Paracetamol Overdose: Analysis of a Sample from a Tertiary Hospital in Eastern Saudi Arabia

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Abstract
Background: Paracetamol overdose is common and has such serious consequences as hepatic toxicity. The aim of this study was to characterize patients in a sample from the Kingdom of Saudi Arabia (KSA) with paracetamol overdose.

Materials and Methods: Retrospective chart review (July 1997 to December 2012) for all patients above the age of 18 years with the diagnosis of paracetamol overdose at a university hospital.

Results: A total of 86 patients with paracetamol overdose were analyzed, about 70% of these patients were young females. 80% were attempts at suicide. 56% of the patients received N-acetylcysteine. Two patients developed hepatic toxicity. There were no mortalities and the average hospital stay was 4.8 ± 4.9 days.

Conclusion: Paracetamol overdose is frequently seen in young females attempting suicide. In KSA, it tends to have a low rate of hepatic toxicity.

Key words: Overdose, paracetamol, toxicity

INTRODUCTION

Paracetamol is an over the counter medicine that is widely used as analgesic and antipyretic. Acute intoxication as self-poisoning is common and occasionally has significant consequences such as hepatic toxicity.\[1\] Paracetamol is a major cause of acute liver failure in the United Kingdom and the United States.\[2-4\] One study reported a lower rate in Asian populations.\[5\] Fasting and alcohol use may increase paracetamol-induced hepatotoxicity.\[6\]

N-acetylcysteine (by replenishing the glutathione stores) is an effective antidote for paracetamol overdose, especially if given early after ingestion of paracetamol.\[7,8\] Patients with acute liver failure may benefit from referral for orthotopic liver transplantation if they meet King’s College criteria.\[9\] A study from the Kingdom of Saudi Arabia (KSA) showed that paracetamol overdose accounts for 30% of intentional drug overdose.\[10\] Previous studies showed that about 55% of paracetamol overdose admissions were females at a median age of 34 years; 45% of these patients had a history of alcohol abuse, and 42% had a history of psychiatric illness.\[11\] The aim of this study was to characterize patients with paracetamol overdose in a sample from the Eastern Province of Saudi Arabia.

MATERIALS AND METHODS

This was a retrospective chart review involving all patients with paracetamol overdose at a tertiary hospital...
in KSA from July 1997 to December 2012. The study was unfunded and hospital institutional review board approved the study protocol. Data were collected from the medical records and hospital database. The international classification and diagnosis nine coding system was used to identify individuals with paracetamol overdose from the medical records. Patients younger than 18 years were excluded. The medical records were reviewed for sociodemographic data, estimation of the amount of paracetamol ingested, paracetamol level, liver function tests, coagulation profile, the use of N-acetylcysteine, duration of hospital stay and in-hospital mortality. Hepatic toxicity was defined as elevation in aspartate aminotransferase (AST) or alanine aminotransferase (ALT) to more than 1000 U/L.\textsuperscript{[12,13]} King’s College criteria were considered met if the arterial pH <7.3 or the patient had encephalopathy with both a prothrombin time >100 s and a serum creatinine concentration >3.4 mg/dL.\textsuperscript{[9]}

**RESULTS**

We identified 129 patients with paracetamol overdose, 45 of whom were excluded because they were younger than 18 years. 86 patients were included in our analysis. Table 1 shows the baseline characteristics and biochemical profile of our patients. Figure 1 shows the mean initial and peak liver enzymes levels of patients. Figure 2 shows the serial paracetamol level during admission. N-acetylcysteine was given in 56% of the cases. 65% of the patients in our sample were single, 33% were married and one patient was divorced. 85% of our patients were educated (63% were high school graduates and 22% were college graduates). Only two cases met the definition of hepatic toxicity. There were no mortalities as a result of paracetamol overdose in our database. The average hospital stay was 4.8 ± 4.9 days.

