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Furosemide and acute pancreatitis
An uncommon entity

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Φουροσεμίδη και οξεία παγκρεατίτιδα:
Μια ασυνήθης οντότητα

Περίληψη στο τέλος του άρθρου

Key words: Diagnosis, Furosemide, Pancreatitis

Until approximately a decade ago, some authors referred to drug-induced acute pancreatitis (DIP) as a mild or moderate clinical condition estimated to occur between 1.4% to 2.0% of all acute pancreatitis (AP) cases; discontinuation of the drug often alleviates symptoms, and normalizes biochemical and radiological parameters, notwithstanding, the course of disease sometimes may present with higher severity and a fulminant outcome.[1–7] Although alcohol abuse and biliary stones are the main (60% to 80%) etiological factors associated with AP,[7] the additional hypothesis (0.1% to 2.0%) of DIP should be discarded whenever some drug has been informed.[2] DIPs may involve ductal and acinar changes, intracellular transport dysfunction, toxic or allergic phenomena; specific toxicity is exceeding rare and develops within 24 hours, while common allergic reactions manifest from one to six weeks after a drug use; the images show pancreas enlargement, indistinct contour, and fat stranding.[2]

The following comments aim to emphasize recent illustrative cases about the DIP due to furosemide.[2–7] A 36-year-old female with nephrotic syndrome and mixed connective tissue disease utilized furosemide for anasarca, and three weeks later her lipase level was 122 U/L, abdominal computed tomography (CT) showed interstitial AP, ultrasound discarded gallstones, and she improved after the stop furosemide considered the most possible etiologic factor. After 10 days using another loop diuretic (bumetanide), she had epigastric pain, lipase level of 907 U/L, and the diagnosis was AP; the diuretic was changed by ethacrynic acid with complete resolution of the manifestations, and authors emphasized this AP with an immune-mediated mechanism related to some metabolite of the sulfa.[3] A 65-year-old woman with diabetes and liver cirrhosis, utilizing insulin, spironolactone, and furosemide, two years before had the confirmed diagnosis of AP six days after the use of this drug, and more recently she had a new episode of furosemide-induced AP with elevated amylase (1,022 IU/L) and lipase (3,122 IU/L) levels, normal images of gallbladder and bile ducts, and classical aspect of edematous pancreas and peripancreatic stranding.[4] Therefore, with the confirmed new DIP by furosemide, the drug was discarded from her schedule in definitive. The case was classified as Ia because more than two previous occurrences had been reported, there was a positive rechallenge with the occurrence of AP after ingestion of furosemide, and recovery was observed twice after discontinuing the drug.[4] The drug-induced classes of AP based on the number of cases, latency period, and re-challenge reactions are Ia (alcohol, α-methyldopa, and cytosine); Ib (trans-retinoic acid, losartan, and amiodarone); II (acetaminophen, estrogen, and tamoxifen); III (captopril, metformin, and naproxen); and IV (ampicillin, and cisplatin).[5] Worthy of note, furosemide was included in class Ia with a minimum number of case reports (n=1), the re-challenge required (yes), the latency established (N/A), and the other alternative etiologies of pancreatitis excluded (yes); the proposed mechanism is a hyper-stimulation of secretions leading to a direct toxic injury and or ischemia.[6] The authors emphasized that DIP may be related to elevated morbidity, longstanding hospitalization, cumbersome costs, and

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delayed diagnosis, and patients with AP of unknown cause must inform potentially involved drugs.[6] DIP-related risk factors were evaluated among 264 case reports between the first quarter of 2004 and the second quarter of 2022, including the following respective groups of drugs: Antineoplastic (13.2%), antidiabetic (10.6%), antibacterial (9.1%), immunomodulatory (4.2%), antipsychotic (2.3%), besides diverse other drugs (60.6%).[7] The final analysis revealed that males, ages between 41 and 54 years, and 36 drugs were risk factors for DIP, the median time to DIP onset was 31 (7–102) days, and about 75% of adverse events occurred within 100 days; these findings can be useful to the early diagnosis and may contribute to future studies on the pathogenesis of DIP.[7]

In conclusion, AP is a rare complication of furosemide use, but it should be considered among differential hypotheses of abdominal acute conditions to enable prompt diagnosis and early discontinuation of the drug.

ΠΕΡΙΛΗΨΗ

Φουροσεμίδη και οξεία παγκρεατίτιδα: Μια ασυνήθης οντότητα

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Το οινόπνευμα και οι χοληφόροι λίθοι είναι οι κύριες αιτιολογίες της οξείας παγκρεατίτιδας, αλλά η φαρμακευτική παγκρεατίτιδα θα πρέπει να λαμβάνεται υπ' όψιν όταν ο ασθενής λαμβάνει φάρμακα. Η φυσιοπαθολογία μπορεί να περιλαμβάνει διαταραχές στους πόρους και στο παρέγχυμα, δυσλειτουργία της ενδοκυτταρικής μεταφοράς και τοξικά ή αλλεργικά αίτια. Η ειδική τοξικότητα είναι πολύ σπάνια και εμφανίζεται τις πρώτες 24 ώρες, ενώ οι αλλεργικές αντιδράσεις εκδηλώνονται μετά από 1–6 εβδομάδες. Οι κλασικές εικόνες περιλαμβάνουν διόγκωση του παγκρέατος με ασαφές περίγραμμα και συσσώρευση λίπους. Αναφέρονται πρόσφατα δεδομένα για την οξεία παγκρεατίτιδα που σχετίζεται με τη φουροσεμίδη.

Λέξεις ευρετηρίου: Διάγνωση, Παγκρεατίτιδα, Φουροσεμίδη

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