Treating staggered paracetamol overdose

**Overview:** Paracetamol hepatotoxicity is the leading cause of acute liver failure in the UK. Liver damage is possible in adults who have taken 10g or more of paracetamol. Ingestion of 5g or more of paracetamol may lead to liver damage if the patient has certain risk factors, including alcoholism and long-term treatment with drugs that induce liver enzymes, such as epilepsy medication and herbal therapy, St John's Wort. The clinical consequences of staggered overdoses are less well understood.

**Current advice:** For suspected paracetamol overdose the MHRA advises immediate medical attention, even if symptoms are limited to nausea or vomiting, and do not reflect the severity of overdose or the risk of organ damage.

Management should be in accordance with established treatment guidelines, see BNF overdose section. Treatment with activated charcoal should be considered if the overdose has been taken within 1 hour. Treatment with N-acetylcysteine may be used up to 24 hours after ingestion of paracetamol, however, the maximum protective effect is obtained up to 8 hours post-ingestion. The effectiveness of the antidote declines sharply after this time.

**New evidence:** A large single centre cohort study examined the clinical impact of staggered overdoses and delayed presentation following paracetamol overdose (Craig et al. 2011).

The study analysed data from 663 patients who were admitted to the Royal Infirmary of Edinburgh between 1992 and 2008 with paracetamol-induced liver injury, of whom 161 (24.3%) had taken a staggered overdose, usually to relieve a variety of common pains, such as abdominal or muscular pains, headache and toothache.

The researchers suggest that prognostic criteria may have reduced sensitivity in staggered overdose patients. This is because despite lower total ingested paracetamol doses and lower admission serum alanine aminotransferase levels, staggered overdose patients were more likely to be encephalopathic on admission, require renal replacement therapy or mechanical ventilation, and had higher mortality compared to single time point overdoses.

They conclude that staggered paracetamol overdoses should be treated as high risk for the development of multiorgan failure, and should be considered for N-acetyl cysteine treatment irrespective of admission serum paracetamol levels.

**Commentary:** "When taken as recommended, paracetamol is a safe and effective analgesic for many types of pain with few side effects and good tolerability. If recommended doses are exceeded, liver damage and acute liver failure may occur.

"People who had taken unintentional overdoses were older, more likely to have a history of alcohol excess, and commonly took compound paracetamol/opioid combination analgesics compared with patients who had taken intentional overdose."
"The mean paracetamol dose in the unintentional overdose group was still high, 11g in 24 hours preceding admission (i.e. markedly higher than recommended daily dose of 4g in 24 hours). The main reason for taking more was trying to relieve untreated pain. Cases of unintentional overdose had greater organ dysfunction on admission and higher mortality. Consequently there should be a low threshold for treatment with acetylcysteine in patients who have taken a staggered unintentional overdose.

"In England and Wales, deaths involving paracetamol have fallen over recent years, largely because of a reduction in deaths involving co- proxamol, which was withdrawn in 2005 (Office for National Statistics 2011). Interestingly, the new study by Craig et al reported a significantly greater proportion of the patients had overdosed unintentionally using combination analgesics between 2003-07 than 1993-97, although this is not supported by the most recent Office for National Statistics mortality data.

"The key messages for patients are clear. If you take more paracetamol than is recommended you won't improve pain control but you may seriously damage your health. When paracetamol does not relieve pain don't think of taking a 'top up' dose, consult a healthcare professional for advice regarding alternative pain management strategies". - Roger Knaggs, Associate Professor in Clinical Pharmacy Practice, University of Nottingham.

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