Case report

Life-threatening hyponatremia due to intravenous n-acetylcysteine treatment in an infant: a case report

Juan Mayordomo-Colunga*, Elene Larrea, Mónica García, Sonsoles Suárez and Julián Rodríguez

Address: Paediatric Emergency Unit, Department of Pediatrics, Hospital Universitario Central de Asturias, Oviedo, Spain

Email: JMC* - jmcolunga@hotmail.com; EL - iujule@hotmail.com; MG - ployin@msn.com; SS - sonsoles.suarez@sespa.princast.es; JR - julian.rodriguez@sespa.princast.es

* Corresponding author

Received: 18 June 2009  Accepted: 17 August 2009  Published: 1 September 2009

Cases Journal 2009, 2:8347 doi: 10.4076/1757-1626-2-8347

This article is available from: http://casesjournal.com/casesjournal/article/view/8347

© 2009 Mayordomo-Colunga et al.; licensee Cases Network Ltd.

This is an Open Access article distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/3.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Abstract

Introduction: N-acetylcysteine has proven to be effective in paracetamol intoxications, but there is no consensus regarding its way of administration. Here, we report a case to highlight the importance of careful management of intravenous n-acetylcysteine.

Case presentation: A two-month old infant was seen in our paediatric emergency department due to paracetamol poisoning after repeated supratherapeutic doses. She was treated with intravenous n-acetylcysteine diluted with dextrose 5%, according to the 20-hour standard protocol. Eight hours later she developed two tonic-clonic seizures and was subsequently intubated. By that time, she had received almost 1 liter of 5% dextrose, and serum sodium was 114 mg/dL. A rapid correction was done with hypertonic saline and the child experienced a good outcome, without any sequelae.

Conclusion: Intravenous n-acetylcysteine administration must be done carefully. Amount of liquid administrated and sodium monitoring should be kept in mind, with special care in small children.

Introduction

Paracetamol is a worldwide-used, safe and effective antipyretic and analgesic for children when used at therapeutic doses. It is nowadays the leading cause of drug poisoning among young children [1]. Repeated supratherapeutic doses with non self-harming intent is an increasing type of paracetamol intoxication, both in adult and paediatric patients [2].

This medication achieves its highest serum levels about four hours after ingestion [3]. Serum paracetamol level determination should be performed at that time if ingested amount is over 150 to 200 mg/kg in a single dose [4,5]. If the value is above the study line of Rumack-Matthew nomogram [6], N-acetylcysteine (NAC) must be administered, either intravenously or orally. Activated charcoal is useful to lower intestinal absorption when ingestion takes place within the previous 60 to 90 minutes [3,7].

Here, we present a case, which derived in a life-threatening condition in an infant due to intravenous administration...
of NAC. We also discuss the use of NAC so as to avoid complications in small children.

Case presentation
A two-month old Caucasian Spanish infant was seen in our pediatric emergency department (PED) because of paracetamol overdosing. She was febrile due to vaccination and her parents gave her three consecutive doses of 500 mg instead of 50 mg of paracetamol (weight 4.7 kg), separated by 6 hours. The infant was brought to our PED two hours after the last dose.

Plasma paracetamol level was determined on arrival (113.5 µg/mL). The child was admitted to the ward and intravenous NAC infusion was started following the standard 20-hour protocol as paracetamol level was high (Table 1).

Eight hours later, the child presented a 2-minutes generalized seizure which responded to intravenous diazepam. Fifteen minutes later, she had another tonic-clonic seizure which also responded to diazepam after 6 minutes. Due to impaired consciousness and suspicion of liver encephalopathy she was intubated and transferred to the pediatric intensive care unit. Blood analysis showed hyponatremia of 114 mEq/L, which was managed with a rapid correction of hypertonic saline until the serum sodium reached 124 mmol/l. Then, sodium was gradually increased via isotonic saline and furosemide boluses. Paracetamol levels were undetectable by 15 hours after admission (Table 1).

The girl was extubated ten hours later, and evolved satisfactorily. She was followed up as an outpatient during the following months, and her neurological status was completely normal.

Discussion
Paracetamol poisoning is the main cause of acute liver failure in adult patients in the West World. In children, paracetamol has fewer toxic effects, but due to its wide use, it remains a concern nowadays. The risk of hepatotoxicity is higher in repeated supratherapeutic doses administration than in single overdose [8]. A frequent mistake in pediatric dose administration is made when the parents miscalcuate the appropriate dose or when there is confusion with paracetamol concentration due to different presentations of the same product [9]. In our case, dosage was ten times higher than the right one [10].

NAC is useful as an antidote for paracetamol overdosing as it increases glutathione, which binds and inactivates the hepatotoxic metabolite N-acetyl-p-benzoquinoneimine. It is indicated when paracetamol plasma concentration is above the study line of Rumack-Matthew nomogram in single overdoses [6]. If time of ingestion is not known or if the patient received repeated supratherapeutic doses, correct risk-stratification cannot be done with the use of Rumack-Matthew nomogram. In those cases, it seems prudent to administer NAC if serum paracetamol concentration is over 20 µg/ml [11]. Moreover, delayed NAC administration has been identified as one of the risk factors to a worse outcome [12]. According to this, the decision of prescribing NAC to our child was correct.

