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Isavuconazole : Does the unique in label regimen fit for a cachectic elderly ?

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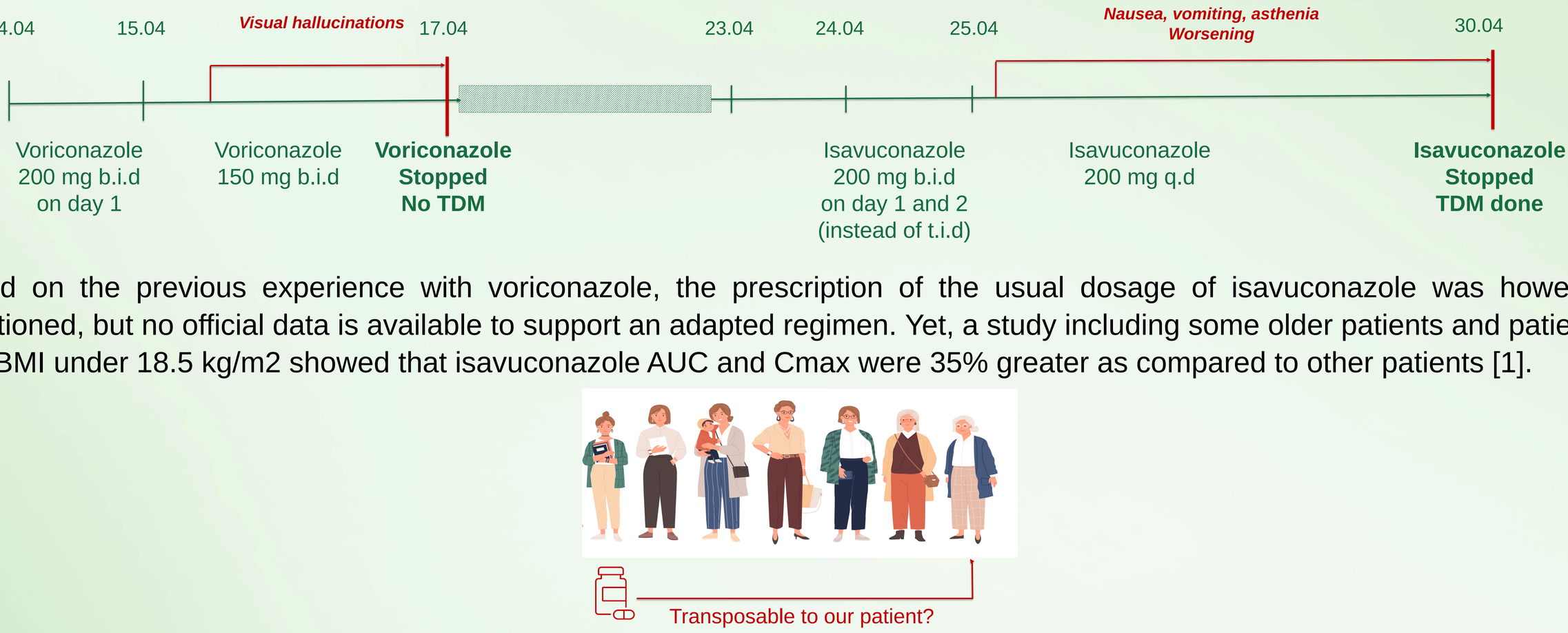
Background

Drug prescription in older patients with cachexia is usually based on clinical trials that do not include this type of patients. Therefore, the in label regimen need usually to be adapted in this population and side effects closely monitored. We present the case of an older cachectic patient treated with isavuconazole. Soon after introduction of the treatment, side effects appeared, suggesting an overexposure.

Case report

A women of 69 years, 36 kg and 1,60 m (BMI of 13 kg/m^2) has been diagnosed with chronic pulmonary aspergillosis. Although she initially refused the treatment for this fortuitous finding, the infection turned into a subacute form of pulmonary aspergillosis requiring the introduction of an antifungal.

Voriconazole was first introduced, with weight-based dosing, but was stopped four days later due to visual hallucinations, a dose-dependent side effect. The infectious diseases consultant suggested a second line treatment with isavocunozale at the unique in label regimen of 200 mg t.i.d on day 1 and 2, then 200 mg q.d.



Based on the previous experience with voriconazole, the prescription of the usual dosage of isavuconazole was however questioned, but no official data is available to support an adapted regimen. Yet, a study including some older patients and patients with BMI under 18.5 kg/m2 showed that isavuconazole AUC and Cmax were 35% greater as compared to other patients [1].

Transposable to our patient?

A dose reduction of isavuconazole was decided with prescription of 200 mg b.i.d on day 1 and 2, then 200 mg q.d. The treatment was stopped on day 7 due to nausea, vomiting and asthenia. A therapeutic drug monitoring (TDM) was performed on day 7 and isavuconazole concentration reached 4.9 mg/l.

Although isavuconazole TDM recommendation is not strong due to a lack of data correlating pharmacokinetics with pharmacodynamics, it can be analyzed that it was above the adequate drug exposure range of [2-3] mg/l [2]. Moreover, a cut-off toxicity appears to be set at 4.6 mg/l [3]. This result suggests that our patient was overexposed and may explain the side effects.

Conclusions

Few specific data on toxicity is usually available for older patients, especially when cachectic or overweight, and even more for drug recently introduced on the market. Dilemma appears when an infection has to be treated rapidly using the best dosage to be effective against the infection and, at the same time, to preserve the health of these vulnerable patients.

References

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