Demographic Information and Clinical and Laboratory Findings in Acetaminophen Poisoning Cases in Rasht, Iran, in 2008

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Received: 15.07.2012 *Accepted: 11.08.2012*

ABSTRACT

Background: Acetaminophen is widely used as an analgesic and antipyretic drug and it is a frequent cause of acute drug poisoning.This study was carried out to investigate the demographic information and clinical and laboratory findings in acetaminophen poisoning patients referred to "17 Shahrivar" and "Razi" educational hospitals, Rasht.

Methods: In this retrospective cross-sectional study, 125 patients with acetaminophen poisoning were studied. Descriptive data were analyzed by SPSS software.

Results: 90 of the patients were women and the mean age of the patients was 21.5±9.06 years. Also, 72.8% of the patients were from urban areas and most of the patients (67.2%) lived in Rasht. Spring was the most common season for the incidence of poisoning. Suicide was the most common pattern of poisoning (91.2%). The mean time interval between poisoning and use of antidote N-acetylcysteine was 4.94±3.5 hours. The most common cause of delayed administration of antidote was failure in diagnosis of poisoning. Overall, 31.2% of the patients had no significant clinical manifestations. In other patients, nausea (50.4%) was the most common clinical symptom. The most common abnormal laboratory findings were prolonged prothrombin time and international normalized ratio (29%). Liver aminotransferases were elevated only in 18% of the patients.

Conclusion: Poisoning with acetaminophen was mainly found in women, 12-20 years of age, in urban areas and spring season. Suicide was the main reason of poisoning. Regarding the most common cause of delay in antidote therapy (failure in poisoning diagnosis), establishment of a toxicology laboratory in Guilan province can help the better management of poisoned patients.

Keywords: Acetaminophen, Poisoning, Rasht, Suicide.

IJT 2012; 681-685

INTRODUCTION

Acetaminophen, also known as paracetamol, N-acetyl-p-aminophenol, and APAP, is an analgesic and antipyretic drug categorized among over-the-counter and prescription products (1,2). Acetaminophen is widely used and it is estimated that more than 1 billion acetaminophen tablets are annually used worldwide (3). Acetaminophen poisoning is common (4). In the UK and USA, acetaminophen was involved in 50% and 10% of poisoning admissions, respectively (4). In a report by Moghadamnia and Ablollahi in Iran, 11.4% of drug-induced poisonings were due to acetaminophen (5).

Acetaminophen generally has few side effects in the recommended therapeutic doses of 1 to 4 g/day but higher doses can be toxic (6). The toxic dose of

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acetaminophen is >7.5 g or >150 mg/kg in human. Chronic ingestions more than 4 g/day may also be toxic (7).

Clinical presentations of acetaminophen poisoning are divided into four phases. The first phase begins shortly after ingestion and can last for 12 to 24 hours. The signs and symptoms are gastrointestinal upset, nausea, vomiting, anorexia, diaphoresis, and pallor but they are not diagnostic and specific. The second phase is up to 48 hours after ingestion. Patients feel better during this phase but laboratory findings can be abnormal. The third phase, if reached, may be specialized by severe hepatic necrosis, typically 3 to 5 days after ingestion. Liver enzyme levels can increase to more than 10,000 IU/L, and lactic acidosis and coagulopathy may ensue. Death can occur in this phase because of acute hepatic failure complications. In the fourth phase, patients who recover generally have complete recovery of liver function without any long-term sequela (1,7,8).

Presentations of acetaminophen poisoning can be unremarkable (7). Hence, it is often diagnosed by taking a thorough history (1). Patients with a history of using alcohol, malnourishment, and use of anti-tubular or anti-epileptic drugs can be at a greater risk for acetaminophen poisoning (7,8).

The serum level of acetaminophen can be used to predict toxicity (7). Management of patients presenting within 24 hours is guided by plasma acetaminophen concentration (4). Rumack-Mathew treatment nomogram is the primary tool used to guide treatment (8) and predicts the probability of hepatotoxicity based on plasma levels and time after ingestion. Decontamination with activated charcoal is the first step in caring for these patients (7). Anti dote therapy is done with N-acetylcysteine (NAC). It can completely protect patients against hepatotoxicity if given within 12 hours of overdose (4).

Early diagnosis and diminishing the time between poisoning and use of antidote NAC can save patients from the complications of acetaminophen poisoning. Therefore, this study was conducted to investigate the demographic information, and clinical and laboratory findings in acetaminophen poisoning and management of patients who referred to 17 Shahrivar Hospital (Pediatric Referral Center of Guilan, Iran) and Razi Hospital, Rasht, Iran, in 2008.

MATERIALS AND METHODS

In this retrospective cross-sectional study, all hospital records of patients with acetaminophen poisoning in "17 Shahrivar" and "Razi" educational hospitals during 2008 were studied. Demographic data including age, gender, habitat (urban or rural), region, season, time elapsed between exposure and admission, cause of poisoning, lag time between poisoning and use of antidote NAC, duration of hospitalization, clinical manifestations, and laboratory findings, were reviewed. Incomplete records of the patients were excluded.

