Sponsored by Pfizer
CeVXpre Unparalleled Access to Pfizer's Investigational Oral Pan-Coronavirus Protease Inhibitor Candidate
Learn More
CeVXpre Register for Our Virtual Conference
Join the Hospital Community Virtual Conference on CeVXpre to Be Served by Three Years
Learn More
HOSPITALIST CAREER LOGIN
Search Jobs and Physician Jobs
Click Here

Clinical, Hospital Medicine

Avoid Pancreatitis Risk

The Hospitalist 2007 December;2007(12)

Author(s): Michelle Cardel, Pharm.D., BCPS

Share: Facebook Twitter Linkedin Email Print

Drugs are an often-overlooked cause of pancreatitis in hospitalized patients,[1,2] Knowing which drugs are associated with acute pancreatic inflammation can help the hospitalist consider such drugs as the cause within their differential diagnosis.

The two most common causes of acute pancreatitis are biliary disease (30%-50%) and chronic alcohol use (35-50%). Drug-induced pancreatitis (DIP) has occurred in more than 100 prescribed medications.[3,4]

Most cases of acute pancreatitis are reversible and resolve on their own within three to seven days after treatment begins. A small number of patients develop severe complications, and their mortality rate rises 30%. Symptoms may last a few days and can include mild to severe epigastric pain that can radiate to the back, chest, flank, or lower abdomen.

Other symptoms can include nausea, vomiting, fever, abdominal tenderness, jaundice, or hypotension. Serum amylase and lipase levels usually rise to three times the upper limit of normal. Use of computerized tomography (CT) or ultrasound can help the diagnosis.

New Warnings

Earlier this year healthcare professionals were warned of updates to the Bicuspiate (pefloxacine sodium) label. The warning was in reference to the co-administration of ceftriaxone and intravenous (IV) calcium-containing infusions either in the same tubing or on different infusion lines.

The current recommendation is that at least 48 hours should pass prior to infusing ceftriaxone and IV calcium-containing solutions in any given patient. Some solutions that should not be combined with ceftriaxone include calcium-containing parenteral nutrition, Ringer's solution, or Hartmann's solution. Calcium-ceftriaxone precipitates can occur and have led to fatalities.—MR

The mechanism of DIP is not known, but is thought to be predominately due to an idiosyncratic reaction, and for a few agents/classes, to intrinsic drug toxicity.5 The incidence of DIP is approximately 1.4%-1%. Not knowing the exact number of prescriptions for each medication and the cases of pancreatitis from each impedes the determination of incidence.

Most data on DIP are from case reports or reviews of complied cases. The validity and severity of DIP is unknown mostly because cases are underreported to MedWatch. Reasons for underreporting include:

- Low index of suspicion for DIP compared with drug-induced hepatotoxicity;
- Milder cases due to missed lower enzyme levels (not routinely ascertained in a metabolic panel);
- Missed latency of exposure; and
- Erroneous classification as alcoholic or biliary disease by default.

Drug-induced pancreatitis is more common in patients who have inflammatory bowel disease, AIDS, cancer, or gastrointestinal disease. It is also common in those who are genetic HIV positive, or who are on immunosuppressive agents.6

An early compilation of DIP reports was published by Lankisch, et al. This was a retrospective evaluation that excluded all other pancreatitis etiologies (e.g., pancreatitis retrograde cholangiopancreatography (ERCP), post-traumatic, post-operative, viral, vascular drugs. Out of 1,653 patients with acute pancreatitis, there were 22 cases of DIP due to the following agents: azathioprine (n=6), mesalamine/sulfasalazine (n=5) didanosine (n=4), estrogens (n=3), furosemide (n=2), hydrochlorothiazide (HCTZ, n=2), metronidazole (n=3). Rechallenge was not attempted for ethical reasons. The mean hospital stay was 25.5 days (range two to 78 days), with an incidence of 1.2%. Two patients died (from AIDS and tuberculosis). The authors noted that other studies show a high fatality rate from azathioprine, did furosemide, and HCTZ.

New Drugs

NEW DRUG

Gramitron injection (Kyleb) has been tentatively FDA approved and is expected to receive final approval and go to market in December, upon patent expiration. Ralfoxiprene (tentrexa), an oral integrase inhibitor, is in a new class of antiretrovirals. This agent was FDA approved for use in combination with other antiretroviral therapy, for treating HIV infection in patients with ongoing viral replication despite treatment.

New Indications

Levofloxacin 750 mg IV injection and oral tablets (Levaxa) have been FDA approved as a five-day, once-daily course for the treatment of complicated urinary tract infections and acute pyelonephritis.

