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Approach to paracetamol intoxication in intensive care: 2 pregnant cases

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Abstract

Acetaminophen (paracetamol) is a commonly used drug during pregnancy and is considered safe. However, it is among the most frequent agents of which overdoses are reported during pregnancy. The most important result of overdose use is hepatotoxicity, which can cause death. We herein present our approach to two pregnant cases we followed up in the intensive care unit due to acetaminophen intoxication.

Keywords: Acetaminophen, Pregnancy, Intoxication, Unit care

Introduction

N-acetyl-para-aminophenol (paracetamol) was discovered in 1889 and entered clinical use in 1955 [1, 2]. Paracetamol is an active metabolite of phenacetin and is used for its analgesic and antipyretic effects [3]. It is among the most used drugs in pregnancy and generally considered safe [4]. However, its overdose is commonly reported during pregnancy [5]. Hepatotoxicity is the most important consequence of paracetamol overdose [7], which may also have renal effects, albeit less frequently [8]. We herein present our clinical approach to two pregnant patients who were followed up in the intensive care unit due to paracetamol intoxication.

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The authors stated that the written consent was obtained from the patients presented with images in the study.

Conflict of Interest
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Case presentation

Case 1

A 23-year-old pregnant patient was admitted to the emergency department after ingestion of 30 tablets of paracetamol (500mg.tb^{-1}), 7 drugs containing iron and folic acid, 24 drugs containing ibuprofen, and 21 drugs containing cyproterone acetate and ethinylestradiol 8 hours ago. On admission to the emergency department, the patient was conscious with a Glasgow coma scale (GCS) of 15 and her vitals were stable. Gastric lavage and activated charcoal were not recommended for the patient who was consulted with the poison counseling hotline. The consultation of the obstetrician was requested due to the pregnancy of the patient and fetal vitality was detected. The patient, who was hospitalized to the intensive care unit for close follow-up, was conscious at the time of admission with stable vital findings. N-Acetyl Cysteine (NAC) treatment was initiated. Daily laboratory values and fetal heart rate were followed and recommendations of the obstetrician were obtained. After 5 days of intensive care follow-up, psychiatry recommendations were received, and she was transferred to the ward uneventfully.

Case 2

An 18-year-old pregnant patient was admitted to the emergency department after ingestion of 20 tablets containing paracetamol. She was conscious with a GCS score of 15 and her vitals were stable. After consultation with the poisoning hotline, gastric lavage and activated charcoal were administered. The consultation of the obstetrician was requested due to the pregnancy of the patient and fetal vitality was detected. The patient, who was taken to intensive care for close follow-up, was conscious at the time of admission with a GCS of 15 and stable vitals. NAC treatment was administered. The suggestions of the obstetrician were obtained by following the daily laboratory values and fetal heart rate. After 3 days of intensive care follow-up, she was transferred to the ward with the recommendations of the psychiatrist uneventfully.

Discussion

Paracetamol is the most common drug that is overdosed during pregnancy [5]. The vast majority of cases of paracetamol toxicity reported during pregnancy involve a large amount of use at one time [9].

N-acetyl-p-benzoquinonimine (NAB), the toxic metabolite of paracetamol, is responsible for the liver toxicity of paracetamol overdose.

N-Acetyl Cysteine (NAC) is an antidote to acetaminophen poisoning. It has been reported that NAC treatment administered in the first eight hours following acute paracetamol intake prevents the development of this liver toxicity to a great extent [6, 7, 10, 11]. NAC, which crosses the placenta, adheres to toxic metabolites formed in both the mother and the fetus and reduces toxicity, can be safely administered to pregnant women [11].

A 17-year-old, 21 weeks pregnant patient used 25 g of paracetamol in two doses of 10 and 15 g 18 and 8 hours before hospitalization, and hepatotoxicity developed. However, a normal pregnancy was achieved with NAC treatment [12]. Another 24-year-old, 27-28 weeks pregnant case used 29 g of paracetamol in less than 24 hours, after which hepatotoxicity and fetal death occurred. However, it has been reported that maternal recovery occurs with NAC treatment [13]. NAC treatment was started immediately in both of our pregnant cases and hepatotoxicity did not occur.

Hepatotoxicity developed in a case in which repeated use of paracetamol in supratherapeutic amounts during pregnancy was reported and subsequently occurred with liver transplantation. Intrauterine fetal death occurred 2 weeks after the operation [14]. This case shows that repeated supratherapeutic intake of paracetamol also has serious morbidity potential.

In order for paracetamol to cause toxicity, the amount of acute overdose should be 150 mg/kg^{-1} (approximately 7.5 g in adults) within 24 hours [11]. However, it should be taken into account that the pharmacokinetics and pharmacodynamics of drugs differ from other patients due to physiological changes in pregnant women [15].

Clinical findings in paracetamol poisoning can be examined in 4 stages:

Stage 1 (30 min-24 hours): Nausea, vomiting, pallor, sweating, lethargy, weakness

Stage 2 (24-72 hours): Increase begins in liver aminotransferase enzymes [16]. Right upper quadrant pain and hepatomegaly can be seen. Increase in prothrombin time (PT) and total bilirubin, oliguria and renal dysfunction can be seen.

Stage 3 (72-96 hours): In addition to the return of clinical symptoms seen in stage 1, signs of jaundice, confusion, hepatic encephalopathy can be seen. Significant increase in liver enzymes and bleeding diathesis may develop. Acute kidney failure and pancreatitis can be seen.

Stage 4 (4 days-2 weeks): Recovery of hepatotoxicity or multiple organ failure (sometimes fatal) may develop [11, 17]. Clinical and laboratory deterioration was not observed in both pregnant patients we followed up, and their fetal vitality continued.

The treatment in paracetamol intoxication includes supportive therapy to prevent the absorption of the drug, antidote therapy and increasing the elimination of the drug. Gastric lavage can be performed to those who are admitted within the first 2 hours of taking the drug and activated charcoal should be administered to those who are admitted in the first 4 hours [18].

NAC, the antidote of paracetamol, can be administered intravenously or orally and is equally effective. Intravenously, 150 mg.kg^{-1} NAC is administered in 200 ml of 5% dextrose, with a 15 minute-loading dose. Subsequently, 50 mg.kg^{-1} NAC in 500 ml 5% dextrose is administered for up to 4 hours, and then 100 mg.kg^{-1} NAC in 1000 ml 5% dextrose is given in 16 hours. The oral loading dose is 140 mg.kg^{-1}. Following this dose, 17 additional doses are administered every 4 hours (70 mg.kg^{-1}) [11].

Anaphylactoid reactions, nausea and vomiting are the reported side effects of NAC treatment [2, 11, 19, 20]. A study conducted in Australia recommends one infusion dose instead of others for simple use [21]. We administered 150mg/kg loading dose of intravenous NAC treatment in 1 hour to two patients. There were no side effects due to NAC in our patients.

Conclusion

NAC treatment is considered safe in the treatment of paracetamol poisoning, which is common in pregnant women. However, large-scale studies are required to support this result.

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