O mecanismo de toxicidade do acetaminofeno se deve à produção de estresse oxidativo. O paracetamol é tão tóxico que ele provoca insuficiência hepática às vezes mortal. Esta droga deveria ser proibida pela vigilância sanitária.

Muito interessante é o fato dos trabalhos catalogados no PubMed que discordem sobre os efeitos colaterais e hepatotóxicos do paracetamol, não possuírem resumos. Será apenas coincidência? “Não vale a pena correr grandes riscos por apenas pequenos sintomas” JFJ.

A Randomized Clinical Trial of Ibuprofen Versus Acetaminophen With Codeine for Acute Pediatric Arm Fracture Pain

Twelve studies were identified, which examined several different outcomes. Three studies examined admissions to liver transplant units; DARE. English language publications between 1998 and 2003 were included. Studies were included if they took place in the United Kingdom and assessed changes in any aspect of paracetamol poisoning following the introduction of the 1998 regulations. RESULTS: Three hundred thirty-six children were randomized to treatment, 169 to ibuprofen and 167 to acetaminophen. Both groups used a median of 4 doses (interquartile range 2, 6.5). The proportion of treatment failures for ibuprofen (20.3%) was lower than for acetaminophen (31.0%), though not statistically significant (difference=10.7%; 95% confidence interval -0.2 to 21.6). The proportion of children who had any function (play, sleep, eating, school) affected by pain when pain was analyzed by day after injury was significantly lower for the ibuprofen group. Significantly more children receiving acetaminophen with codeine reported adverse effects and did not want to use it for future fractures. CONCLUSION: Ibuprofen was at least as effective as acetaminophen with codeine for outpatient analgesia for children with arm fractures. There was no significant difference in analgesic failure or pain scores, but children receiving ibuprofen had better functional outcomes. Children receiving ibuprofen had significantly fewer adverse effects, and both children and parents were more satisfied with ibuprofen. Ibuprofen is preferable to acetaminophen with codeine for outpatient treatment of children with uncomplicated arm fractures.

PMD: 19692147

Ibuprofen provides analgesia equivalent to acetaminophen-codeine in the treatment of acute pain in children with extremity injuries: a randomized clinical trial

OBJECTIVES: This study compared the analgesic effectiveness of acetaminophen-codeine with that of ibuprofen for children with acute traumatic extremity pain, with the hypothesis that the two medications would demonstrate equivalent reduction in pain scores in an emergency department (ED) setting. METHODS: This was a randomized, double-blind, clinical trial of children during the first 3 days after discharge from the emergency department (ED). The primary outcome was failure of the oral study medication, defined as use of the rescue medication. Pain medication use, pain scores, functional outcomes, adverse effects, and satisfaction were also assessed. RESULTS: Three hundred thirty-six children were randomized to treatment, 169 to ibuprofen and 167 to acetaminophen. Both groups used a median of 4 doses (interquartile range 2, 6.5). The proportion of treatment failures for ibuprofen (20.3%) was lower than for acetaminophen (31.0%), though not statistically significant (difference=10.7%; 95% confidence interval -0.2 to 21.6). The proportion of children who had any function (play, sleep, eating, school) affected by pain when pain was analyzed by day after injury was significantly lower for the ibuprofen group. Significantly more children receiving acetaminophen with codeine reported adverse effects and did not want to use it for future fractures. CONCLUSION: Ibuprofen was at least as effective as acetaminophen with codeine for outpatient analgesia for children with arm fractures. There was no significant difference in analgesic failure or pain scores, but children receiving ibuprofen had better functional outcomes. Children receiving ibuprofen had significantly fewer adverse effects, and both children and parents were more satisfied with ibuprofen. Ibuprofen is preferable to acetaminophen with codeine for outpatient treatment of children with uncomplicated arm fractures.

PMD: 19624576

Restricting paracetamol in the United Kingdom to reduce poisoning: a systematic review.

BACKGROUND: Paracetamol poisoning is implicated in about 150-200 poisoning deaths per year in England and Wales. We review previous studies assessing the effectiveness of regulations introduced in 1998 to restrict sales of paracetamol and reduce paracetamol poisoning. METHODS: We searched the following electronic databases: MEDLINE, EMBASE, CINHAL, HIMIC, COCH, APC, CENTRAL and DARE. English language publications between 1998 and 2003 were included. Studies were included if they took place in the United Kingdom and assessed changes in any aspect of paracetamol poisoning following the introduction of the 1998 regulations. RESULTS: Twelve studies were identified, which examined several different outcomes. Three studies examined admissions to liver transplant units;...
all reported reductions. Eight studies evaluated severity of paracetamol poisoning; three reported reductions but five did not. Five out of six studies reported reductions in hospital admissions. One study reported reduced mortality in England and Wales after 1 year while another found no difference in Scotland 2 years after the regulations were introduced. Two studies observed a significant reduction in over-the-counter sales. Studies suffered from several limitations including short follow-up periods, no case definition for paracetamol poisoning and lack of comparison groups. CONCLUSIONS: The limitations of these studies make it difficult to draw firm conclusions. They do, however, suggest that the 1998 regulations may have been associated with reduced admissions to liver units and liver transplants, reduced hospital attendance due to paracetamol poisoning and reduced sales of paracetamol. Further research is needed to fully evaluate the impact of the 1998 regulations. In the future, formal evaluation of the impact of similar interventions should be an integral part of policy formation.

