

Acetaminophen Overdose in Jamaica

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ABSTRACT

Acetaminophen is a dose dependent hepatotoxin which is frequently associated with intentional self-harm. Forty-nine cases of parasuicide attempts involving paracetamol only or in combination with another drug were treated at the UHWI, Jamaica, between 1994–2004. The majority were women (84%) and the mean age was 23 years. Acetaminophen was the only agent ingested in 71% of cases; 29% involved an additional drug. Patients presented an average of 6.5 hours after ingestion (range 1–45 hours). Serum transaminases were elevated in 18% of cases and N-acetylcysteine (NAC) therapy given in 55%. The mean duration of hospitalization was three days. One patient developed liver failure and there were no deaths. Education of the public and medical profession is needed to increase awareness of the potential toxic effects of acetaminophen overdose. N-acetylcysteine therapy should be given early in suspected cases.

Sobredosis de Acetaminofén en Jamaica

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RESUMEN

El acetaminofén es una hepatotóxina dosis-dependiente, frecuentemente asociada con intenciones auto-destructivas. Cuarenta y nueve casos de intentos parasuicidas que involucraban paracetamol o combinación con otra droga, fueron tratados en el UHWI, Jamaica, entre 1994-2004. En la mayoría de los casos se trataba de mujeres (84%) y la edad promedio fue 23 años. El acetaminofén fue el único agente ingerido en 71% de los casos; 29% involucraron un medicamento adicional. Las transaminasas en suero fueron elevadas en 18% de los casos y se aplicó terapia de N-acetil-cisteína en el 55% de los casos. La duración promedio de hospitalización fue de tres días. Uno de los pacientes tuvo un fallo hepático y no hubo muertes. Se requiere la educación del público y la profesión médica a fin de aumentar la conciencia sobre los efectos tóxicos potenciales de la sobredosis de acetaminofén. La terapia con N-acetil-cisteína (NAC) debe aplicarse tan pronto como el caso despierte sospecha.

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INTRODUCTION

Acetaminophen (paracetamol) is a commonly used analgesic which can be purchased by consumers over the counter and is responsible in 30% to 50% of cases of accidental and non-accidental drug overdose (1). Acetaminophen overdose, either alone, or in combination with other drugs, is the commonest cause of intentional self-harm (1) and also accounts for 60% of cases of acute liver failure leading to orthotopic liver transplant in the United Kingdom (UK) and the United States of America (USA) (2, 3).

Acetaminophen is potentially hepatotoxic resulting in a dose dependent destruction of hepatocytes through its meta-

bolite N-acetyl-P-benzoquinone-imine (NAPQI) (4). Normally, 95% of ingested acetaminophen is conjugated with sulfate and glucuronide and excreted via the kidneys and 5% is metabolized via cytochrome p 450 (CYP2E1) to form NAPQI which is usually conjugated by glutathione and is excreted by the kidneys as a water soluble conjugate. N-acetyl-P-benzoquinone-imine is formed in excess when the normal conjugation of acetaminophen to water soluble metabolites in the liver is overwhelmed by toxic ingestion. At toxic levels, glutathione becomes fully consumed and NAPQI binds to hepatocyte cell proteins resulting in necrosis through disruption of normal membrane integrity (3).

The recommended maximum adult dose of acetaminophen is 4g in 24 hours. The toxic effects are usually seen in patients taking above 7g in 24 hours (5). However, this threshold is lower in alcoholics who exhibit induction of cyto-

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chrome p 450 and therefore metabolize acetaminophen to its toxic component more rapidly (4).

There has been no previous study reported on the effects of acetaminophen overdose in Jamaica. This study reviews the clinical features and outcomes of patients with a parasuicide event with acetaminophen overdose, seen at the University Hospital of the West Indies, Jamaica, over a ten-year period from 1994 to 2004.

