

Seizure after a massive infusion of N-acetylcysteine and successful treatment with a good outcome



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Abstract

Objective: N-acetylcysteine is frequently used as an efficacious antidote for acetaminophen toxicity. It prevents liver injury induced by paracetamol and in most cases the overdose of acetylcysteine produces mild clinical effects.

Case Presentation: Here we describe a patient who self-treated himself by acetylcysteine after acetaminophen toxicity. Approximately 5 hours after receiving 140 g of acetaminophen, the patient developed confusion, hypotension as well as seizures and also had coagulopathy and acute kidney injury. Other causes of these symptoms were overdose of acetaminophen and amoxicillin. Finally, the patient was treated by extensive supportive therapy and got healed.

Conclusion: This case suggests that massive IV acetylcysteine overdose can cause serious life-threatening conditions. The purpose of reporting this case is to increase the awareness among medical staff concerning adverse reactions revealed after a massive overdose of N-acetylcysteine and their arrangement as well as describing the way of management of such problems. The seizure was one of the manifestations in our case and it is so rare. This indicates that massive dosing of acetylcysteine could form irreversible damages in the brain, so it is very important to start the management as soon as possible and monitor patients precisely.

Keywords: Acetylcysteine, Acetaminophen, Amoxicillin, seizure, Coagulopathy, Nephropathy

Introduction

N-acetylcysteine is frequently used as an efficacious antidote for acetaminophen toxicity. The recommended protocol of therapy is based on 150 mg/kg over 1 hour, followed by 50 mg/kg over 4 hours followed by 100 mg/kg over 16 hours. Dosing mistakes are frequent. N-acetylcysteine has a wide therapeutic range and severe outcomes are unusual (1). In this research, we aim to explain the adverse effects that were seen after acetylcysteine overdose due to a mistake caused by the patient self-treatment and the way of successful management performed by the medical team.

Case Presentation

A 31-year-old male medical staff with a weight of 75 kg ingested 17×500 mg of acetaminophen tablets and 10×500

mg of amoxicillin capsules in order to suicide. After 1 hour he regretted and he knew the way of treatment of intoxication so denied going to the hospital and treated himself by 70 vials of N-acetylcysteine 2 g/10 mL. At the time of admission, the chief complaint of the patient was frequent nausea and vomiting accompanied by fatigue. The patient had no history of prior illness or disease. In a quick approach he had a pulse rate of 130 beats per minute, respiratory rate of 16 breaths per minute, blood pressure of 100/70 mm Hg, temperature 36.5°C and O₂ saturation of 94.4%. In addition, he had intact mental status and unremarkable physical examination. Besides, his electrolytes, renal function, liver function, and complete blood count (CBC) were all within normal limits. We fixed nasogastric tube and gastric washing was done. After all procedures were done, the patient was suffering from



severe respiratory distress and airway management was performed and the patient was prepared to be transferred to the Toxicology department. After three hours he had a seizure. The airway breathing circulation (ABC) Protocol was performed and benzodiazepine therapy was started, the type of seizure was generalized tonic-clonic and lasted for about 3 minutes and then stopped. The neurology service was consulted and sodium valproate drip for 5 hours was recommended. The patient had no history of epilepsy or seizure before and at the time of admission, he had hypotension and tachycardia. The laboratory data included Bun of 20 mg/dL, creatinine of 2.1 mg/dL, aspartate transaminase (AST): 58 IU/L, alanine aminotransferase (ALT): 69 IU/L and in the CBC thrombocytopenia of 50 000 platelets was seen. The tests were repeated after one hour and the results were blood urea nitrogen (BUN) of 70 mg/dL, creatinine 2.9 mg/dL, platelets of 42000, and serum electrolytes were normal. The patient was prepared for hemodialysis and the CV-line was fixed, then the first dialysis was conducted on the first day of admission, the day after he underwent for 4 hours of heme-dialysis due to the disturbances of laboratory indices and received 1 unit of fresh frozen plasma and 10 packs of platelets. The required tests were requested and the results were largely distorted and the patient needed another hemodialysis and then because of platelet reduction, he received another pack of platelets. After this prescription, the coagulation indices were prothrombin time (PT)=12 seconds, partial thromboplastin time (PTT)=32 seconds, international normalized ratio (INR)=1 and platelets=150 000. The following day when the laboratory tests were still distorted, the patient was sent for another dialysis for 2 hours and then he received another 5 packs of platelet because of further reduction in platelet counting. On the sixth day after overdose, the laboratory tests were as follows: BUN=20 mg/dL, Cr=1.3 mg/dL, AST=108 IU/L, ALT=17 IU/L, PT=10 seconds, PTT=30 seconds, INR=1 second, and platelets count=183 000. Ultimately, he was healthy again and felt better and stayed in the ward for some days. After the tenth day, he was discharged in a healthy condition with laboratory tests within normal limits.

