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HUMAN BIOLOGY

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BCH 306

Question:

Write on the various ways to assess the integrity of liver following an exposure to a named toxicant.

Answer

Acetaminophen (also named paracetamol or APAP) is not a Nonsteroidal anti-inflammatory drugs ⋯ synthesis by the action of inhibition of prostaglandin G/H synthase 1 and 2. Prostaglandin G/H synthase ⋯ 1 and 2 catalyze the arachidonic acid to prostaglandin G2, and also catalyze prostaglandin G2 to ⋯ prostaglandin H2 in the metabolism pathway. Decreased prostaglandin synthesis in many animal model's cell is caused by presence of acetaminophen. ⋯ (NSAIDs). However, it still can be used to treat pain and fever. Acetaminophen can block prostaglandin.

Acetaminophen (APAP) is metabolized primarily in the liver. Glucuronidation is the main route, accounting for 45-55% of APAP metabolism, and is mediatied by UGT1A1, UGT1A6, UGT1A9, UGT2B15 in the liver and UGT1A10 in the gut. APAP can also by metabolized via sulfation, accounting for 30-35% of the metabolism. In the liver, this step is catalyzed by the sulfotransferases SULT1A1, SULT1A3, SULT1A4, SULT1E1 and SULT2A1. Moreover, APAP can also be activated to form the toxic N-acetyl-p-benzoquinone imine (NAPQI) under the mediation of CYP3A4, CYP2E1, CYP2D6 CYP1A2, CYP2E1 and CYP2A6.

The definition of hepatotoxicity after acetaminophen overdose is a serum aspartate aminotransferase or alanine aminotransferase of 1000 international units/L or greater.

* serum acetaminophen level

* serum AST and ALT

WAYS TO ASSESS THE INTEGRITY OF LIVER AFTER EXPOSURE TO ACETAMINOPHEN

1. Obtain liver function tests (LFTs). Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) concentrations begin to rise within 24 hours after an acute ingestion and peak at about 72 hours. In severe overdose, transaminase elevation can be detected as early as 12-16 hours' post-ingestion. Toxicity is defined as serum AST or ALT concentrations greater than 1000 IU/L. A rapid progression of transaminase values to 3000 IU/L or greater reflects severe hepatotoxicity. Include bilirubin and alkaline phosphatase concentrations.

A proposed strategy for predicting hepatotoxicity involves multiplying the acetaminophen concentration times the ALT concentration. Products and risk levels are as follows:

* < 1500 - Low risk

* 1500-10,000 - Low to moderate risk

* > 10,000 - High risk

2. Acetaminophen may be quantified in blood, plasma, or urine as a diagnostic tool in clinical poisoning situations or to aid in the medicolegal investigation of suspicious deaths. The concentration in serum after a typical dose of paracetamol usually peaks below 30 mg/l, which equals 200 µmol/L.[42] Levels of 30 – 300 mg/L (200 – 2000 µmol/L) are often observed in overdose patients. Postmortem blood levels have ranged from 50 – 400 mg/L in persons dying due to acute overdosage. Automated colorimetric techniques, gas chromatography and liquid chromatography are currently in use for the laboratory analysis of the drug in physiological specimens.

3. Clinical or biochemical evidence of liver toxicity may develop in one to four days, although, in severe cases, it may be evident in 12 hours.[39] Right-upper-quadrant tenderness may be present and can aid in diagnosis. Laboratory studies may show evidence of liver necrosis with elevated AST, ALT, bilirubin, and prolonged coagulation times, particularly an elevated prothrombin time.[40] After paracetamol overdose, when AST and ALT exceed 1000 IU/L, paracetamol-induced hepatotoxicity can be diagnosed.[39] In some cases, the AST and ALT levels can exceed 10,000 IU/L.