



Screening for Unsuspected Paracetamol Toxicity in Emergency Department Patients with Elevated ALT

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Background

Paracetamol overdose is a major cause of hepatotoxicity occasionally requiring liver transplantation. However if the toxicity is recognised, treatment with N-Acetyl Cysteine (NAC) can markedly reduce liver damage.

Paracetamol overdose may be intentional or unintentional, resulting from overzealous or unregulated self-medication. Patients are at risk of accidental overdose due to the multitude of preparations available which contain paracetamol and the range of indications (see figure 1 and box). A recent study found that of 131 unintentional overdoses, 38% had taken 2 or more paracetamol-containing products simultaneously.¹

Accidental overdose may not be revealed through history taking due to patient forgetfulness or lack of specific questioning and may have a worse outcome than an intentional overdose, in part be due to lack of recognition of the problem.²

Aim

We investigated the use of serum paracetamol measurements to screen for unsuspected paracetamol toxicity in patients presenting to the Emergency Department (ED) with elevated liver enzymes. The aim was to evaluate the efficacy of this protocol for preventing cases of paracetamol-induced liver toxicity.

Methods

For a period of one year, all blood samples from ED with serum ALT > 50 U/L were reflexively tested for paracetamol concentration³.

Serum ALT was measured using an Olympus AU2700 analyser using Olympus reagents and Roche calibrator and paracetamol was measured using an Abbott AxSYM analyser with Abbott reagents. Paracetamol measurements were made as soon as the ALT test was completed and the results were reported for patient management. The therapeutic interval for paracetamol is 10 – 20 mg/L.

The testing program was audited for frequency of positive results. Chart review was used to assess effect on patient management and efficacy of history taking.

The project was approved by the SVH Human Research Ethics Committee.

Results

Data Summary		
Number of samples	1038	2.8 per day
No paracetamol detected	832	80%
Paracetamol present < 10 mg/L	153	15%
Paracetamol 10 - 20 mg/L	43	4%
Paracetamol > 20 mg/L	10	1%

Of the 53 patients with paracetamol > 10 mg/L, 19 had received their paracetamol in hospital. Of those subjects not given paracetamol in hospital 22 (65%) did not have paracetamol ingestion noted during initial history.

Two patients were administered N-acetylcysteine (NAC) based on the screening. In one case NAC may have prevented more severe liver dysfunction (case 1), in the other case the NAC was ceased and the patient discharged.

In other cases the paracetamol result provided important clarification of the presentation (eg case 2).

Paracetamol in Australia



Figure 1. Examples of paracetamol available in Australia

Example Case Histories

CASE 1: 24F with UTI & Cystitis. ALT=101. Fevers, nausea, vomiting, crying, refusing iv therapy. Admitted to regular alcohol and cocaine use, laxative abuse and anorexia nervosa. There was no indication on admission that she had taken a paracetamol overdose, and hence no routine level was taken. Study paracetamol = 30 mg/L. Following paracetamol result repeat medication history identified high doses of paracetamol in previous days for pain (up to 10 x 500mg tablets for 4 days). Denied acute OD. NAC commenced. ALT and AST resolved without worsening liver function. **Study paracetamol result identified unsuspected hepatotoxic paracetamol concentration allowing NAC treatment. Follow-up revealed possible deliberate attempt at self-harm.**

