ORIGINAL ARTICLE

Paracetamol overdose: an evidence based flowchart to guide management

C I Wallace, P I Dargan, A L Jones

Emerg Med J 2002;**19**:202–205

A flowchart for the management of patients with paracetamol poisoning is presented to help clinicians in the emergency department.

Paracetamol is the commonest drug taken in overdose in the United Kingdom. While the management of early paracetamol poisoning is straightforward, the management of late presenting cases, cases presenting after a staggered overdose, and patients with risk factors for paracetamol poisoning can be much more complex. The authors have developed and present here an evidence based flowchart that will guide clinicians step by step through the investigation and treatment of all patients presenting to hospital after this common, but often difficult to manage overdose. As well as a management guideline this flowchart can be used as an educational tool.

BACKGROUND

Paracetamol is the commonest drug taken in overdose in the United Kingdom, accounting for 48% of all poisoning admissions to hospital and an estimated 100–200 deaths per year.[1–6] However, junior doctors' knowledge about the management of paracetamol poisoning is poor.[7]

The management of patients who present early (less than 15 hours) after ingestion of a single paracetamol overdose is straightforward. If the patient has taken a potentially toxic dose of paracetamol, management is guided by the plasma paracetamol concentration; treatment with N-acetylcysteine in patients with a toxic plasma paracetamol concentration provides complete protection against paracetamol induced hepatotoxicity.[8] However, when cases stray from this simple scenario (such as with staggered overdoses, patients with high risk factors for paracetamol poisoning, or late presentation), management decisions are more complex.[9–11]

Current guidelines for paracetamol poisoning are based on the consensus recommendations of the UK National Poisons Information Service (NPIS), they have also been adopted by the Royal College of Paediatrics and Child Health as a Good Practice Consensus Statement. The guidelines have been circulated to all accident and emergency departments in the form of a poster in prose format and we support their use.[12]

Our aim is to provide an evidence based, easy to follow, and visually attractive management guideline for paracetamol poisoning, aimed at emergency and general physicians (particularly junior doctors) dealing with this common, but often difficult to manage overdose. The flowchart that we present will guide the clinician through the management of a patient presenting with a paracetamol overdose in a stepwise fashion. It can also be used as an educational tool because it indicates the evidence (or lack of it) for each management step. It therefore augments the current NPIS paracetamol poster.[12] The flowchart is a guideline however, and not a protocol, and individual decisions will need to be made for every patient based on their particular circumstances.

METHODS

We conducted a literature search of Medline, Toxline, and Embase using the terms "paracetamol" and "acetaminophen" with "intoxication", "poisoning" and "overdose". No language was barred and no other limitations were placed. The retrieved abstracts were reviewed and the most pertinent articles were reviewed in more detail. In addition, we took into account the consensus recommendations from the UK Toxicology Group (National Poisons Information Service (NPIS), Paracetamol Information Centre, and British Association of Accident and Emergency Medicine) on which the current UK guidelines for the management of paracetamol poisoning are based. This evidence base was then used to construct an algorithmic flowchart to guide the clinician through the management of both simple and complex paracetamol poisoning in a stepwise fashion.

RESULTS

See figure 1 for the flowchart used to guide the management of patients with paracetamol poisoning, together with the supporting references from the literature.[8–45]

The paracetamol flowchart is structured around a few crucial branchpoints in the following order. Is the patient presenting after a single or staggered overdose? What is the time after ingestion? What are the results to the relevant investigations? Based upon the results of these questions, the clinician is guided through the appropriate steps in investigation and treatment of the paracetamol overdose. So that the flowchart can be used as a stand alone tool to guide patient management we have included the standard UK plasma paracetamol treatment nomogram,[8 12 37] together with information boxes on risk factors for paracetamol poisoning,[13–19] doses of N-acetylcysteine [8 40] and management of adverse reactions to N-acetylcysteine.[41 42]

Correspondence to:
Dr A Jones, National Poisons Information Service, Guy's and St Thomas' NHS Trust, Avonley Road, London, SE14 5ER, UK;
alison.jones@gstt.sthames.nhs.uk

