

Voriconazole-induced QT-corrected (QTc) interval prolongation, bradycardia, hypothermia, mydriasis in an immunosuppressed patient with Ewing.

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Abstract:

Background: Invasive aspergillosis is an important cause of increased mortality and morbidity in immunocompromised patients. Early treatment of probable aspergillosis by voriconazole is recommended by many authors. Nevertheless direct possible lethal complications must be taken into account. **Methods:** we describe a case of voriconazole adverse events in a 18 y old patient treated for aplasia by antibiotics and caspofungin. He remained febrile: Voriconazole initiated for digestive mycosis, caught, endemic aspergillosis. Second injection was badly tolerated (fever 40 °, dyspnea, chills, myalgias, hypotension) leading to stop Voriconazole. Few hours later, bradycardia (36 bpm/mn), QT c interval prolongation (QTc 482ms), bilateral mydriasis, hypothermia appeared. Others risks for cardiac events were studied: prior cardiotoxic chemotherapy; lightly low calcemia and magnesemia , negative T ondes, traducing major potassium deficit in cardiac cells, in spite of initially normal kaliemia (4.6 mmol/l) mild hypokalemia (3.3 meq/l). Systemic infection was eliminated, cerebral MRI normal, blood dosage of voriconazole at 80 h and 96 h after last dose negative. We discontinued potentially arrhythmogenic drugs. Specific treatment consisted of electrolyte disturbances correction, IV atropine, scopolamine patch. 24 h holter ECG revealed neither torsades de pointes nor ventricular tachycardia. QT c interval remained longer for 3 days. Onde T was normalised at day 6, with disappearance of bradycardia and hypothermia ,without any cardiac event. **Results:** Azole family antifungal agents were pointed out as arrhythmogenic (QTc prolongation, torsades de pointes) in combination or alone. Few data reported bradycardia and QT c prolongation with voriconazole, although the drug package insert warns about such reactions. Furthermore, none case of mydriasis was reported but noted in Pfizer American data file(< 2% of case). **Conclusions:** Careful monitoring of QTc prolongation and bradycardia in patients receiving voriconazole is mandatory, particularly those with electrolyte disturbances, concomitant QT prolonging drugs, and /or receiving toxic cardiac chemotherapy.

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