Collected data were analyzed by SPSS software (version 18, USA). Values were presented as frequency and mean ± standard deviation.

RESULTS

Of the 125 patients poisoned with acetaminophen, 122 referred to Razi Hospital and the rest three referred to "17 Shahrivar" Hospital. Overall, 90 patients (72%) were women and 71 patients (56.8%) were 12-20 years old and 48 patients (38.4%) were 20-40. The mean age of the patients was 21.5±9.06 years and they ranged in age from 74 years to 4 months. Also, 91 patients (72.8%) resided in city and most of the patients (67.2%) lived in Rasht. Spring (32.8%) was the season with the highest incidence of poisoning.

Suicide (91.2%) was the most common reason of poisoning. Overall, 6

patients (4.8%) were poisoned accidentally; three with large amount of an unknown solution and 3 with unawareness of the toxic effects of drugs. Five patients (4%) used acetaminophen with codeine component.

Antidote was administrated to 70 patients. The mean time between poisoning and use of antidote NAC was 4.94±3.5 hours which ranged from 1 to 12 hours. Antidote was administrated only to 48 patients (34.8%) in proper time (the first 8 hours after overdose) and in 22 patients (17.6%), it was administrated after 8 hours. Oral and injected NAC were used in 38 (54.3%) and 32 (45.7) patients, respectively. The most common causes of delayed administration are noted in Table 1. The mean hospitalization period was 19.39±12.9 hours with range of 1 to 96 hours. Overall, 58.4% of the patients were hospitalized for 12-24 hours and 43 patients (34.4%) were discharged in less than 12 hours with personal satisfaction.

Also, 31.2% of the patients had no significant clinical manifestations. In other patients, nausea (50.4%) was the common clinical symptoms (Figure1).

Laboratory findings were available in 100 patients that were normal in 44 patients. Abnormal laboratory findings included increased prothrombin time (PT) and international normalized ratio (INR) (29%), elevated liver aminotransferases (18%), anemia (14%), increased white blood cell (WBC) count (8%), elevation in bilirubin level (4%), and respiratory alkalosis (3%).

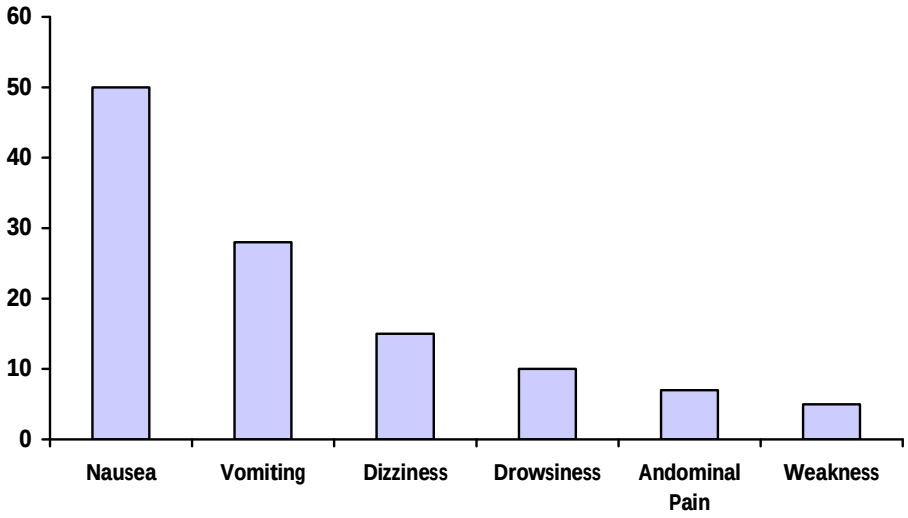

Figure 1. Manifestation of acetaminophen poisoning

Table 1. Causes of delayed antidote administration

Cause of delayed administration of antidote	Number	Percent
Failure in diagnosing poisoning	30	39
Late referral	16	20.8
Discharge with personal satisfaction	14	18.2
Incorrect treatment	12	15.5
Late admission	5	6.5
Total	77	100

DISCUSSION

Intoxication with acetaminophen is a common challenge for poisoning treatment centers (9). In this study, 125 patients with presumed acetaminophen poisoning were reviewed. Since the serum level of acetaminophen was not evaluated, comparison was done circumspectly.

Similar to other studies, female patients formed the majority of the patients. In a report by Suppapitiporn, the age of all patients ranged from 15 to 25 years old and 80.8% of the patients were female (10). Alaniz studied 128 adult patients with mean age of 38 years and 51 patients with mean age of 14.3 years and observed that 78 (60.9%) of the adult patients presented with intentional toxic ingestion compared with the 82.4% intentional ingestion in the pediatric cases (6). Schiødt *et al.* studied 71 patients, 50 of whom were classified as having taken acetaminophen in suicidal attempts and 21 as having been accidentally poisoned (11). The suicidal patients had ingested almost twice as much acetaminophen as those in the accidental-overdose group (11). In the present study, most of the patients aged 12-40 years and the common cause of ingestion was suicide (91.2%). This can be due to the greater prevalence of suicide among young patients.

