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**Toxicology Society, Singapore (TSS) Consensus Statement on Acetylcysteine for Paracetamol Overdose**

* **Recommends administering the first dose of intravenous acetylcysteine over one hour instead of 15 minutes.**
* **Treatment with acetylcysteine is not contraindicated in patients with hypersensitivity or previous anaphylactoid reaction to N-acetylcysteine**

**Background:**

Paracetamol overdose can potentially cause liver damage and death. Intravenous acetylcysteine is the antidote of choice to treat paracetamol overdose locally. Its efficacy when given within 8 hours of the overdose is recognized.

Following the release of “Paracetamol overdose: new guidance on use of intravenous acetylcysteine” by the Commission on Human Medicines (CHM), UK, in September 2012, TSS reviewed our local guidelines and concurred with the CHM recommendations to administer the first dose of intravenous acetylcysteine over one hour instead of 15 minutes.

**Rationale**

1. N-acetylcysteine is an effective antidote for all patients overdosed on paracetamol who are at risk of developing hepatotoxicity. As most dose-related adverse reactions to acetylcysteine occur within the first hour of infusion, these may be reduced if the initial infusion is extended from 15 minutes to 60 minutes. Management is mainly supportive for these adverse reactions, with temporarily stopping or slowing of the infusion, and administration of antihistamines. This is evidence-based but practiced only sporadically in various hospitals locally. In some cases, acetylcysteine infusion was stopped.

The current practice of infusing the initial dose over any range between15 minutes to 60 minutes is dependent on the treating physician.

As such, TSS recommends administering the first dose of intravenous acetylcysteine over one hour to standardise practice and to reduce dose related adverse effects.

1. Adverse effects are usually described as anaphylactoid reactions, manifested as flushing, rash, wheeze or hypotension. Severe life-threatening reactions although rare, may occur in susceptible persons, such as those with asthma. However, this should not contraindicate the use of acetylcysteine in the treatment of paracetamol overdose. Even if a patient has a previous reaction to intravenous acetylcysteine, the benefits of administering acetylcysteine would still outweigh the risks. Thus such patients should receive treatment. Any 'hypersensitivity-like' reactions ascribed to acetylcysteine are likely to be anaphylactoid in nature and therefore may not occur on repeated exposure.

**References**

1. Drug Safety Update September 2012, vol 6, issue 2: A1
2. <http://www.mhra.gov.uk/home/groups/pl-p/documents/drugsafetymessage/con184709.pdf>. Accessed 7 August 2013
3. Daly FF, Fountain JS, Murray L, Graudins A, Buckley NA; Panel of Australian

and New Zealand clinical toxicologists. Guidelines for the management of

paracetamol poisoning in Australia and New Zealand--explanation and elaboration.

A consensus statement from clinical toxicologists consulting to the Australasian

poisons information centres. Med J Aust. 2008 Mar 3;188(5):296-301. Review.

1. Keays R, Harrison PM, Wendon JA, et al. Intravenous acetylcysteine in paracetamol induced fulminant hepatic failure: a prospective controlled trial. BMJ 1991; 303: 1026-1029.