Belotaxine 60 mg tablets (Eviclot) have been FDA approved to reduce the risk of invasive breast cancer in two populations of postmenopausal women: those with osteoporosis and those at high risk for invasive breast cancer.

Additionally, Trivedi, et al., evaluated cases reported in the literature or unpublished cases from 1966 through 2004. They then classified the drugs into one of three categories based on strength of evidence of DIP association:

Class I included medications causing more than 20 reported cases with at least one case following rechallenge. Class II were medications causing more than 10 but fewer than 20 reported cases with/without a positive rechallenge, and Class III were all medications in 10 or fewer cases or unpublished reports (FDA or pharmaceutical company reports). Following are some of the most common reports from drugs available in the U.S.:

- Class I: dd (n=883), asparaginase (n=177), azathioprine (n=89), valproic acid (n=85), pentavalent antimonials (pentamidine to treat leishmaniasis, n=83), pentamidine (n=79), mercaptopurine (n=78), didanosine (n=59), estrogens (n=42), opioids (n=42), tetracycline (n=34), cytosine (n=29), steroids (n=25), sulfamethoxazole/trimethoprim (SMZ-TMP, n=24), sulfasalazine (n=23), furosemide (n=21), azathioprine (n=21).
- Class II: rifampin, lamivudine, scintadox, calcitonin/salmon, acetaminophen, interferon alfa-2b, enalapril, HCTZ, cisplatin, erythromycin; and
- Class III: mumarous agents, including the following class(s): sprulons, macrolides, angiotensin-converting enzyme inhibitors (ACEI), statins, and others.

Most recently Badalov, et al., evaluated cases from Medline (through July 1, 2006) and classified them based on levels of evidence. These levels were:

- Definite (imaging study or autopsy confirmed diagnosis);
- Probable (typical symptoms present and threefold increase in amylase and/or lipase); or
- Possible (all others, not included in the final analysis).

Cases were further subclassified into four classes:

- Class Ia (3 or more cases with positive rechallenge, excluding all other causes): codeine, conjugated estrogens, enalapril, lisinopril, methotrexate, mesalamine, pravastatin (other statins), procainamide, simvastatin, sulfonic, sulfa drugs, tetracycline, and valproic acid.
- Class Ib (1 or more cases with positive rechallenge, not excluding all other causes): ampicillinate, azathioprine, clomiphene, cytosine arabinoside, dapsone, dexamethasone (other steroids), estrogens, furosemide, fluoxetine, lamivudine, losartan, 6-MP, methotrexate, methyldopa, nelfinavir, omeprazole, pentamidine, SMZ-TMP, and trans-retinoic acid (oral topical).
- Class II (four or more cases, consistent latency in 75% of cases): acetaminophen, clozapine, dd, erythromycin, l-asparaginase/pegaspargase, pentamidine, propofol, and tamoxifen.
- Class III (two or more cases, no consistent latency, no rechallenge): alendronate, captopril, carbamazepine, ciflorexe, HCTZ, interferon, lisinopril, meltirtinx, mirtazapine, naproxen, and others; and
- Class IV (one case, no other cites, without rechallenge): too numerous.

Additionally, the Australian Adverse Drug Reactions Advisory Committee reported on the top 12 DIP-associated medications (n=814 reports implicating 695 drugs). The most commonly reported drugs included azathioprine, did, valproate, stavudine, simvastatin, clozapine, lamivudine, estrogens, prednisolone, olanzapine, celecoxib and 6-MP, which are listed in each medication's Australian product information.

The following drugs/classes have been implicated in causing DIP:

- AIDS therapies: did, pentamidine;
- Antimicrobials: metronidazole, sulfonamides, tetracyclines;
- Diuretics: furosemide, HCTZ;
- Anti-inflammatories: mesalamine, salicylates, sulindac, sulfasalazine;
- Immunosuppressants: azathioprine, mercaptopurine, methotrexate; and
- Neuropsychiatric agents: valproic acid.

The American Gastroenterology Association Institute has developed a guide for managing acute pancreatitis. Additionally, they note that when assessing DIP, consider prescription, over-the-counter, and herbal products, too.7 Pancreatitis can occur with certain drugs or medication classes, some more often than others.

Consider DIP in the differential diagnosis of patients who present with or develop epigastric pain. Question all patients with acute pancreatitis about their medication use as a possible cause for the disease. Assessment of amylase/lipase will aid in the diagnosis. To prevent further compromise in cases where DIP is suspected, hold the offending agent (and substitute if possible) to decrease further episodes. TH

Michele M Kirchner is a freelance medical writer based in New York City.

