We aimed to assess the expected acetylcysteine concentration time profiles following delivery of modified acetylcysteine regimens proposed for those at high and low risk of hepatotoxicity. In addition, we will determine acetylcysteine concentrations post-cessation of abbreviated infusions” wong et al (2017).

Abstract:

PURPOSE: Paracetamol overdose is common and is treated with acetylcysteine to prevent the development of hepatotoxicity. N-acetyl-p-benzoquinone imine (NAPQI) is the toxic metabolite of paracetamol overdose. We aimed to assess the expected acetylcysteine concentration time profiles following delivery of modified acetylcysteine regimens proposed for those at high and low risk of hepatotoxicity. In addition, we will determine acetylcysteine concentrations post-cessation of abbreviated infusions.

METHOD: We performed pharmacokinetic simulations using Berkeley Madonna (version 8.3.23.0) comparing the time course of acetylcysteine concentration during and after the cessation of an abbreviated 12-h regimen (250 mg/kg) using a two-bag infusion and
compared this to the standard 21-h three-bag (300 mg/kg) regimen. We also simulated extended duration acetylcysteine regimens and other increased dosing strategies that have been recommended in specific paracetamol poisoning scenarios.

RESULTS: A more sustained serum concentration is achieved when the acetylcysteine loading dose is delivered over 4 h using the two-bag compared to the 1-h loading dose of the three-bag regimen. When administering an abbreviated 12-h acetylcysteine regimen, circulating acetylcysteine is detectable for 8 h after cessation of the infusion. This may provide a continued hepatoprotective effect if NAPQI is still being generated after the infusion is ceased.

CONCLUSION: This pharmacokinetic simulation study is an important step in determining plasma acetylcysteine concentrations that are likely to be achieved using various modified treatment regimens. Importantly, for patients at low risk of liver injury after acute overdose, acetylcysteine is likely to be detectable many hours post-cessation of a 12-h regimen. This should provide a safety factor against development of hepatotoxicity for any ongoing paracetamol metabolism after cessation of the acetylcysteine infusion.

Reference:


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