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# Efficacy of a Two Bags Acetylcysteine Regimen to Treat Paracetamol Overdose (2NAC Study)

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BACKGROUND/OBJECTIVES: Previous studies of paracetamol overdose treatment show that a 2-bag, 20-hour intravenous (IV) acetylcysteine regimen decreased incidence of non-allergic anaphylactic reactions compared to the 3-bag, 21-hour IV regimen. We evaluated the efficacy and safety of the 2-bag IV acetylcysteine regimen.

METHODS: This is a mixed retrospective/prospective observational study of paracetamol overdose from 2009 to mid-2019 in Australian centres currently using a 2-bag IV acetylcysteine regimen (200mg/kg over 4 hours, 100mg/kg over 16 hours). Outcomes are compared to a historical cohort treated at the same centres with a 3-bag IV acetylcysteine regimen. For the primary analysis: subjects had single, acute ingestions, a serum paracetamol-concentration performed 4 to 24-hours post-ingestion which was on or above the Rumack-Matthews treatment-nomogram line. The primary outcome was development of acute liver injury (ALI), defined as peak ALT >150 IU/L and double baseline.

RESULTS: Out of 6419 paracetamol overdose presentations to nine treatment centres, 2763 received acetylcysteine. For the primary analysis, 1003 received the 2-bag and 783 received the 3-bag acetylcysteine regimen. When presentation bloods were performed 8-hours post-overdose, 18 (2.6%) developed ALI with the 2-bag regimen vs 15 (2.6%) with the 3-bag regimen (p=0.98 OR 1 95% CI: 0.50-2). When presentation bloods were performed 8 to 24-hours post-overdose, 66 (20%) developed ALI with the 2-bag regimen vs 46 (21 %) with the 3-bag regimen (p=0.51, OR 0.86, 95% CI 0.56-1.3). The incidence of hepatotoxicity (ALT>1000 IU/L) with the 2-bag regimen was: 49 (4.9%) vs 43 (5.5%) with the 3-bag regimen (p=0.56, OR 0.88, 95% CI: 0.58-1.3)). Cutaneous and systemic non-allergic anaphylactic reactions were identified in: 20 (3%) with 2-bag vs 64 (8.1%) with 3-bag regimen (p=<0.0001, OR 0.2, 95% CI: 0.13-0.38).

CONCLUSIONS: In this multi-centre study, the 2-bag IV acetylcysteine regimen was as efficacious as the 3-bag IV regimen and resulted in significantly less non-allergic anaphylactic reactions.