Most of the admitted patients were from urban areas, especially Rasht city. This distribution can be attributed to the ease of access to referral centers for patients who live in that region.

The strongest predictor of severe hepatotoxicity was delayed N-acetyl cysteine treatment or no antidote therapy in patients consuming more than 10g of paracetamol or with toxic serum paracetamol levels (12). In our study, antidote was administrated only to 56% of the patients. In addition, antidote was administrated to only 34.8% of the cases in proper time. This study showed that the most common cause of delayed administration of antidote was failure to diagnose the poisoning (39%). This can be due to the non-specific manifestations of acetaminophen intoxication. On the other hand, the serum level of acetaminophen as a predictor of poisoning was not evaluated by the laboratories in this region. Late referral and discharge with patients' request and consent were the other causes of delayed antidote administration. It indicates that in the view of people, acetaminophen is not a toxic drug. Late admission was another cause of delayed antidote administration due to the large number of the patients referring with poisoning.

In this study, the majority of the patients were discharged within 12-24 hours. Betten *et al*. stated this interlude was sufficient to treat patients without risk factors of hepatotoxicity (13). The mean hospitalization period was 19.39±12.9 hours ranging from 1 to 96 hours. Also, 58.4% of the patients were hospitalized for 12-24 hours. Suppapitiporn reported that the length of hospitalization varies from 1 to 21 days with the mean duration of 3.48 days (10).The early symptoms of acetaminophen poisoning are often nausea or they are absent, leading to concern that potentially toxic ingestions might be missed due to a poor history (8). Presentations of the patients in this study were similar to previous studies and most of them were asymptomatic. Nonetheless, nausea was the most common manifestation of acetaminophen poisoning.

Suppapitiporn found that one third of patients with acetaminophen poisoning had three fold the abnormal level of liver aminotransferases (10). In the present study, the most common abnormal laboratory findings were prothrombin time (PT) prolongation and international normalized ratio (INR) (29%). Liver aminotransferases were elevated only in 18% of the patients.

CONCLUSION

Poisoning with acetaminophen was mainly found in women, 12-20 years of

age, in urban areas in spring season. Suicide was the main reason of poisoning. Noticing the delay in antidote therapy (failure in poisoning diagnosis), establishment of laboratories competent in measurement of serum levels of acetaminophen can help the better management of poisoned patients. As a limitation of the present study, variables like the ingested dose of acetaminophen, past history of suicide, alcohol use, and smoking were not surveyed. Thus reviewing these variables in future studies is suggested.

ACKNOWLEDGEMENTS

The authors would like to indicate their thanks to Guilan University of Medical Sciences who supported this study and to statistician who analysed the data.

REFERENCES

1. Schilling A, Corey R, Corey M, Eghtesad B. Acetaminophen: old drug, new warnings. Cleveland Clinic journal of medicine. 2010;77(1):19-27.
2. Sumioka I, Matsura T, Yamada K. Acetaminophen-induced hepatotoxicity: still an important issue. Yonago Acta Med. 2004;47(2):17-28.
3. Quallich LG, Brown JW, Shehab TM, Fontana RJ. Management of acetaminophen hepatotoxicity: a survey of practicing physicians. JCOM. 2001;8(6):25-32.
4. Dargan PI, Jones AL. Acetaminophen poisoning: an update for the intensivist. Critical care-London. 2002;6(2):108-10.
5. Moghadamnia A, Abdoilahi M. An epidemiological study of poisoning in northern lslamic. Eastern Mediterranean Health Journal. 2002;8(1):88-94.
6. Alaniz C, Janusz J. A retrospective study of the etiologies and outcomes of patients admitted to a university hospital with presumed acetaminophen toxicity. Hospital Pharmacy. 2007;42(2):126-32.
7. Bartlett D. Acetaminophen toxicity. J Emerg Nurs. 2004;30(3):281-3.
8. Rowden AK, Norvell J, Eldridge DL, Kirk MA. Updates on acetaminophen toxicity. Medical Clinics of North America. 2005;89(6):1145-60.
9. Agreement C. Acetaminophen poisoning: an evidence-based consensus guideline for out-of-hospital management. Clinical Toxicology. 2006;44:1-18.
10. Suppapitiporn S. Attempted suicide by acetaminophen ingestion. 2003;47(11):713-25.
11. Schiødt FV, Rochling FA, Casey DL, Lee WM. Acetaminophen toxicity in an urban county hospital. New England Journal of Medicine. 1997;337(16):1112-8.
12. Ayonrinde O, Phelps G, Hurley J, Ayonrinde O. Paracetamol overdose and hepatotoxicity at a regional Australian hospital: a 4-year experience. Internal medicine journal. 2005;35(11):655-60.
13. Betten DP, Cantrell FL, Thomas SC, Williams SR, Clark RF. A prospective evaluation of shortened course oral N-acetylcysteine for the treatment of acute acetaminophen poisoning. Annals of emergency medicine. 2007;50(3):272-9.