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CLINICAL RESEARCH



Assessing the impact of a new medical toxicology service on the treatment of paracetamol overdose at a large tertiary care hospital

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ABSTRACT

Background: Paracetamol overdose is the most common cause of acute liver failure in the United States. Administration of acetylcysteine is the standard of care for this intoxication. Laboratory values and clinical criteria are used to guide treatment duration, but decision-making is nuanced and often complex and difficult. The purpose of this study was to evaluate the effect of the introduction of a medical toxicology service on the rate of errors in the management of paracetamol overdose.

Methods: This was a single center, retrospective, cohort evaluation. Patients with suspected paracetamol overdose were divided into two groups: those attending in the 1 year period before and those in the 1 year after the introduction of the medical toxicology service. The primary outcome was the frequency of deviations from the established management of paracetamol intoxication, using international guidelines as a reference.

Results: Fifty-four patients were eligible for the study (20 pre-toxicology-service, 34 post-toxicology-service). The frequency of incorrect therapeutic decisions was significantly lower in the post-toxicology service implementation versus the pre-implementation group ($P = 0.005$).

Discussion: Our study suggests that a medical toxicology service reduces the incidence of management errors, including the number of missed acetylcysteine doses in patients with paracetamol overdose. The limitations include the retrospective study design and that the study was conducted at a single center, which may limit generalizability.

Conclusions: The implementation of a medical toxicology service was associated with a decrease in the number of errors in the management of paracetamol overdose.

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Paracetamol; acetylcysteine; poisoning; medical toxicology; error

Background

Poisoning is a major global public health concern and one of the leading causes of injury-related death in the emergency department [1]. It constitutes between 0.5% and 5% of emergency department presentations [2], strains the healthcare system, and increases the workload of front-line healthcare personnel [3]. Emergency department personnel may sometimes lack the experience and/or knowledge needed to treat certain types of intoxication [4,5]. As drug-related hospitalizations, morbidity and mortality continue to increase, there is a need for cost containment without compromise to the quality of care [6].

Paracetamol is the most widely used non-prescription analgesic in the world [7], and it is commonly taken, deliberately or unintentionally, in overdose. It is a leading cause of fatalities following toxic ingestion, accounting for over 300 deaths in the United States in 2020 [8], and is the most common cause of acute liver failure in the United States [9]. Acetylcysteine is the mainstay of treatment for this overdose [10], and individualized treatment is imperative to reduce the

risk of hepatic failure or death; management of paracetamol overdose with acetylcysteine is often complex and must be individualized [11]. Implementation of guidelines for paracetamol poisoning may improve patient management [12].

Medical/clinical toxicologists are physicians with specialized knowledge in unintentional and intentional overdoses, occupational exposure to toxins, adverse drug reactions, drug-drug interactions, and envenomation. They have a positive impact on knowledge translation, resource allocation, length of stay, and a number of other related outcomes [13,14]. Bedside medical toxicology consultation has the additional benefit of enabling and facilitating a more accurate and detailed history and physical examination, advising on the assessment of clinical trends, and providing information regarding the availability and use of the laboratory and ancillary data – all in real time [15].

Studies evaluating the overall effectiveness of newly developed medical toxicology services have been performed [6,16], but changes in the outcomes of specific intoxications have not been published.

The purpose of this study was to evaluate the effect of the introduction of a medical toxicology service on the rate of errors in the management of paracetamol overdose.

Methods

This was a single center, retrospective cohort evaluation of adult and pediatric patients admitted for paracetamol overdose. The study was conducted at an 800-bed university-affiliated tertiary care referral center with 200 adult and pediatric emergency department beds and over 250,000 emergency department patient visits annually. Prior to that time, patients suffering from intoxication were treated by a variety of different services and specialties, accessing a regional poison center by phone when necessary.

Study patients were divided into one of two groups: those attending in the year *before* and those attending in the year *after* the establishment of a medical toxicology service at our institution in September 2015. A pediatric resident screened all identified patients for inclusion and abstracted baseline characteristics and outcome data from the electronic health records. Data were entered onto a Microsoft Excel® 2013 spreadsheet (Microsoft Corporation, Redmond, WA) and included age, sex, study time period (before or after initiation of the medical toxicology service), use of gastric decontamination or specific antidote treatment, including route of administration, adverse reaction, any deviations from published therapeutic guidelines for the management of paracetamol intoxication (see definitions below), and length of stay. Extracted laboratory values included aspartate aminotransferase activity, alanine aminotransferase activity, international normalized ratio, serum paracetamol concentration and its timing. Demographic and clinical features were presented as numbers or percentages for categorical variables, and as the mean and standard deviation for continuous variables. Statistical comparisons of variables were performed using non-parametric association tests (Chi-square or Fisher's exact test), with $P < 0.05$ indicating significance. A binary logistic regression model was performed to analyze the need for hospital admission.

The study was approved by the hospital ethics committee and was exempted from patient consent due to the retrospective nature of the study and because all data were anonymous.

Study definitions:

1. Acute paracetamol intoxication within a period of ≤ 8 h: ingestion of >200 mg/kg for patients <6 years of age and in adults and adolescents ingestion >10 g.
2. Repeated supra-therapeutic ingestion: >6 g or 150 mg/kg per 24 h period for 48 h or longer, or ingestion of a toxic amount over a period >8 h.

An incorrect therapeutic decision was defined as a deviation from the standard of care in treating paracetamol intoxication [17] as follows:

- i. Activated charcoal administration when not indicated.
- ii. Measurement of paracetamol concentration <4 h after ingestion.
- iii. Acetylcysteine treatment was provided when not indicated, as per the Rumack-Matthew nomogram, in the setting of acute intoxication [17].
- iv. Acetylcysteine treatment was not given when indicated.