References

1. Lankisch PG, Dohge M, Gottesleiner F. Drug-induced acute pancreatitis: incidence and severity. Gut 1995 Oct;37(4):565-567.
2. Elsobky A, Pearson NL. Drug-induced pancreatitis. Can Pharm J. 2006;139(6):58-60.
3. Trowill CD, Pitchumoni CS. Drug-induced pancreatitis: an update. J Clin Gastroenterol. 2005 Sept;39(8):709-716.
4. Badalov N, Baradarian R, Iwarsx K, et al. Drug-induced pancreatitis: an evidence-based review. Clin Gastroenterol Hepatol. 2007 Jun;5(6):648-661.
5. Vege SS, Chari ST. Etiology of acute pancreatitis. In: UpToDate. Rose, BD (Ed), UpToDate, Wellham, Mass., 2007.
6. Simon A. Drug-induced pancreatitis. Aust Adv Drug Reactions Bull. 2006 Dec;25(6):22.
7. American Gastroenterological Association Institute Medical Position Statement on Acute Pancreatitis. Gastroenterology. 1998 Sep;115(3):763-764.

NEXT ARTICLE:
In the Literature >

Comments (Be the first to comment)

Clinical
Hospital Medicine with COVID-19 vaccination refusals
Feb 01, 2022
COVID-19 Stories: Accounts of a Pandemic Year
Feb 01, 2022
"Beyond a reasonable doubt": Hospitalists in the courtroom
April 01, 2021
Use of COVID-19 high-titer convalescent plasma
April 01, 2021
The COVID-19 pivot in hospitals
April 01, 2021
Hospital medicine during COVID-19
Feb 01, 2021
Hospital medicine pivots amid COVID-19
Feb 01, 2021
Longitudinal assessment of hospital-acquired SARS-CoV-2 infection
Feb 01, 2021
MORE >

Quality
Hospitalist Improvement Innovations Network: Improving care transitions
Feb 01, 2022
Depression screening in primary care: Changing outcomes, changing lives
Feb 01, 2022
Cardiac rehab after cardiac arrest surgery associated with improved survival
Feb 01, 2022
Virtual is the new real
Feb 01, 2022
Reliable care and hospital discharge: Implementing a transitional care bundle
Feb 01, 2022
MORE >

Public Policy
Congressional reexamination between Medicare payment cuts
Feb 01, 2022
April 2022
Senate confirms Murthy as Surgeon General
Feb 01, 2022
March 28, 2022
AHRQ and partner nation to medicine collaborate
Feb 01, 2022
March 28, 2022
What the 3 billion COVID-19 tests mean for hospitalists
Feb 01, 2022
March 28, 2022
Precision Medicine Initiative Cohort Program and Mrk2 enhancer
Feb 01, 2022
March 28, 2022
MORE >

Practice Management
Prospective and retrospective health care
Feb 01, 2022
About use or Rice Infections Prevention Stifling Spread of Antibiotics
Feb 01, 2022
The COVID-19 pivot in hospitals
April 01, 2021
Hospitalists Hit Hard by COVID-19 Pandemic
April 01, 2021
Longitudinal assessment between diverse groups and hospital COVID-19 outcomes
Feb 01, 2021
MORE >

From the Society
SHM Advocating Care of Elder Hospitalized Patients
March 31, 2021
Hospital Medicine Hospitalist Dual Certification Exam Scheduled
March 31, 2021
Opening of aspects of patient care through telehealth, TBLC, PINE
March 31, 2021
Roundtable discussion: The Hospitalist Dual Certification Exam
March 31, 2021
A hospitalist pod: Hospital Medicine, HTC
March 31, 2021
MORE >

Video
Critical care and COVID-19: Do and don'ts
March 31, 2021
Treatment options for COVID-19 in the hospitalized patient
March 31, 2021
Managing the COVID-19 hospital flow at UCSF Medical Center
March 31, 2021
Cards: ref: Hospitalist COVID affecting confidence in hospitalists
March 31, 2021
COVID-19 Vaccine Hub provides transfer information for hospitalists
March 31, 2021
MORE >

THE PUBLICATION
About Us
Contact Us
Feedback
Advertising
Editorial Board
Subscribe
Online Submission
Hospital Leader Blog
Podcast
Privacy Policy
Do Not Sell My Personal Information
Advertise
Editorial Calendar
Facebook
Twitter
Instagram
Linkedin
Rss

SPECIALTY FOCUS
Critical Care
Emergency Medicine
Leadership Training
Mediation Reconciliation
Pediatrics
Telehealth
Transitions of Care

TOP SECTIONS
Quality
Clinical
Practice Management
Public Policy
Video
From the Society

An Official Publication of the Society of Hospital Medicine
Powered by Wordpress
© Copyright 2021 The Hospitalist. All rights reserved.