PMID: 15590709

**Drug-induced hepatotoxicity or drug-induced liver injury**


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Drug-induced hepatotoxicity is underreported and underestimated in the United States. It is an important cause of acute liver failure. Common classes of drugs causing drug-induced hepatotoxicity include antibiotics, lipid lowering agents, oral hypoglycemics, psychotropics, antiretrovirals, acetaminophen, and complementary and alternative medicines. Hepatotoxic drugs often have a signature or pattern of liver injury including patterns of liver test abnormalities, latency of symptom onset, presence or absence of immune hypersensitivity, and the course of the reaction after drug withdrawal.

PMID: 19442919

**Acute liver failure associated with a prolonged course of acetaminophen at recommended dosages in pediatric age**


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Acetaminophen is considered as a safe analgesic and antipyretic drug in paediatric age. The main problem in the use of acetaminophen is acute liver failure after an overdose or an acute intoxication. We report a case of fulminant liver failure and spontaneous recovery in a patient treated with a prolonged course of acetaminophen at recommended dosages.

PMID: 19431953

Results of a prospective study of acute liver failure at 17 tertiary care centers in the United States.


Comment in:


Summary for patients in:


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BACKGROUND: Because acute liver failure is rare, related data have been sparse. Studies have suggested that viral hepatitis is the most common underlying cause of this condition. OBJECTIVE: To describe the clinical features, presumed causes, and short-term outcomes of acute liver failure. DESIGN: Prospective cohort study. SETTING: 17 tertiary care centers participating in the U.S. Acute Liver Failure Study Group. PATIENTS: 308 consecutive patients with acute liver failure, admitted over a 41-month period. MEASUREMENTS: Detailed clinical and laboratory data collected during hospitalization, including outcome 3 weeks after study admission. RESULTS: 73% of patients were women; median age was 38 years. Acetaminophen overdose was the most common apparent cause of acute liver failure, accounting for 39% of cases. Idiosyncratic drug reactions were the presumptive cause in 13% of cases, viral hepatitis A and B combined were implicated in 12% of cases, and 17% of cases were of indeterminate cause. Overall patient survival at 3 weeks was 67%. Twenty-nine percent of patients had liver transplantation, and 43% survived without transplantation. Short-term transplant-free survival varied greatly, from 68% for patients with acetaminophen-related liver failure to 25% and 17% for those with other drug reactions and liver failure of indeterminate cause, respectively. Coma grade at admission appeared to be associated with outcome, but age and symptom duration did not. CONCLUSIONS: Acetaminophen overdose and idiosyncratic drug reactions have replaced viral hepatitis as the most frequent apparent causes of acute liver failure. Apparent cause and coma grade at admission were associated with outcome. Although transplantation may improve patient survival, it was unavailable or unnecessary for most patients.

PMID: 12484709

**Prevention of hepatocarcinogenesis and increased susceptibility to acetaminophen-induced liver failure in transaldolase-deficient mice by N-acetylcysteine**


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Although oxidative stress has been implicated in acute acetaminophen-induced liver failure and in chronic liver cirrhosis and hepatocellular carcinoma (HCC), no common underlying metabolic pathway has been identified. Recent case reports suggest a link between the pentose phosphate pathway (PPP) enzyme transaldolase (TAL; encoded by TALDO1) and liver failure in children. Here, we show that Taldo1-/- mice spontaneously developed HCC, and Taldo1-/- mice had increased susceptibility to acetaminophen-induced liver failure. Oxidative stress in Taldo1-/- livers was characterized by the accumulation of sedoheptulose 7-phosphate, failure to recycle ribose 5-phosphate for the oxidative PPP, depleted NADPH and glutathione levels, and increased production of lipid peroxidation. Furthermore, we found evidence of hepatic mitochondrial dysfunction, as indicated by loss of transmembrane potential, diminished mitochondrial mass, and reduced ATP/ADP ratio. Reduced beta-catenin phosphorylation and enhanced c-Jun expression in Taldo1-/- mice reflected adaptation to oxidative stress. Taldo1-/- hepatocytes were resistant to CYP450-mediated acetaminophen-induced apoptosis in vitro and in vivo. Remarkably, lifelong administration of the potent antioxidant N-acetylcysteine (NAC) prevented acetaminophen-induced liver failure, restored Fas-dependent hepatocyte apoptosis, and blocked hepatocarcinogenesis in Taldo1-/- mice. These data reveal a protective role for the TAL-mediated branch of the PPP against hepatocarcinogenesis and identify NAC as a promising treatment for liver disease in TAL deficiency.

PMID: 19436114