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Hepatic injury due to combined choline-deprivation and thioacetamide administration: an experimental approach to liver diseases.

Al-Humadi H[1], Theocharis S, Dontas I, Stolakis V, Zarros A, Kyriakaki A, Al-Saigh R, Liapi C.

Author information

- [1]Department of Pharmacology, Medical School, National and Kapodistrian University of Athens, 75 Mikras Asias Str., 11 527, Athens, Greece.

Abstract

BACKGROUND:

The induction of prolonged choline-deprivation (CD) in rats receiving thioacetamide (TAA) is an experimental approach of mild hepatotoxicity that could resemble commonly presented cases in clinical practice (in which states of malnutrition and/or alcoholism are complicated by the development of other liver-associated diseases).

AIM:

The present study aimed to investigate the time-dependent effects of a 30-, a 60- and a 90-day dietary CD and/or TAA administration on the adult rat liver histopathology and the serum markers of hepatic functional integrity.

METHODS:

Rats were divided into four main groups: (a) control, (b) CD, (c) TAA and (d) CD + TAA. Dietary CD was provoked through the administration of choline-deficient diet, while TAA administration was performed ad libitum through the drinking water (300 mg/l of drinking water).

RESULTS:

Histological examination of the CD + TAA liver sections revealed micro- and macro-vesicular steatosis with degeneration and primary fibrosis at day 30, to extensive steatosis and fibrosis at day 90. Steatosis was mostly of the macrovesicular type, involving all zones of the lobule, while inflammatory infiltrate consisted of foci of acute and chronic inflammatory cells randomly distributed in the lobule. These changes were accompanied by gradually increasing mitotic activity, as well as by a constantly high alpha-smooth muscle actin immunohistochemical staining. The determination of hepatocellular injury markers such as the serum enzyme levels' of alanine aminotransferase and aspartate aminotransferase demonstrated a decrease at day 30 (they returned to control levels at days 60 and 90). However, the determination of those serum enzymes used for the assessment of cholestatic liver injury (gamma-glutamyltransferase, alkaline phosphatase) revealed a constant (time-independent) statistically-significant increase versus control values.

CONCLUSIONS:

Long-term combined dietary CD and TAA administration could be a more realistic experimental approach to human liver diseases involving severe steatosis, fibrosis, stellate cell activation and significant regenerative hepatocellular response.