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Acute Renal Failure and Hemolytic Uremic Syndrome in Overdose With N-acetyl Cysteine After Acetaminophen Poisoning

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Abstract

Context: Acetylcysteine is an effective treatment for acetaminophen poisoning. The preparation and dose calculation of acetylcysteine is associated with medical errors. The prevalence of this error is 34% globally.

Case report: A 15-year-old girl took an overdose of acetaminophen in a suicide attempt. Acetylcysteine intravenous was ordered. Due to the medication error by the nurse, she received a 10-fold overdose of intravenous acetylcysteine in both initial loading dose and maintenance dose, at first day. On the second day, the patient showed abdominal pain, nausea, vomiting, and elevated liver enzymes. Her hemoglobin, hematocrit, and platelet quickly decreased. Subsequently, she developed oliguria, anuria, and rising serum creatinine levels. The patient was diagnosed with uremic hemolytic syndrome. She underwent hemodialysis and was treated with plasmapheresis, blood transfusions, and platelets.

Discussion: The effects of acetaminophen poisoning and acetylcysteine overdose may be much more severe and have a greater impact on patient survival than each poisoning alone. Timely and accurate treatment measures can help prevent long-term side effects.

Keywords: Acetylcysteine, Renal Failure, Medication Error

1. Context

Acetaminophen is one of the most commonly used drugs for suicide attempts in the world (1). There are several medications available as an antidote to acetaminophen (2). However, the primary antidote to acetaminophen overdose is N-acetyl cysteine (2). N-acetyl cysteine (NAC) has been recognized as an effective antidote for acetaminophen poisoning via oral or intravenous administration (3). However, intravenous NAC is associated with the occurrence of many side effects (4). These short-term side effects may include nausea and vomiting, anaphylactic reactions such as flushing, shortness of breath, cough, tachycardia, rash, pruritus, bronchospasm, and hypotension (3). Hemolysis, cerebral edema, renal failure, and death are associated with high NAC doses (5). This study aimed to investigate Hemolytic Uremic Syndrome (HUS), kidney failure, and permanent dialysis due to a high NAC dose in a 15-year-old girl who attempted suicide by acetaminophen poisoning.

2. Case presentation

A 15-year-old girl was hospitalized due to the ingestion of 30 acetaminophen 500 mg tablets. In the emergency department of a local hospital, gastric lavage was performed. Activated charcoal was given to the patient, and NAC treatment was started. The treating physician ordered NAC intravenously following 150 mg/kg for one hour, followed by 9 mg/kg over 20 hours. Due to medication error by the nurse, mistakenly 45 vials of two grams (equivalent to 90 grams) as an initial loading dose and 90 grams in 20 hours as a maintenance dose were infused for the patient. The NAC infusion was discontinued one hour into the maintenance dose. Thus, the patient received a 10-fold overdose of

IV NAC when given 45 vials (90 grams) of the initial loading dose and 450 mg as a maintenance dose of acetylcysteine. The patient developed allergic reactions, including nausea, hot flashes, erythema, and pruritus. Because of the patient's above symptoms, NAC infusion was stopped, and hydrocortisone injection was used to reduce allergic reactions. However, because the patient's care quality was not sufficient, she was referred to a poison center at the university hospital. She was transferred to the intensive care unit.

Unfortunately, due to the fear of legal problems, the poison center was not informed of NAC overdose. In the poisoning center, the patient showed abdominal pain, nausea, vomiting, and elevated liver enzymes. Thus, the patient was visited by a gastroenterologist for better evaluation. Serum amylase and lipase were normal. Based on the Gastroenterologist consulting, the NAC at the dose of 5 mg/kg in 500 mL dextrose 5% over 24 h was infused. On the second day of hospitalization, abdominal pain decreased, and NAC administration was discontinued. However, the patient showed elevated serum creatinine levels (Cr = 4.9) and markedly decreased urine output (< 50 cc in 24 hours), for which nephrology consultation was performed. Concurrently, the patient's blood hemoglobin (from 12.5 g/dL to 7 g/dL) and platelet levels ($45 \times 1{,}000/mm^3$) decreased, and NAC infusion was discontinued. The patient's condition worsened, so the catheter was inserted in the subclavian vein, and hemodialysis lasted around two hours. In peripheral blood smear, 5 to 7 schistocytes per field were revealed, and according to the set of clinical symptoms, her final hematologic diagnosis was HUS. Then, plasmapheresis was performed daily for up to seven days. Ultrasound showed that the kidney's size was normal, but the renal cortex was highly echogenic. One week after dialysis and plasmapheresis, urine output increased, but the high serum creatinine level did not decrease.