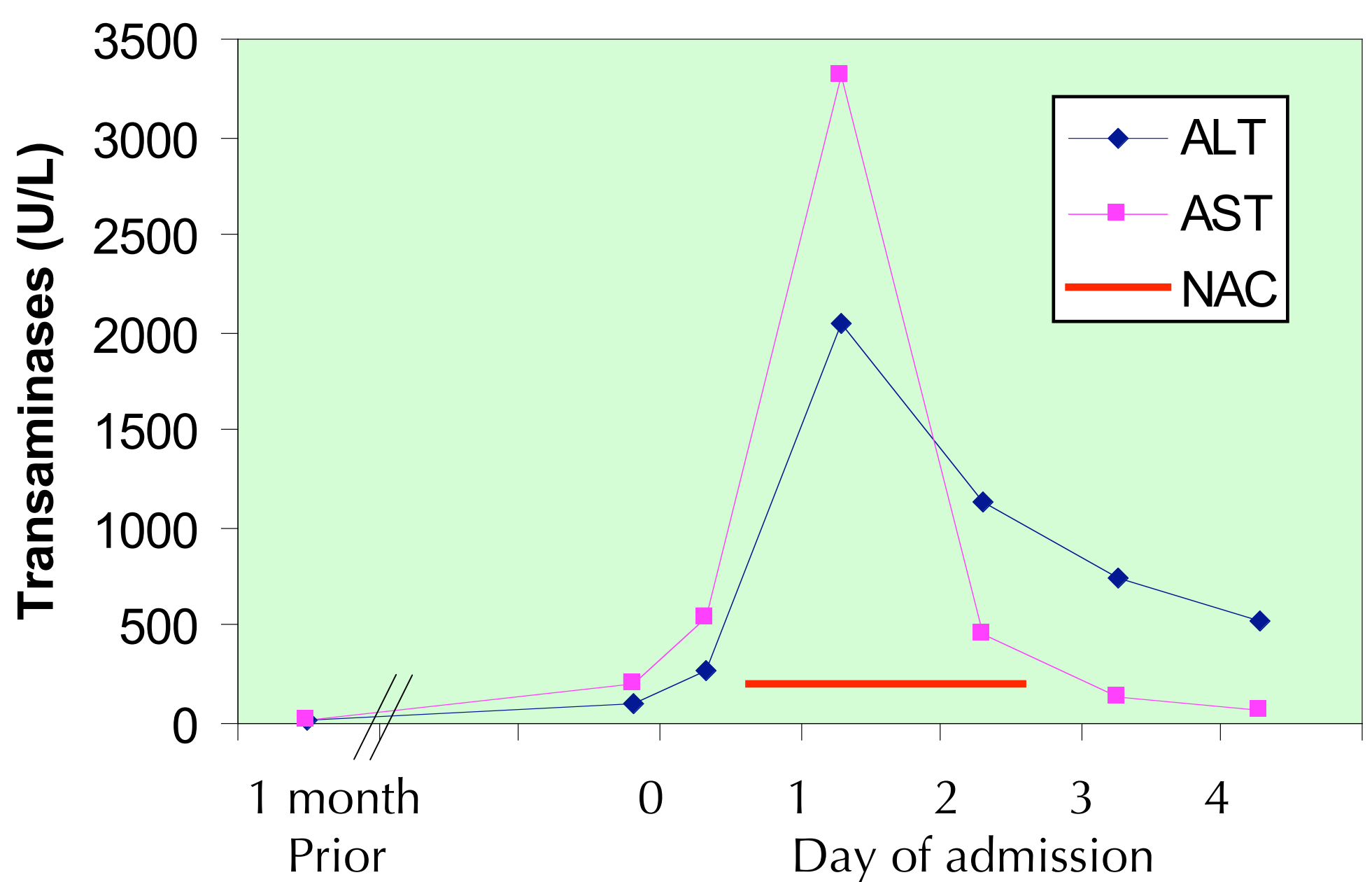


Figure 2. ALT and AST from case 1. The red line shows the period of NAC infusion.

CASE 2: F19 with post-tonsillectomy bleeding. ALT = 88, paracetamol = 11 mg/L, nil initial history of paracetamol ingestion. Following paracetamol result, specific medication history revealed > 8 Panadeine Forte® tablets a day for the past few days. Paracetamol discontinued, patient observed, repeat ALT=10. Discharged. **Study paracetamol result clarified possible cause of raised ALT.**