Results

Fifty-four patients with suspected paracetamol overdose were included in the final analysis: 20 in the pre-toxicology service and 34 in the post-toxicology service cohort. Demographic and clinical characteristics are summarized in Table 1. No toxicologist was involved in the pre-toxicology service cohort, whereas all 34 (100%) post-toxicology service patients underwent a medical toxicologist consultation. The pre- and post-toxicology service implementation groups were similar in terms of baseline laboratory values and the presence of pre-existing hepatic laboratory abnormalities. The average length of stay was 2.85 days in the pre-toxicology service cohort and 1.97 days in the post-toxicology service cohort ($P = 0.01$). In addition, patients in the pre-toxicology service implementation cohort experienced more management errors (see Table 2).

Table 1. Clinical characteristics of study patients.

Characteristic	Pre-medical toxicology service (n = 20)	Post-medical toxicology service (n = 34)	P-value
Age, years, mean \pm standard deviation	34 \pm 17	33 \pm 16	0.12
Female sex, n (%)	13 (65%)	25 (74%)	0.5
Site of admission, n (%)			0.6
Emergency department	13 (65%)	24 (71%)	
Intensive care unit	3 (15%)	2 (5.9%)	
Ward	4 (20%)	8 (24%)	
Paracetamol concentration, mean \pm standard deviation	132 \pm 86	159 \pm 100	0.62
Aspartate aminotransferase activity U/L, mean \pm standard deviation	343 \pm 956	443 \pm 1,918	0.2
Alanine aminotransferase activity U/L, mean \pm standard deviation	509 \pm 1,771	375 \pm 1,419	0.2
International normalized ratio, mean \pm standard deviation	1.18 \pm 0.19	1.31 \pm 0.61	0.8
Received acetylcysteine n (%)	19 (95%)	33 (97%)	0.7
Adverse reaction to acetylcysteine n (%)	1 (5.6%)	3 (9.4%)	0.6
Activated charcoal administered, n (%)	3 (15%)	5 (15%)	>0.9
Length of hospital stay, days	2.85	1.97	0.01

Table 2. Incorrect therapeutic decisions experienced by study patients before and after the introduction of a medical toxicology service.

Characteristic	Pre-medical toxicology service (n = 20)	Post-medical toxicology service (n = 34)	P-value
Incorrect therapeutic decision, n (%)	10 (50%)	7 (20%)	0.02
Activated charcoal administration not indicated	3*	0	0.04
Paracetamol concentration measured <4 h post-ingestion	5	7**	0.7
Acetylcysteine treatment not indicated	6	0	0.001
Acetylcysteine treatment not given when indicated	3	0	0.04

*These three patients received charcoal inappropriately at 11, 14 and 15 hours after non-massive ingestions.

**In all seven of these post-toxicology service patients the samples were drawn in the emergency department *prior* to medical toxicology service consultation.

Discussion

Our study suggests that a medical toxicology service reduces the incidence of management errors, including the number of missed acetylcysteine doses in patients with paracetamol overdose. The new toxicology service optimized the timely and appropriate administration of acetylcysteine and led to an increase in the frequency of individualized treatment plans.

Correct and timely management of paracetamol overdose can reduce hepatotoxicity, unnecessary blood sampling, and hospital admission [18]. Many of the errors in the management of paracetamol intoxication could be reduced by a clear understanding of the differences between acute versus supratherapeutic and chronic intoxications. In particular, the appropriate use of the Rumack-Matthew nomogram has been shown to reduce unnecessary investigations and administration of acetylcysteine [19].

A reduction in unnecessary treatment and admission rates, as shown in our study, represents an improvement in quality of care. A bedside medical toxicologist, actively involved in the ongoing care of intoxicated patients, was able to provide nuanced management that led to substantial and significant improvements in the care of paracetamol intoxicated patients. Even with a knowledge of the Rumack-Matthew nomogram, busy emergency department physicians may not always be able to provide such care.

Cost savings resulting from the establishment of a medical toxicology service are difficult to quantify, being dependent on multiple variables, including the number of toxicologists and the volume of patients. Although we found a statistically significant decrease in management errors of paracetamol intoxication and in the length of stay following the introduction of a medical toxicology service, our study was not designed or intended to perform a cost analysis of a toxicology service. It is likely, however, that a reduction in inappropriate testing, the appropriate use of laboratory resources and reduced hospital length of stay would lead to institutional cost savings. As increased healthcare economic pressures exert increasing influence over hospitalizations and observation, a prospective study examining this issue would be of value.

In 12 of our patients, the initial paracetamol concentration was drawn too early, five in the pre-toxicology service and seven in the post-toxicology service group. In all post-toxicology service patients, this was because the specimens were obtained in triage before requesting medical toxicology service consultation. This highlights the need for the medical

toxicologist to impart more knowledge and information to physicians and nurses involved in the treatment of intoxicated patients, and argues for early medical toxicology consultation.

This study has several limitations. The retrospective nature of the study poses a limitation as data collection relied on physician charting. Secondly, the study was conducted at a single center, limiting generalizability to other institutions whose patient populations and resources may be dissimilar to ours.

Conclusions

The introduction of a medical toxicologist-driven medical toxicology service was associated with a decrease in management errors in the treatment of patients with paracetamol intoxication. Early medical toxicology involvement with intoxicated patients may help promote the appropriate use of a treatment nomogram and reduce inappropriate investigations and the unnecessary administration of acetylcysteine.

Author contributions

The authors Eli Bronshtein and Or Segev have made an equal contribution to this paper.

Disclosure statement

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