SUBJECTS AND METHODS

A review was performed of patients' medical records at the University Hospital of the West Indies (UHWI), Jamaica, for the ten-year period from 1994 to 2004. The International Classification and Diagnosis (ICD) 9 and 10 coding systems was used to identify individuals with a parasuicide event involving paracetamol, using paracetamol, acetaminophen and parasuicide as the key search terms. Information was obtained with regards to patients' age, gender, weight and date of presentation to hospital. The agent ingested whether only acetaminophen or in combination with another drug, dosage, time between ingestion and presentation to hospital were also obtained. Results of liver transaminases, prothrombin time, serum albumin and bilirubin or whether the patient was admitted to hospital were documented. Whether N-acetylcysteine (NAC) therapy or gastric lavage was given, duration of admission to hospital, history of alcohol use and psychiatric history were also recorded.

RESULTS

In the 10-year interval between 1994 and 2004, 49 cases presented to the emergency department, UHWI, with parasuicide attempt involving paracetamol overdose, either alone or in combination with another drug. There were 41 (84%) females and eight (16%) males. The age ranged from 14 to 39 years, with a mean age of 23 years. There were ten cases in 2001 and 2004, six cases in 1999, five cases in 2000, four cases in 2003 and three cases in 2002 (Figure). Thirty-five

(71%) cases involved paracetamol as the only drug ingested. Paracetamol and antibiotics were ingested in five (10%), paracetamol and NSAIDs in three (6%) and paracetamol and antidepressants in three (6%) cases. The others combined paracetamol with miscellaneous drugs. The paracetamol dosages ingested, estimated from patient's or caregiver's history, ranged from 2g to 30g. In two cases, no estimate of the ingested dose was recorded. In five cases, the estimated dose recorded was below accepted criteria for toxic overdose (range 2g to 4g). Chronic alcohol intake was present in five (10%). A psychiatric history was present in five (10%). Patients presented an average of 6.5 hours (range 1–45 hours) after ingestion.

Serum transaminases (SGOT, AST) were evaluated at presentation in 40 (82%) of the cases. Four of the cases without serum transaminases were estimated to have taken a non-toxic dose of paracetamol. No record of transaminases was present in five of the cases in which toxic doses were ingested. Serum transaminase (SGOT, AST) was elevated at presentation in 9/49(18%) cases, one patient had marked elevation (6900 IU/l) whilst the others had levels between 4 – 6 times the upper limit of normal. Serum albumin was normal in 28 cases, low in two and was not recorded in 15 cases. The prothrombin time was normal in 21 cases. It was not done in 17 and elevated in only one case.

Gastric lavage was performed in twenty-six (53%) patients. N-acetylcysteine was administered in twenty-seven (55%) patients soon after presentation. Forty-five patients (92%) were admitted to hospital. Duration of admission ranged from one to eight days with a mean of three days. One patient developed liver failure and there were no deaths.

DISCUSSION

Acetaminophen is one of the most widely used analgesics and antipyretics worldwide (3). It is a dose dependent hepatotoxin and acetaminophen overdose is the commonest aetiology of acute liver failure in the USA and UK, and the incidence of this problem is increasing (2, 3, 6).

Acetaminophen overdose is usually diagnosed by the appropriate history suggesting toxic ingestion and confirmed by serum acetaminophen levels. In many patients, there is a delay in seeking medical attention as symptoms may be delayed or an overdose may be taken unintentionally. Unintentional liver damage from self-medication for pain or fever with acetaminophen is well recognized (2). Also, in severe cases, the diagnosis may be delayed as patients frequently develop encephalopathy quite rapidly preventing an adequate history.

In the present study, 71% of cases involved only acetaminophen ingestion. In the remaining cases (29%), other agents were also ingested. This is similar to a recent study on acetaminophen hepatotoxicity in which 22% of patients ingested two drugs including narcotic analgesics (2).