References

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Anagrain, Capadex, Chem-Mart Chemadol, Chemists' Own Cold & Flu Day/Night, Chemists' Own Cold & Flu Relief Tablets, Chemists' Own Coldeze Tablets, Chemists' Own Dolased Analgesic-Calmative, Chemists' Own Dolased Day/Night Pain Relief, Chemists' Own Hayfever Sinus Relief Tablets, Chemists' Own Pain Tablets, Chemists' Own Pain Tabsules, Chemists' Own Paracetamol 500 mg Tablets, Chemists' Own Paracetamol Capsules, Chemists' Own Paracetamol Pain & Fever Drops, Chemists' Own Sinus-Pain Relief Tablets, Codalgin, Codalgin Forte, Codalgin Relief, Codapane, Codapane Forte, Codral 4 Flu Tablets, Codral Cold & Flu Tablets, Codral Cough, Cold & Flu Day & Night Capsules, Codral Daytime/Nighttime Tablets, Codral Pain Relief, Demazin Cold and Flu Tablets, Demazin Cough Cold and Flu Tablets, Di-Gesic, Dimetapp Cold & Flu Day Relief Liquid Caps, Dimetapp Cold & Flu Night Relief Liquid Caps, Dimetapp Cold, Cough & Flu - Day & Night Liquid Caps, Dolaforte, Duatrol SR, Dymadon Co, Dymadon Forte, Dymadon, Dymadon P, Febridon Tablets & Febridon Clear Effervescent Soluble Tablets, Fiorinal, Fiorinal - Dental, Gold Cross Paracetamol Tablets, Herron Paracetamol, Hexal Comfarol Plus, Lemsip Max, Lemsip Original Lemon, Lemsip Pharmacy Flu Strength - Daytime, Lemsip Pharmacy Flu Strength - Nighttime, Logicin Flu Strength Day & Night Tablets, Mersyndol, Mersyndol DayStrength, Mersyndol Forte, Metomax, Norgesic, Orthocol Cold & Flu, Orthocol Day & Night Cold & Flu, Orthocol Night Cold and Flu, Painstop Day-Time Pain Reliever, Painstop Night-Time Pain Reliever, Panadeine, Panadeine Forte, Panadeine-15, Panadol, Panadol Allergy Sinus, Panadol Cold & Flu, Panadol Extend, Panadol Osteo, Panadol Sinus, Panadol Sinus Day/Night, Panalgesic, Panamax, Panamax Co., Paracetamol Soluble Tablets, Paradox, Parahexal, Paralgin, Parke-Davis Day & Night Cold & Flu Capsules, Parmol, Perfalgan, Prodeine Forte, Prodeine-15, Sinutab Sinus and Pain Relief, Sinutab Sinus, Allergy and Pain Relief, Sudafed Daytime/Nighttime Relief Tablets, Sudafed Sinus Pain Relief, Sudafed Sinus Pain and Allergy Relief, Terry White Chemists Paracetamol, Tylenol, Tylenol Allergy Sinus, Tylenol Cold & Flu, Tylenol Cold & Flu Non-Drowsy, Tylenol Sinus.

Paracetamol preparations available in Australia (MIMS)

Discussion

In order to implement a screening program it must have sufficient sensitivity and specificity for the condition as well as a suitable cost-benefit analysis.

During the year of this study no patient was identified at risk of requiring transplantation, however liver some liver function may have been preserved in one case (case 1) and important clinical information was obtained in several cases (eg case 2).

Since completing this study, a publication has shown that ALT is elevated (>80 U/L) in over 50% of patients receiving maximal recommended paracetamol treatment⁴. This indicates poor specificity of modest increases in ALT for paracetamol overdose. Using a higher ALT concentration for screening would reduce sensitivity for elevated paracetamol concentrations (data not shown).

The high frequency of paracetamol administered in hospital detracts from the specificity of testing for pre-admission overdosing.

A calculation of the expected frequency of listing for liver transplant in Australia on the basis of paracetamol overdose suggests presentation of about 1 case per 9 million per year.

On the basis of a poor cost-benefit ratio, the screening protocol was not brought into routine practice.

Conclusions

The screening protocol identified the high frequency of paracetamol use in ED patients and the low sensitivity of routine history taking.

The protocol identified only two patients for direct intervention but assisted with interpretation of other cases.

Given the low frequency of unsuspected severe paracetamol toxicity, and low sensitivity and specificity, this process was not brought into routine practice.

This study highlights the importance of an accurate medication history. Additionally, unintentional chronic paracetamol toxicity should be considered in cases of elevated transaminases.

Acknowledgements

We thank the laboratory staff in Chemical Pathology for screening the ALT results and performing the paracetamol measurements. The study was supported with a grant from the SydPath research fund.