with tacrolimus and receiving concomitant treatment with voriconazole or isavuconazole over a two-year period in a class 5 hospital according to cluster classification was performed.
- The variables collected included age, plasma levels of tacrolimus for ten days after the start of combination, and toxicity associated with azole throughout treatment with it. The standard deviation of tacrolimus levels was calculated to determine which of the antifungals had generated more oscillation in plasma levels.
- For qualitative variables, absolute and relative frequencies were obtained and for quantitative variables the median and interquartile range. For hypothesis contrast, the Fisher’s exact test or the Mann-Whitney U test was performed according to the type of variable.

Results

- 45 patients
  - Voriconazole N=23
    - 60 (56-67) years
  - Isavuconazole N=22
    - 63 (65-68) years

  TOLERANCE TO TREATMENT

  - Patients had side effects associated with the azole
    - Isavuconazole 28.57%, Voriconazole 82.6% (p<0.005)
  - Patients had to suspended treatment due to these side effects
    - Isavuconazole 6%, Voriconazole 47.82% (n=11) (p<0.005)

CONCENTRATIONS OF TACROLIMUS

- Concentrations of tacrolimus greater than 20ng/ml (toxic concentration) within ten days since the combination started
  - Isavuconazole 14.3% (n=3)
    - Voriconazole 34.8% (n=8) (p=0.1685)
  - Median standard deviation of tacrolimus plasma concentration
    - Isavuconazole 3.17ng/ml (1.4-5)
      - Voriconazole 3.76ng/ml (2.89-4.5) (p=0.272)
  - Patients who temporarily discontinued tacrolimus treatment due to high-level concentration and associated toxicity
    - Isavuconazole 18.2% (n=4)
      - Voriconazole 34.8% (n=8) (p=0.1685)

COMPARATION OF MOST COMMON SIDE EFFECTS

- Neurological toxicity
  - Voriconazole 20% Isavuconazole 10% (p<0.005)
- Hepatotoxicity
  - Voriconazole 20% Isavuconazole 10% (p<0.005)
- Digestive toxicity
  - Voriconazole 20% Isavuconazole 10% (p<0.005)

Conclusions

Treatment with isavuconazole resulted in fewer tacrolimus poisoning, although the difference was not statistically significant. In addition, treatment with isavuconazole was found to be safer, had fewer side effects and did not require antifungal discontinuation.