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 overdose 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 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 AU12700 analyser using Olympus reagents and Roche calibrator and was measured using an Abbott AxSYM analyser using Olympus reagents and Roche calibrator and

The testing program was audited for frequency of positive paracetamol result identified unsuspected hepatotoxicity.

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

Results

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).

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.

Discussion

During the year of this study no patient was identified at risk of requiring transplantation, but liver 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 treatment. 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.

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References