According to the patient's needs, dialysis and plasmapheresis sessions were performed until the 47th day of hospitalization. Echocardiography was carried out for the patient on the 11th, 24th, and 38th days that showed 50%, 35% and 40%, respectively. During hospitalization, the patient had many respiratory problems, including dyspnea, acute pulmonary edema, and hemoptysis, but controlled by ventilation, antibiotic therapy, and bronchoscopy procedures such as bronchoalveolar lavage. During hospitalization, the secondary workup for high Cr levels was performed; C3 and C4 were less than standard, and ANA (antinuclear antibody), pANCA (perinuclear antineutrophil cytoplasmic antibody), cANCA (cytoplasmic-anti neutrophilic cytoplasmic antibodies), dsDNA (anti-double stranded DNA), CH50 (Hemolytic Complement) levels were within the normal limits. Because of the low serum complement level and HUS, we performed a renal biopsy on the 45th day of admission for ruling out glomerulonephritis like lupus nephritis. Before the renal biopsy, the patient received intravenous immunoglobulin and corticosteroids. In the renal biopsy, pathological processes were consistent with HUS changes, glomerular ischemia, glomerulosclerosis as glomeruli, and acute tubular necrosis (ATN) evidence. Finally, the patient with a permanent central venous catheter was discharged from the hospital with permanent dialysis three times a week for three hours each.

3. Discussion

Acetaminophen toxicity is the most common cause of poisoning worldwide (3). Every year, many patients are impaired due to these medical errors, while most of these errors are preventable (6). Acetylcysteine, the primary antidote for acetaminophen poisoning, is used both orally and intravenously to prevent liver damage (7). It is effective if given within 8-10 hours of acetaminophen ingestion (8). However, due to the complexity of the NAC treatment regimen, it may cause errors in the calculation of doses by medical staff (7). The prevalence of this error is 34% in the world (9). In this study, renal failure and hemolytic uremic syndrome associated with acetylcysteine overdose were investigated in a 15-year-old girl with intentional acetaminophen poisoning. The patient arrived at the hospital in approximately less than an hour, and a large amount of acetaminophen was removed from the patient's stomach. It seems that most of the complications that occurred for this patient were related to an overdose of acetylcysteine. The interaction between acetaminophen and acetylcysteine in patient survival is more than intoxication with either alone (10). In most previous studies, patients went to the hospital late, and this led to increasing acetaminophen absorption of paracetamol (1, 3, 7). This increased the interaction of acetaminophen and acetylcysteine, which increased the risk of hepatotoxicity and death in patients (10). Taking acetylcysteine orally and intravenously is associated with side effects. Adverse side effects associated with intravenous administration include flushing, rash, nausea, vomiting, and itching, besides tachycardia, bronchospasm, and hypotension in severe cases (1, 3). They occur in the first two hours after infusion in 15% of patients (3, 11).

Some patients presented oliguria, anuria, uremia, and a 40% reduction in GFR on the first day of overdosing on NAC, leading to acute kidney failure (12). The second day after admission, this patient developed anuria, elevated serum creatinine levels, low red blood cells, low platelets, and the presence of schistocytes in a peripheral blood smear, which confirmed HUS. She underwent hemodialysis every two days for one week and plasmapheresis ev-

ery day for one week and until the 47th day of hospitalization according to the patient's need. Tubular necrosis and nephrotoxicity are also seen in one to two percent of acetaminophen poisoning cases, which is also seen in cases of NAC overdose with or without liver poisoning (3). A kidney biopsy performed on the 45th day of hospitalization showed ischemia and evidence of glomerulosclerosis in most glomeruli. Fortunately, this patient responded well to treatment procedures, but she was undergoing permanent hemodialysis. However, it seems that patient care and young age are more related to patient survival.

3.1. Conclusions

Patients should be transferred to the hospital as soon as possible without wasting time to prevent the interaction of the effects of acetaminophen and its overdose with acetylcysteine. Timely and accurate treatment measures can help prevent long-term side effects. the physician orders should be rechecked by head nurses for preparing a medication, and be careful enough to match the information such as the name of the drug, drug form, and dose prescribed with the pharmacy's product for use in the patient.

Footnotes

Authors' Contribution: Conceptualization: Reza Asadzadeh, Zahra Khalighi; Data collection: Nahid Mamizadeh; Writing the original draft: Aliashraf Mozafari, Marzieh Hadavi, and Abas Ghaysouri; Writing, review, editing, and investigation: All authors.

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