DSEN ABSTRACT

Mechanisms of drug-induced pancreatitis: overview of reviews and case reports

Summary

- Based on 166 included articles (27 reviews, 139 case reports), nine broad mechanism categories for drug-induced pancreatitis were identified: direct or indirect toxic effects, pancreatic duct blockage and hypertension, immune-mediated mechanisms, genetic predisposition, non-pancreatic organ dysfunction, cellular-level pancreatic dysfunction, blood chemistry abnormality, altered pancreatic blood flow, and alteration of inflammatory mediators or cellular protective pathways.
- While many hypotheses for DIP mechanisms exist, many are supported by little or no evidence from the literature.
- As many drugs have multiple associated mechanisms, overall mechanisms of drug-induced pancreatitis remain relatively unclear at this time.

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What is the issue?

- The mechanisms by which drugs can induce acute pancreatitis are largely unknown and likely mediated via multiple pathways.

What was the aim of the study?

The following research question was addressed:

- What mechanisms of drug-induced pancreatitis (DIP) have been described in the literature?

We systematically reviewed the literature to identify the mechanisms postulated for DIP therein.

How was the study conducted?

- A protocol was developed a priori and registered with PROSPERO. We searched MEDLINE, Embase, the Cochrane Library, and additional sources to identify reviews reporting mechanisms for DIP with cited evidence. As well, studies identified in a related systematic review of case reports (DSEN query 16-04b) as reporting a mechanism for DIP with cited evidence were included. Well-established systematic review methods were used for screening and data extraction. We developed categories that reflected the general pathophysiological processes underpinning the mechanisms reported in the included studies. We also summarized mechanism data for each drug or drug class for which data had been reported.

What did the study find?

- Twenty-seven review articles and 139 case reports were included. Nine mechanism categories were identified from within these studies: (1) direct or indirect toxic effects, (2) pancreatic duct blockage and hypertension, (3) immune-mediated mechanisms, (4) genetic predisposition, (5) non-pancreatic organ dysfunction, (6) cellular-level pancreatic dysfunction, (7) blood chemistry abnormality, (8) altered pancreatic blood flow, and (9) alteration of inflammatory mediators or cellular protective pathways.
- DIP is thought to occur mainly due to idiosyncratic reactions (i.e., specific to an individual due to rare, usually unknown factors inherent to that individual at that point in time that predisposes toward DIP). Many specific DIP mechanisms have been hypothesized; however, there is often little clinical evidence supporting them, and the translatability of preclinical evidence for DIP mechanisms is questionable due to high exposure levels that are not clinically relevant.
- Many drugs have multiple hypothesized mechanisms and are not easily classified into broad mechanism categories. Thus, mechanisms for DIP remain generally unclear.

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