Letter

NAC: still the way to go

Amit K Gupta, Gar M Chan, Howard A Greller and Mark K Su

Department of Emergency Medicine, North Shore University Hospital, 300 Community Drive, Manhasset, NY 11030, USA

Corresponding author: Amit K Gupta, agupta1@hotmail.com

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See related research by Yang *et al*., http://ccforum.com/content/13/2/R55

We would like to thank Yang and colleagues for their attempt to determine the possibility of delayed hepatic recovery with *N*-acetylcysteine (NAC) administration in acetaminophen-induced hepatotoxicity [1]. We are concerned, however, about the possible consequences that may arise from their conclusions.

Owing to the wide availability of acetaminophen, intentional and unintentional overdoses are one of the leading causes of liver failure in the world [2]. NAC is currently a highly effective and safe antidote to treat acute acetaminophen overdose, and is most efficacious when administered within 8 hours of ingestion [3]. Furthermore, one landmark study showed that even in patients who presented with delayed acetaminophen-induced fulminant hepatic failure, intravenous NAC administration improved survival versus control individuals (48% vs. 20%) [4]. Another study found that the infusion of acetylcysteine in patients with acetaminophen-induced liver failure resulted in an increase in mean oxygen delivery and in an increased mean arterial pressure [5].

It is difficult to believe that the mouse model of Yang and colleagues has any correlation to humans, since the already established human data are so overwhelmingly positive. The amount of acetaminophen administered in their study caused hepatotoxicity but did not induce death, and therefore is not applicable to real-life situations where people may ingest potentially fatal doses of acetaminophen.

It is not clear to us why the authors came to explore this study topic. The conclusions drawn from their article are potentially dangerous and should be viewed with caution and scepticism.

Authors' response

Runkuan Yang, Keita Miki, Xin He, Meaghan E Killeen and Mitchell P Fink

We would like to point out the following factors.

Firstly, NAC treatment was effective at the 24 hours timepoint in our study.

Also, the main treatment duration in the paper of Keays and colleagues was 20 hours [4]. Even though a low dose of NAC infusion was continued after the main treatment, this therapy was discontinued when patients recovered from encephalopathy. It is not clear for how long this NAC treatment was given in surviving patients and in nonsurviving patients.

Finally, Harrison and colleagues' patients were treated with NAC for 4 hours and 15 minutes [5] – the treatment was therefore not prolonged.

Acetaminophen is frequently used by patients with chronic pain. Acetaminophen hepatotoxicity in these patients is treated with NAC for longer than the standard 20 hours in some hospitals. At present, NAC is also used to treat nonacetaminophen-induced hepatotoxicity [6,7]. The median duration of NAC administration in children with nonacetaminophen-induced acute liver injury is 5 days (range, 1 to 77 days) [7]. There are, however, only limited data available on the efficacy and safety of NAC. It is therefore important to know the safety and efficacy of prolonged NAC therapy.

NAC = *N*-acetylcysteine.

Competing interests

The authors declare that they have no competing interests.

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