Accepted for publication
29 October 2001

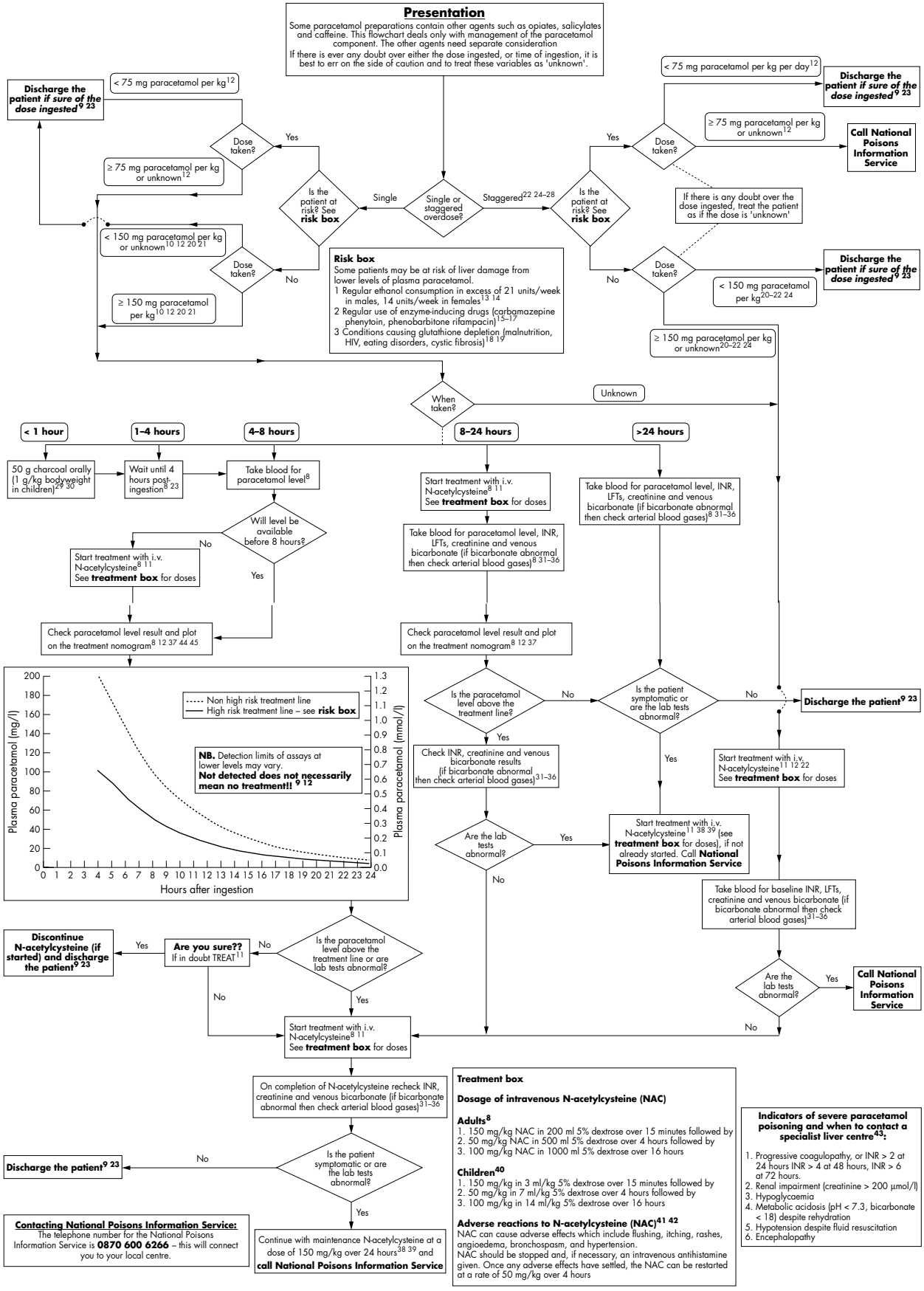

Figure 1 Paracetamol overdose: a flowchart to guide management. (The numbers in superscripts relate to the supporting references).

