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ORIGINAL REPORT

# Effects of delay in infusion of N-acetylcysteine on appearance of adverse drug reactions after acetaminophen overdose: a retrospective study†

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SUMMARY

**Purpose** To investigate the relationship between different types of adverse drug reaction (ADR) and late time to N-acetylcysteine (NAC) infusion in patients presenting to the hospital with acetaminophen overdose.

**Methods** This is a retrospective study of patients admitted to the hospital for acute acetaminophen overdose over a period of 5 years (1 January 2004 to 31 December 2008). The primary outcome of interest was the relationship between ADR, if any, and late time to NAC infusion. Parametric and non-parametric tests were used to test differences between groups depending on the normality of the data. SPSS 15 was used for data analysis.

**Results** Of 305 patients with acetaminophen overdose, 146 (47.9%) were treated with intravenous NAC and 139 (45.6%) were included in this study. Different types of ADR were observed in 94 (67.6%) patients. Late time to NAC infusion was significantly associated with cutaneous anaphylactoid reactions when compared to patients without this type of ADR ($p < 0.001$). However, there were no significant differences in time to NAC infusion between patients with and without the following ADR: gastrointestinal reactions ($p = 0.11$), respiratory reactions ($p = 0.77$), central nervous reactions ($p = 0.64$), and cardiovascular reactions ($p = 0.63$).

**Conclusion** Late time to NAC infusion is a risk factor for developing cutaneous anaphylactoid reactions, suggesting, rather than proving, that early NAC infusion ($\leq$8 hours) may be protective against this type of ADR. Copyright © 2010 John Wiley & Sons, Ltd.

KEY WORDS — acetaminophen; adverse drug reaction; cutaneous anaphylactoid reactions; N-acetylcysteine; overdose

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## INTRODUCTION

Acetaminophen (Paracetamol) is the most common drug taken in overdose in the world. It is frequently used as an over-the-counter analgesic and antipyretic for minor aches and pains.[1,2] Despite excellent safety for therapeutic uses, it is also one of the most common agents deliberately ingested in self-poisoning episodes and a leading cause of hepatotoxicity and nephrotoxicity.[3,4]

Since the early 1970s, N-acetylcysteine (NAC) has been used as an antidote to acetaminophen overdose.[5] Multiple protocols for the administration of NAC in the patient with acetaminophen overdose exist for both the oral and intravenous routes. There has been much discussion of the pros of oral *versus* intravenous administration of NAC in the literature and each therapeutic protocol has its supporters.[5] Both have been shown to be equally effective.[6,7] Orally, NAC has been shown to have a minimal adverse effect profile, consisting mostly of nausea and vomiting, and increased tolerance can be achieved with co-administration of an antiemetic such as metoclopramide or ondansetron.[8] The intravenous preparation was approved by the US Food and Drug Administration (FDA) for use in the United States in 2004. Intravenous NAC has been the standard treatment for acetaminophen overdose in

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†The authors declare no conflict of interest.