



Sunset at Navarre Beach

PIC QUESTION OF THE WEEK: 9/1/08

Q: What are some of the important clinical characteristics of drug-induced pancreatitis?

A: Pancreatitis is most often associated with gallstones and alcohol abuse, but drugs are responsible for nearly 2% of the cases in the general population and up to 40% of cases in HIV positive patients. Some characteristics of pancreatitis include abdominal pain, nausea, and levels of serum lipase and amylase that are two to three times the upper limit of normal. Several mechanisms have been proposed as causes of drug-induced pancreatitis including hypersensitivity, accumulation of toxic metabolites, spasm of the sphincter of Oddi, and intrinsic toxicity related to overdose. Hypertriglyceridemia may be a contributing factor. The onset of symptoms of pancreatitis varies, depending on the associated mechanism, but can range from an almost immediate reaction to one requiring several months of drug administration. Unlike many adverse effects, pancreatitis is not often associated with an entire class of drugs. The exceptions to this rule are the *statins*, most ACE inhibitors, and a large number of nucleoside reverse transcriptase inhibitors (NRTI). Three NRTIs (didanosine, stavudine, zalcitabine) include Black Box warnings regarding pancreatitis. Cases of pancreatitis have been reported with several of the agents in each of these groups. There are many additional drugs that have been associated as possible causes of pancreatitis. Based on the number of reported cases and documentation of positive re-challenge, drugs have been categorized into one of three groups/classes based on suggested causality- definite, probable, and possible. Class I medications are defined as those with at least 20 or more reported cases and at least one report of positive re-challenge. Examples include asparaginase, azathioprine, cytarabine, didanosine, estrogens, exenatide, furosemide, mercaptopurine, mesalamine, opiates, pentamidine, steroids, sulfamethoxazole/trimethoprim, sulfasalazine, sulindac, tetracycline, and valproic acid. Class II drugs have been implicated in more than 10 cases, but less than 20, and are considered to have a probable association with acute pancreatitis. Acetaminophen, carbamazepine, cisplatin, enalapril, erythromycin, hydrochlorothiazide, interferon alfa-2b, lamivudine, metformin, octreotide and rifampin are examples of Class II compounds. Finally, Class III medications includes an extensive list of medications associated with 10 or fewer cases reported in the literature or drugs for which unpublished reports have been submitted to the FDA and/or manufacturer. Drug-induced pancreatitis can be a severe condition as evidenced by the recent FDA Alert regarding reported cases of hemorrhagic or necrotizing pancreatitis associated with exenatide (Byetta). In cases of suspected drug-induced pancreatitis, the offending drug must be withdrawn and the patient should be treated immediately.

References:

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Ashley M. Bartell and Alaina E. Fairley, Pharm.D. Candidates

The PIC Question of the Week is a publication of the Pharmaceutical Information Center, Mylan School of Pharmacy, Duquesne University, Pittsburgh, PA 15282 (412.396.4600).