DISCUSSION

Paracetamol remains the most common agent taken in overdose in the UK,[4 5] but junior doctors' knowledge about the management of paracetamol poisoning remains poor,[7] despite the availability of UK guidelines as a poster in prose format.[12] The management of paracetamol poisoning has been reviewed in detail elsewhere and these review articles complement our management flowchart for readers who wish to study the background literature in more detail.[9 10 23 46]

A study by Hardern *et al* [47] showed that the management of paracetamol poisoning is improved if staff have access to guidelines, but found no difference between the performance of prose and flowchart formats. However, two further studies, one in the US [48] and one in the UK [49] have shown that physicians prefer practice guidelines in the form of evidence based algorithms that are "user friendly". The management of paracetamol overdose entails multiple steps in both investigation and treatment. We feel that the presentation of these management decisions in the algorithmic, flowchart format that we present means that each step in the process can be focused upon separately (whereas the entire body of prose guidelines may need to be assimilated before understanding the individual steps). The management flowchart deals with both the well defined early cases and more complex cases such as patients with risk factors for paracetamol poisoning, staggered overdoses, and late presenters.

This flowchart will guide physicians through the management of the majority of patients presenting with a paracetamol overdose from the time of presentation to hospital to the time that they are medically fit for discharge. There are however situations where further advice tailored to the management of an individual patient from either a clinical toxicologist at the National Poisons Information Service, or a hepatologist at a liver transplant unit may be required and this has been indicated on the flowchart. This particularly applies to patients presenting either after a staggered paracetamol overdose or later than 24 hours after a single paracetamol overdose, where both the efficacy and mechanism of action of N-acetylcysteine are controversial.[8 11 21] Patients with established hepatotoxicity, with markers of severe toxicity outlined in the flowchart, such as coagulopathy, should be discussed early with a hepatologist, as meticulous supportive care is critical to a good outcome in such cases.[43 50]

CONCLUSION

Paracetamol is by far the commonest substance involved in self poisoning in the UK. While the management of early paracetamol poisoning is straightforward, the management of late presenting cases, cases presenting after a staggered overdose and patients with risk factors for paracetamol poisoning can be much more complex. We have developed an evidence based, easy to follow management guideline in the form of a flowchart that will guide clinicians step by step through the investigation and treatment of all patients presenting to hospital after a paracetamol overdose.

ACKNOWLEDGEMENT

The authors would like to thank Professor Laurie Prescott and Dr Alex Proudfoot for reviewing the flowchart and for their helpful comments.

Contributors

Craig Wallace and Paul Dargan were responsible for the literature review and designed the management flowchart. Alison Jones reviewed the literature review and the management flowchart. All three authors were involved in the writing of the paper and all three authors will act as guarantors.

Authors' affiliations

C I Wallace, P I Dargan, A L Jones, National Poisons Information Service, Guy's and St Thomas' NHS Trust, London, UK

Conflicts of interest: AJ has acted as an advisor to Glaxo Smith Kline, Cumberland Pharmaceuticals. Oxford Pharmaceuticals support the outreach educational activity of the London Centre of the National Poisons Information Service. AJ and PD have acted as advisors to Orphan Drugs (Europe) and have received funding to attend meetings from Glaxo Smith Kline.