There is no consensus regarding NAC administration as it seems to be effective if used both intravenously and orally [7,12,13]. Some advantages for intravenous administration are that it can be used in patients at risk of impaired consciousness and its shorter duration when compared to oral one. Oral dose of n-acetylcysteine involves a large volume and would greatly increase the risk of regurgitation and aspiration, mostly if liver failure develops which could impair conscious level.

Protocols as the 20-hour one used in our case must be abandoned in small patients for intravenous NAC administration. According to them, patients are given a loading dose of 150 mg/kg of NAC in 40 to 200 ml of 5% dextrose over 15 minutes, followed by 50 mg/kg in 500 ml of 5% dextrose over 4 hours and then 100 mg/kg in 1000 ml of 5% dextrose over the next 16 hours. By eight hours of treatment, our child had received 950 mL of 5% dextrose. If the protocol would have been completed, she would have received up to 361.7 ml/kg of free water. Therefore, NAC concentration should be of 40 mg of NAC per ml of 5% dextrose [11,14] or drug information sheet for patients weighing 10 kg should be followed (Acetadote®). This should avoid complications as cerebral edema or hyponatremia [14].

In conclusion, intravenous NAC administration must be done carefully. Amount of liquid administrated and sodium monitoring should be kept in mind, with special care in small children.

Consent
Written informed consent was obtained from the patient parents’ for publication of this case report. A copy of the

| Table 1. Blood determinations at admission (PED), at the time seizures developed (WARD) and after rapid correction with hypertonic saline in the pediatric intensive care unit. PED: pediatric emergency department; PICU: pediatric intensive care unit |
|----------------|--------|--------|
| Glucose (mg/dl) | 117    | 290    | 137    |
| Sodium (mg/dl)  | 134    | 114    | 124    |
| AST (U/l)       | 64     | 57     | 61     |
| ALT (U/l)       | 39     | 36     | 38     |
| Serum paracetamol level (µg/mL) | 113.5  | 17.8   | 7.8    |
written consent is available for review by the Editor-in-Chief of this journal.

**Competing interests**
The authors declare that they have no competing interests.

**Authors’ contributions**
JMC and EL and CR drafted the manuscript. MG, SS and JR revised the literature. All authors read and approved the final version of the manuscript.

**References**
1. Mintegi S, Fernandez A, Alustiza J, Canduela V, Mongil I, Caubet I, Clerigue N, Herranz M, Crespo E, Fanjul JL, Fernandez P, Humayor J, Landa J, Munoz JA, Lasarte R, Nunez FJ, Lopez J, Molina JC, Perez A, Pou J, Sanchez CA, Vazquez P. Emergency visits for childhood poisoning: a 2-year prospective multicenter survey in Spain. *Pediatr Emerg Care* 2006, 22:334-338.
2. Kozer E, McGuigan M. Approaches toward repeated supratherapeutic doses of paracetamol in children: a survey of medical directors of poison centres in North America and Europe. *Drug Saf* 2002, 25:613-617.
3. Anderson BJ, Holford NH, Armishaw JC, Aicken R. Predicting concentrations in children presenting with acetaminophen overdose. *J Pediatr* 1999, 135:290-295.
4. Alander SW, Dowd MD, Bratton SL, Kearns GL. Pediatric acetaminophen overdose: risk factors associated with hepatocellular injury. *Arch Pediatr Adolesc Med* 2000, 154:346-350.
5. Burillo-Puuste G, Mintegui S, Munne P. Changes in pediatric toxic dose of acetaminophen. *Am J Emerg Med* 2004, 22:323.
6. Rumack BH, Matthew H. Acetaminophen poisoning and toxicity. *Pediatrics* 1975, 55:871-876.
7. Brok J, Buckley N, Gloed C. Interventions for paracetamol (acetaminophen) overdose. *Cochrane Database Syst Rev* 2006, 19:CD003328.
8. Rivera-Penera T, Gugig R, Davis J, McDiarmid S, Vargas J, Rosenthal P, Berquist W, Heyman MB, Ament ME. Outcome of acetaminophen overdose in pediatric patients and factors contributing to hepatotoxicity. *J Pediatr* 1997, 130:300-304.
9. Kubic A, Burda AM, Bockewitz E, Wahl M. Hepatotoxicity in an infant following supratherapeutic dosing of acetaminophen for twenty-four hours. *Semin Diagn Pathol* 2009, 26:7-9.
10. Fernandez LA, Mintegui RS, Martinez Gonzalez MJ. Paracetamol poisoning in infants aged less than six months: dosage errors. *Am Pediatr (Bac)* 2004, 60:177-179.
11. Heard KJ. Acetylcysteine for acetaminophen poisoning. *N Engl J Med* 2008, 359:285-292.
12. Kanter MZ. Comparison of oral and i.v. acetylcysteine in the treatment of acetaminophen poisoning. *Am J Health Syst Pharm* 2006, 63:1821-1827.
13. Prescott L. Oral or intravenous N-acetylcysteine for acetaminophen poisoning? *Ann Emerg Med* 2005, 45:409-413.
14. Sung L, Simons JA, DAYNEKA NL. Dilution of intravenous N-acetylcysteine as a cause of hyponatremia. *Pediatrics* 1997, 100:389-391.