Letter to the Editors

Paracetamol (acetaminophen) overdose and
acetylcysteine administration: should the United
Kingdom adopt a single '150-line'?

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For more than 30 years acetylcysteine has been recognized as an effective antidote after paracetamol overdose, and is capable of preventing liver failure if given sufficiently early after ingestion [1]. The National Poisons Information Service in the United Kingdom advises acetylcysteine based on the extent of paracetamol exposure and the presence of additional risk factors [2]. The Prescott nomogram, or so-called '200-line' is used to indicate acetylcysteine treatment and is plotted from 200 mg l⁻¹ (1320 µmol l⁻¹) at 4 h to 30 mg l⁻¹ (200 µmol l⁻¹) at 15 h [1]. A '100-line' allows more aggressive treatment of patients considered at high risk of liver injury due to prior use of drugs capable of inducing hepatic P450 enzymes, regular excess ethanol consumption, malnutrition or the presence of established liver disease [3, 4]. In the United States, Australia and elsewhere, risk assessment is based solely on a paracetamol concentration above the so-called '150-line', plotted 25% lower than the standard Prescott nomogram [5]. Few comparative data exist concerning the various international methods.

The impact of adopting a single '150-line' vs. the current United Kingdom method was studied in an existing dataset of 1045 patients who presented to the Emergency Department of the Royal Infirmary of Edinburgh within 24 h of paracetamol ingestion at a single time point [6]. Paracetamol concentrations were considered with reference to the different nomograms and between-group comparisons made using two-tailed Yate's corrected Chi square proportional tests (MedCalc statistical software v.11.1.1.0, Mariakerke, Belgium).

If the '150-line' was used as the sole indicator for acetylcysteine administration, then a similar number of patients would have been included compared with the existing United Kingdom criteria: 262 vs. 273, representing 1.1% (95% CI -3.3, 5.4%) fewer patients ($P = 0.6344$). However, this would have resulted in treatment of 55 additional patients above the '150-line' without risk factors and 66 high risk patients between the '100-line' and '150-line'

Table 1

Administration of acetylcysteine according to the paracetamol concentration and presence of risk factors

[Paracetamol]	<i>n</i>	Acetylcysteine
Above '200-line'		
No risk factors	99	93 (93.9%)
High risk	64	64 (100.0%)
Total	163	157 (96.3%)
Between '150-line' and '200-line'		
†No risk factors	55	29 (52.7%)
High risk	44	44 (100.0%)*
Total	99	73 (73.7%)
Between '100-line' and '150-line'		
No risk factors	96	21 (21.9%)
‡High risk	66	63 (95.5%)*
Total	162	84 (51.9%)
Below '100-line'		
No risk factors	424	16 (3.8%)
High risk	197	23 (11.7%)
Total	621	39 (6.3%)
All		
No risk factors	674	159 (23.6%)
High risk	371	194 (52.3%)*
Total	1045	353 (33.8%)

* $P < 0.005$ vs. 'no risk factors'. †All would receive treatment if using the '150-line',
‡none would receive treatment if using '150-line'.

would no longer have been treated (Table 1). Paracetamol concentrations were above the '200-line' in 163 patients (15.6%, 95% CI 13.3, 18.2%), above the '150-line' in 262 (25.1%, 95% CI 22.1, 28.3%) and above the '100-line' in 424 patients (40.6%, 95% CI 36.8, 44.6%).

Acetylcysteine was administered to around 10% more patients than actually met the existing criteria, perhaps indicating some uncertainty surrounding the definition of high risk patients. Adoption of the '150-line' would remove the need for clinical risk assessment so that the need for

treatment could be ascertained in a more objective manner. The '150-line' approach appears to be acceptable to the majority of Directors of Poison Control Centres in the United States and Europe, despite different international guidelines [7]. A limitation of the present findings is that they are derived from a single hospital, and might not be applicable to other institutions or regions with different patient characteristics.

In conclusion, the '150-line' method would identify a similar overall number of patients. However, the resulting population would have a distinct pattern of paracetamol exposure and different risk factor profiles from the population identified by the current United Kingdom criteria. The subgroup of greatest interest are high risk patients with paracetamol concentrations between the '100-line' and '150-line' that currently receive antidote but would no longer do so according to the '150-line' method. Too few data exist to address adequately the likely risk of acute liver injury in this subgroup, and this issue may only be addressed by very large prospective studies involving multiple institutions. More data are needed in order to optimize clinical care and achieve greater international harmonization.

Competing Interests

There are no competing interests to declare.

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