**DISCUSSION**

Paracetamol overdose is not uncommonly seen in clinical practice and as shown in Figure 3, it accounts for 23% of all drug overdose in adults seen at our hospital. As far as we know, this is the first study that specifically describes paracetamol overdose in KSA. More than 70% of our patients were young females, and 80% were attempts at suicide. This observation can imply a social problem, and the need for a cultural program aimed at improving health, especially since a recent study has shown that family conflicts were the common cause of suicide attempts.\textsuperscript{[14]} The predominance of paracetamol overdose in high school graduates has been shown in other self-poisoning related studies.\textsuperscript{[15]}

Hepatotoxicity was seen in only two cases accounting for 2.3% of all paracetamol overdose. The first patient was a 19-year-old female who accidentally ingested 4.5 g of paracetamol and had a peak AST and ALT levels at 1957 U/L and 1898 U/L respectively. The second patient was another 19-year-old female who ingested 15 g of paracetamol in a suicide attempt and had a peak AST and ALT levels at 1293 U/L and 1641 U/L respectively. Neither patient met the King’s College criteria for acute liver failure. Marzilawati et al.\textsuperscript{[5]} reported a low rate (7.3%) of hepatotoxicity in Asian patients

**Table 1: Baseline characteristics and biochemical profile of patients**

<table>
<thead>
<tr>
<th>Patient characteristics</th>
<th>n = 86</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>24.4±6.6</td>
</tr>
<tr>
<td>Sex (male %)</td>
<td>28</td>
</tr>
<tr>
<td>Nationality (Saudi %)</td>
<td>80</td>
</tr>
<tr>
<td>Ingestion type %</td>
<td></td>
</tr>
<tr>
<td>Accidental</td>
<td>20</td>
</tr>
<tr>
<td>Suicidal</td>
<td>80</td>
</tr>
<tr>
<td>Marital status %</td>
<td></td>
</tr>
<tr>
<td>Single</td>
<td>66</td>
</tr>
<tr>
<td>Married</td>
<td>33</td>
</tr>
<tr>
<td>Divorced</td>
<td>1</td>
</tr>
<tr>
<td>Dose of paracetamol ingested (mg)</td>
<td>8244±4445</td>
</tr>
<tr>
<td>Paracetamol level (mg/L)</td>
<td>76.4±52.8</td>
</tr>
<tr>
<td>ALT level (U/L)</td>
<td>58.1±202.9</td>
</tr>
<tr>
<td>AST level (U/L)</td>
<td>45.5±211.7</td>
</tr>
<tr>
<td>Alkaline phosphatase level (U/L)</td>
<td>94.5±51.9</td>
</tr>
<tr>
<td>Gama-glutamyl transpeptidase level (U/L)</td>
<td>27.8±25.9</td>
</tr>
<tr>
<td>INR</td>
<td>1.4±1.7</td>
</tr>
<tr>
<td>Serum creatinine (mg/dL)</td>
<td>0.8±0.18</td>
</tr>
</tbody>
</table>

\textsuperscript{1}INR – International normalized ratio; ALT – Alanine aminotransferase; AST – Aspartate aminotransferase

**Figure 1: Mean liver enzymes levels**
with paracetamol overdose and suggested that ethnic differences in paracetamol metabolism may contribute to hepatic toxicity. Another possible explanation for the lower rate of paracetamol-induced hepatic toxicity is related to the dose ingested. Hepatic toxicity has been associated with doses >10 g,[16,17] while the mean dose of paracetamol ingested in our sample was about 8.2 g. One possible contributor to the lower hepatic toxicity in this sample is the fact that alcohol consumption is rare in the Saudi population because of religious and cultural reasons. Chronic ingestion of alcohol increases CYP2E1 activity leading to reduced glutathione levels predisposing patients with paracetamol overdose to hepatic toxicity.[18,19]

N-acetylcysteine is the antidote for paracetamol overdose as it prevents paracetamol-induced hepatic injury by restoring hepatic glutathione level, especially when administered within 8 h of the overdose.[7,20,21] In our sample, 56% of the patients received N-acetylcysteine (60% received the intravenous form of the medicine and 40% received the oral form). N-acetylcysteine was given according to Rumack and Matthew normogram and the dose was calculated according to body weight.[12,22] These calculations are based on information obtained from western countries and may not be accurate when applied to different populations. Since people in the west tend to have higher body weights, our patients might have been given excessive doses of N-acetylcysteine. This could have lowered the rate of hepatic toxicity seen in our sample.

Our study has certain limitations; the first being its retrospective nature, the small sample size and a single-center study. Also, our sample had no information on the consumption of alcohol and the time lapse between ingestion and presentation.

CONCLUSION

Paracetamol overdose is frequently seen in young females attempting suicide. In Saudi Arabia, the rate of hepatic toxicity tends to be low. Larger studies are needed to make generalization of our findings feasible.

REFERENCES