## P001 [ID#4]

# Comparison of Adverse Reactions to a 2 vs 3 Bag IV Acetylcysteine Regimen During Treatment of Paracetamol Overdose

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**BACKGROUND/OBJECTIVES**: Previous studies have shown that a 2-bag 20-hour intravenous (IV) acetylcysteine regimen reduced the incidence of non-allergic anaphylactic reactions compared to the 3-bag 21-hour IV regimen for treatment of paracetamol overdose. We evaluated the safety and adverse reactions of the 2-bag IV acetylcysteine regimen in a larger international collaborative study.

**METHODS**: This is a prospective cohort study of Australian centres using a 2-bag IV acetylcysteine regimen (200mg/kg over 4 hours, 100mg/kg over 16 hours) for paracetamol overdose, with data analysed from early 2014 to late 2018. Outcomes were compared with patients from the Canadian Acetaminophen Overdose Study (CAOS) treated with a 3-bag IV acetylcysteine regimen (150mg/kg over 15-60 min, 50mg/kg over 4 hours, 100mg/kg over 16 hours), 1980 to 2005. All subjects who receive acetylcysteine were included in the study. Outcomes including adverse reactions and mortality attributed to paracetamol overdose are reported. Adverse events to acetylcysteine included cutaneous (oedema, facial flushing, pruritus, urticaria) and systemic reactions (hypotension, respiratory symptoms).

**RESULTS**: Out of 15,037 paracetamol overdose presentations to 43 treatment centres, 7,663 received acetylcysteine. Study criteria were met in 1208 receiving the 2-bag and 6,455 receiving the 3-bag acetylcysteine regimen. Median years of age was 21 (IQR 17,32) vs 24 (17,37) in the 2 vs 3-bag acetylcysteine regimen, respectively. Median time to acetylcysteine was 7 hours (IQR 6,12) for the 2-bag vs 9.3 hours (6.2,19) for the 3-bag regimen. The incidence of cutaneous and systemic non-allergic anaphylactic reactions was: 22 (1.8%) with the 2-bag vs 528 (8.2%) with the 3-bag regimen ($p<0.0001$, OR 0.2, 95%CI: 0.13-0.32). Mortality attributable to acetylcysteine was zero in both cohorts.

**CONCLUSIONS**: In this multi-centre study, the 2-bag IV acetylcysteine regimen resulted in significantly less non-allergic anaphylactic reactions compared to the 3-bag IV acetylcysteine regimen.