REFERENCES

1 **Fagan E**, Wanna G. Reducing paracetamol overdoses. *BMJ* 1996;**313**:1417–18.
2 **Atcha Z**. Paracetamol related deaths in England and Wales, 1993–1997 (Office for National Statistics). *Health Stat Q* 2000;**1**:5–9.
3 **Gunnel D**, Hawton K, Murray V *et al*. Use of paracetamol for suicide and parasuicide in the UK and France: are restrictions on availability justified? *J Epidemiol Community Health* 1997;**51**:175–9.
4 **Thomas SHL**, Horner JE, Chew K *et al*. Presentation of poisoned patients to accident and emergency departments in the North of England. *Hum Exp Toxicol* 1996;**15**:466–70.
5 **Bialas MC**, Reid PG, Beck P *et al*. Changing patterns of self-poisoning in a UK health district. *Q J Med* 1996;**89**:893–901.
6 **Hawton K**, Fagg J. Trends in deliberate self poisoning and self injury in Oxford, 1976–1990. *BMJ* 1992;**304**:1409–11.
7 **Hulbert DC**, Bray GP, Beckett MW. The management of paracetamol poisoning by junior doctors. *J Accid Emerg Med* 1995;**12**:66–7.
8 **Prescott LF**, Illingworth RN, Critchley JA *et al*. Intravenous N-acetylcysteine: the treatment of choice for paracetamol poisoning. *BMJ* 1979;2:1097–100.
9 **Vale JA**, Proudfoot AT. Paracetamol (acetaminophen) poisoning *Lancet* 1995;**346**:547–52.
10 **Prescott LF**. Paracetamol overdosage: pharmacological considerations and clinical management. *Drugs* 1983;**23**:290–314.
11 **Jones AL**. Mechanism of action and value of N-acetylcysteine in the treatment of early and late acetaminophen poisoning: a critical review. *J Toxicol Clin Tox* 1998;**36**:277–85.
12 **NPIS**. *Management of acute paracetamol poisoning*. Guidelines agreed by the UK National Poisons Information Service 1998. Supplied to Accident and Emergency Centres in the United Kingdom by the Paracetamol Information Centre in collaboration with the British Association for Accident and Emergency Medicine.
13 **Prescott LF**. Paracetamol, alcohol and the liver. *Br J Clin Pharmacol* 2000;**49**:291–301.
14 **Bray GP**, Mowat C, Muir DF *et al*. The effect of chronic alcohol intake on prognosis and outcome in paracetamol overdose. *Hum Exp Toxicol* 1991;**10**:435–8.
15 **Wright N**, Prescott LF. Potentiation by previous drug therapy of hepatotoxicity following paracetamol overdose. *Scott Med J* 1973;**18**:56–8.
16 **Smith JA**, Hine ID, Beck P *et al*. Paracetamol toxicity: is enzyme induction important? *Hum Exp Toxicol* 1986;**5**:383–5.
17 **Minton N**, Henry JA, Frankel RJ. Fatal paracetamol poisoning in an epileptic *Hum Exp Toxicol* 1988;**7**:33–4.
18 **Buhl R**, Jaffe HA, Holroyd KA, *et al*. Systemic glutathione deficiency in symptom-free HIV-seropositive individuals. *Lancet* 1989;ii:1294–8.
19 **Whitcomb DC**, Block GD. Association of acetaminophen hepatotoxicity with fasting and ethanol use. *JAMA* 1994;**272**:1845–50.
20 **Wendel A**, Jaeschke H, Gloger M. Drug induced lipid peroxidation in mice – protection against paracetamol induced liver necrosis by intravenous liposomally entrapped glutathione. *Biochem Pharmacol* 1982;**31**:3601–5.
21 **Prescott LF**. *Paracetamol (acetaminophen). A critical bibliographic review*. London: Taylor and Francis, 1996.
22 **Linden CH**, Rumack BH. Acetaminophen overdose. *Emerg Clin North Am* 1984;**2**:103.
23 **Prescott LF**, Critchley JA. The treatment of acetaminophen poisoning. *Ann Rev Pharmacol Toxicol* 1983;**23**:87–101.
24 **Henretig FM**, Selbst SM, Forrest C, *et al*. Repeated acetaminophen overdosing causing hepatotoxicity in children: clinical reports and literature review. *Clin Pediatr* 1989;**28**:525–8.
25 **Agran PF**, Zenk KE, Romanowsky SG. Acute liver failure and encephalopathy in a 15 month old infant. *Am J Dis Child* 1983;**137**:1107–14.
26 **Swetnam SM**, Florman AL. Probable acetaminophen toxicity in an 18-month old infant due to repeated overdosing. *Clin Pediatr* 1984;**23**:104–5.
27 **Smith DW**, Isakson G, Frankel R, *et al*. Hepatic failure following ingestion of multiple doses of acetaminophen in a young child. *J Pediatr Gastroenterol Nutr* 1986;**5**:822–5.
28 **Douidoar SM**, Ali-Khali I, Hakersang RW. Severe hepatotoxicity , acute renal failure and pancytopenia in a young child after repeated acetaminophen overdosing. *Clin Pediatr* 1994;**33**:42–5.
29 American Academy of Clinical Toxicology; European Association of Poison Control Centres and Clinical Toxicologists. Position statement: single-dose activated charcoal. *J Toxicol Clin Toxicol* 1997;**35**:721–41.
30 **Buckley NA**, Whyte IM, O'Connell DL, *et al*. Activated charcoal reduces the need for N-acetylcysteine treatment after acetaminophen (paracetamol) overdose. *J Toxicol Clin Toxicol* 1999;**37**:753–7.