Discussion

N-acetylcysteine has two mechanisms of action. In paracetamol overdose, acetylcysteine acts as a hepatoprotective agent by restoring hepatic glutathione, serving as a glutathione substitute, and enhancing the nontoxic sulfate conjugation of acetaminophen. It also acts as mucolytic and exerts mucolytic action through its free sulfhydryl group which opens up the disulfide bonds in the mucoproteins thus lowering mucous viscosity. The recommended protocol of therapy is based on 150 mg/kg over 1 hour, followed by 50 mg/kg over 4 hours and then by 100 mg/kg over 16 hours (2). Here the patient was stable right before the infusion of acetylcysteine, and

after receiving massive infusion about 140 g, he developed hypotension and got tachycardia. These types of reactions are highlighted in previous studies (3). Hypotension could be due to anaphylactoid reactions and the severity of overdose manifestations depends on intravenous or oral prescription. The most common adverse reactions reported are nausea, vomiting, tachycardia and severe manifestations such as anaphylactoid reactions include shock, rash, urticaria, angioedema, bronchospasm and rarely hypotension are related to a massive overdose of N-acetylcysteine (4). In the present case, upon his arrival in our department, he started developing generalized tonic-clonic seizure that lasted for three minutes. He had no history of epilepsy or seizure before and it occurred only once in the period of admission and was well-controlled by dripping of sodium valproate. Neurological assessment was normal. Development of seizures was reported before, while a massive overdose of acetylcysteine happened. In one case reported from Montreal, a girl who was 30 months started clonic status epilepticus in the left side of her body after receiving 2450 mg/kg of acetylcysteine and she died ultimately because of cerebral edema and the increasing of Intracranial Pressure (5). In another case reported in 2011, a 21-year-old female developed delirium and seizures that progressed to cerebral edema, uncal herniation, and ultimately severe brain injury (1). Our patient's laboratory tests showed progressive levels of urea and creatinine that caused acute renal failure. In general, N-acetylcysteine has been reported to protect the kidney from injury induced by contrast media, ischemia, and toxins and does not cause kidney problems. But in the reviews performed in this article, in rare cases, overdose of this substance leads to nephrotoxicity and increased BUN/Cr (2). As we know the patient also ingested 10×500 mg amoxicillin capsules that can develop acute renal failure as mentioned in many previous researches (6-8). Based on the lab tests checked for the patient, there were obvious coagulopathy and reduction in platelets count. These kinds of disturbances are not reported with acetylcysteine but are reported as common adverse reactions of acetaminophen overdose (9-12). The patient underwent hemodialysis 4 times in 4 days repeatedly and this way of management made his laboratory tests normal. He was finally discharged with a health condition after 10 days of admission. This indicates the on-time diagnosis and highlights that the rapid dialysis can help remove intoxication.

Conclusion

The purpose of reporting this case is to increase the awareness among medical staff concerning adverse reactions revealed after a massive overdose of N-acetylcysteine and their arrangement as well as describing the way of management of such problems. The seizure was one of the manifestations in our case and it is so rare. This indicates that massive dosing of acetylcysteine

could form irreversible damages in the brain, so it is very important to start the management as soon as possible and monitor patients precisely.

Ethical issues

This article does not contain any test on human participants or animals.

Authors' contributions

PRN: performing of the study and writing of the draft KS, MHK :concept and design MA and TS: data collection and interpretation of the data

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