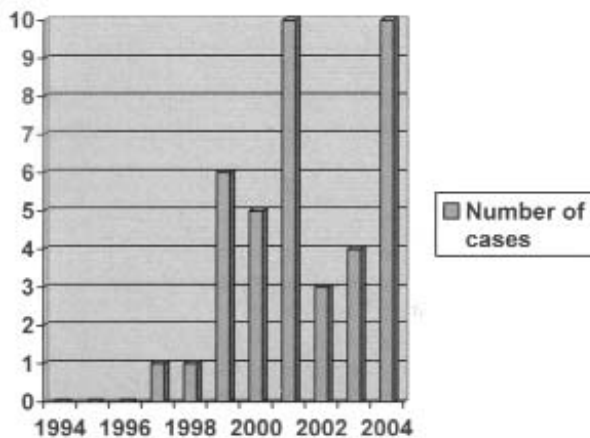


Figure: Number of paracetamol overdose cases per year

Acetaminophen may cause elevation of serum transaminases even when used in therapeutic doses (6). In the present study, the serum transaminases were elevated in only 18% of patients. In another study, it was found that over one-third of patients taking therapeutic doses of acetaminophen had significant elevation of serum transaminase levels. All were asymptomatic. In addition, acetaminophen concentration in serum was near or below the limits of assay detection (6). However, measurement of serum acetaminophen protein adducts, which represents liver injury specific to acetaminophen, may reliably identify acetaminophen hepatotoxicity in doubtful cases (3).

The risk of severe and possibly fatal liver damage after overdosage cannot be adequately assessed from either the amount ingested or early symptoms (7, 8). The biochemical indicators which suggest paracetamol induced severe hepatic injury are grossly elevated serum transaminases (greater than 1000 IU). O'Grady *et al* have validated criteria which are used to assess the severity of paracetamol ingestion and the likelihood of benefiting from a liver transplant (9). These criteria utilize the serum prothrombin time, serum creatinine, pH and presence or absence of hepatic encephalopathy.

Acetaminophen overdose is treated by administering NAC which is a glutathione precursor. When administered soon after overdose, it replenishes mitochondrial and cytosolic glutathione stores that have been depleted (7). It is most effective when administered within the first eight hours of ingestion. The decision to administer NAC is guided by a nomogram comprising the acetaminophen level determined from a serum sample (5). N-acetylcysteine, a powerful antioxidant, may protect against further hepatic damage. Treatment less than ten hours after overdose is highly likely to prevent death and likely to result in fewer patients developing severe liver damage (7). It may also be beneficial when administered up to 24 hours after ingestion in reducing the morbidity associated with acetaminophen toxicity. It may also be of benefit in acetaminophen-induced fulminant hepatic failure. In the present study, NAC was administered in over half of the patients soon after presentation and may have contributed to the satisfactory outcomes of patients in this series.

In order to decrease the morbidity and mortality of acetaminophen toxicity, specific measures should be considered. Education of the public, pharmacists and physicians regarding the potential toxic effects of acetaminophen is important. In the UK, legislation to reduce the size of packs of acetaminophen sold over the counter, and thus the number of tablets available in the household, has significantly reduced the size of overdoses with consequent reduction in morbidity

and mortality (10, 11). In addition, physicians must consider acetaminophen, in patients presenting with suicide attempts and since specific therapy is available, it is important to measure serum acetaminophen and to administer NAC in patients with or without clinical liver involvement. If toxic ingestion is suspected clinically, NAC should be administered even in the absence of detectable acetaminophen levels or without a nomogram.

There are several limitations with the present study. This study was a retrospective review and although all cases of acetaminophen parasuicides were identified from the UHWI coding system, missed and unreported cases may have been excluded. In addition, the data obtained from the files were not uniform for all cases. The dose of paracetamol ingested may not have been accurate as this depended on patients and family members recall and estimation. It is difficult to estimate the overall problem of acetaminophen overdose in Jamaica in this review. The number of cases is relatively small compared to developed countries. A prospective study is needed to determine prevalence of this problem and should include surveillance of all parasuicides for overdose.

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