31 **Singer AJ**, Carracio TR, Mofenson HC. The temporal profile of increased transaminase levels in patients with acetaminophen induced liver dysfunction *Ann Emerg Med* 1995;**26**:49–53.
32 **Harrison PM**, O'Grady JG, Keays RT, *et al*. Serial prothrombin time as a prognostic indicator in paracetamol induced fulminant hepatic failure *BMJ* 1990;**301**:964–6.
33 **Record CO**, Iles RA, Cohen RD, *et al*. Acid-base and metabolic disturbances in fulminant hepatic failure *Gut* 1975;**16**:144–9.
34 **Blantz RC**. Acetaminophen, acute and chronic effects on renal function. *Am J Kidney Dis* 1996;**28**:S3–6.
35 **Eguia L**, Materson BJ. Acetaminophen-related acute renal failure without fulminant liver failure. *Pharmacotherapy* 1997;**17**:363–70.
36 **Prescott LF**, Proudfoot AT, Creegen RJ. Paracetamol induced acute renal failure in the absence of fulminant liver damage. *BMJ* 1982;**284**:421–2
37 **Rumack BH**, Matthew H. Acetaminophen poisoning and toxicity. *Pediatrics* 1975;**55**:871–6.
38 **Keays R**, Harrison PM, Wendon JA, *et al*. Intravenous acetylcysteine in paracetamol-induced fulminant hepatic failure: a prospective controlled trial. *BMJ* 1991;**303**:1026–9.
39 **Harrison PM**, Keays R, Bray GP, *et al*. Improved outcome of paracetamol induced fulminant hepatic failure by late administration of acetylcysteine. *Lancet* 1990;**335**:1572–3.
40 The Medicines Committee of the Royal College of Paediatrics and child Health and Neonatal and Paediatric Pharmacists Group. *Medicines for Children 1999*. London: Royal College of Paediatrics and Child Health Publications, 1999.
41 **Dawson AH**, Henry DA, McEwen J. Adverse reactions to N-Acetylcysteine during treatment for paracetamol poisoning. *Med J Aust* 1989;**150**:329–31.
42 **Bailey B**, McGuigan MA. Management of anaphyalctoid reactions to intravenous N-Acetylcysteine. *Ann Emerg Med* 1998;**31**:710–15.
43 **Makin A**, Williams R. The current management of paracetamol overdosage. *Br J Clin Pharmacol* 1994;**48**:144–8.
44 **Prescott LF**, Wright N, Roscoe P, *et al*. Plasma paracetamol half-life and hepatic necrosis in patients with paracetamol overdosage. *Lancet* 1971;i:519–22.
45 **Gazzard BG**, Hughes RD, Widdop B, *et al*. Early prediction of the outcome of a paracetamol overdose based on an analysis of 163 patients. *Postgrad Med J* 1977;**53**:243–47.
46 **Makin A**, Williams R. The current management of paracetamol overdosage. *Br J Clin Pharmacol* 1994;**48**:144–8.
47 **Hardern RD**, Hodgson LC, Hamer DW. Flow diagram or prose: does the format of practice guidelines matter? *Eur J Emerg Med* 1998;**5**:241–4.
48 **Stone TT**, Kivalahan CH, Cox KR. Evaluation of physician preferences for guideline implementation. *Am J Med Qual* 1999;**14**:170–7.
49 **Hardern RD**, Hampshaw S. What do accident and emergency medical staff think of practice guidelines. *Eur J Emerg Med* 1997;**4**:68–71.
50 **O'Grady JG**, Wendon J, Tan KC, *et al*. Liver transplantation after paracetamol overdose. *BMJ* 1991;**303**:221–3.