

Pancreatitis Associated with the Use of Itraconazole

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Introduction: Acute pancreatitis is a relatively rare, but serious clinical disorder with high mortality. The acute inflammation of the pancreas is believed to be caused by inappropriate intra-pancreatic activation of digestive enzymes, which leads to subsequent auto-digestion. Clinical symptoms are acute and constant pain in the epigastric area or the right upper quadrant. The most frequent causes of acute pancreatitis are alcohol abuse and cholelithiasis, comprising 70–80% of all cases.[1] Drugs are a relatively rare cause of acute pancreatitis, with an estimated incidence of 0.1–2%.[2] In literature reviews various different drugs have been associated with pancreatitis. Literature on itraconazole-induced pancreatitis is as far as we know limited to only one Dutch case report.[3]

Aim: To call attention to the assumed association between itraconazole and pancreatitis by presentation of four cases.

Methods and Results: The Netherlands Pharmacovigilance Centre Lareb, maintaining the voluntary adverse drug reaction reporting system in the Netherlands received four case reports of pancreatitis associated with use of itraconazole. Indication for use was onychomycosis for two female patients, 50/67 years old, and tinea pedis for two male patients, 55/15 years old. Time to onset varied from 3 days to 7 weeks after start of the medication. The diagnosis pancreatitis was confirmed by lab tests. In two of these cases, recurrent use of itraconazole resulted in recurrent symptoms. All four patients had been using relatively high doses of itraconazole. The database of the WHO Collaborating Centre contains 34 additional reports of pancreatitis on itraconazole. Mechanism of itraconazole-induced pancreatitis: Given the low incidence and poor predictability of this adverse drug reaction, an idiosyncratic cause seems plausible. The relatively short time period to onset and the rapid de- and rechallenge that were reported are in line with an immune response.[4] However, relatively high doses of itraconazole were used in all four cases, which would be in favor of an accumulation of a toxic metabolite.[5]

Conclusions: The presented cases suggest a causal relation between itraconazole and pancreatitis. More data on this association are needed. We intend to stimulate awareness of this association among physicians, so they can inquire about the possible use of itraconazole while diagnosing patients with unexplained abdominal complaints. Given the mild indication for the use of itraconazole and the seriousness of this possible adverse drug reaction, physicians may wish to reconsider the prescription of itraconazole to patients with risk factors for drug-induced pancreatitis.

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