Near-fatal drug toxicities in newborn babies: A Case Series

Abstract

Background: Neonates are highly vulnerable to drug toxicities because of their age-related limitations in drug metabolisms and renal excretion. Lack of the knowledge and/or education for medical professionals about the right dose administration and the lack of neonate-specific formulations are the additional dilemmas.

Cases Presentation: Here, we reported six neonates presented with severe drug toxicities, including acetaminophen, digoxin, theophyllin, lidocaine and opium and they were successfully treated in NICU at Amirkola Children's Hospital, Babol– in the north of Iran. Most of the toxicities were originated from the lack knowledge of physician or parents for selecting the right drug and dose of drug for newborn babies.

Conclusions: Better education of medical professional and parents are needed to avoid neonatal drug toxicities.

Keywords: Toxicity, Neonatal, Drug, Acetaminophen, Digoxin, Theophyllin, Lidocaine and Opium

Case Series

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Introduction

Neonates are at great risk to develop drug toxicities because of immaturity of their drug metabolism and disposal mechanism [1, 2]. These limitations determine the efficacy and/or safety of a therapeutic or inadvertent drug exposure [3, 4]. So a strict policy must be undertaken when a drug is administered in and outpatient clinic and also for neonates admitted to the hospital. Furthermore, the treatments of severe drug toxicity in neonatal period including peritoneal dialysis or hemodyalisis have several limitations in neonatal period in developing countries. Here, we reported six neonates presented with severe drug toxicities, including acetaminophen, digoxin, theophyllin, lidocaine and opium and they were successfully treated in NICU at Amirkola Children's Hospital, Babol– in the north of Iran.

Cases Presentation

Case 1:

A term newborn was brought to the outpatient clinics of our hospital because of vomiting and bad general condition. He was visited 3 days ago and referred to a cardiologist because of a harsh systolic murmur, which was found on routine physical examination. Lanoxin elixir 50 µg/ml (GlaxoSmithKline company) with a dose of 0.2 mL BD was commenced by cardiologist for the diagnosis of large VSD, but because of misinterpretation by pharmacist he received 2 ml TDS (Instead of 0.2 ml BD) for 4 doses. He developed severe digoxin toxicity. He was admitted to NICU immediately and a two-volume blood exchange transfusion was done for two times. Plasma digoxin level has

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not been measured, because of its unavailability. His general condition recovered and he was discharged with maintenance dose of digoxin and a good general condition.

Case 2:

A full term, well baby with moderate hyperbilirubinemia was visited by a pediatrician at 4th day of life and he was given erroneously Phenobarbital to treat hyperbilirubinemia. Theophyllin retard tab 250 mg was given to the baby instead of phenobarbital tab 15 mg by a pharmacist. He developed vomiting and severe convulsions. So he was admitted to NICU and mechanical ventilation started because of respiratory failure and exchange transfusions was done for two times. After recovery for 7 days, he was discharged with phenobarbital as a maintenance therapy for his seizure and abnormal brain CT scan. He is now alive without need for medication for seizure.

Case 3:

A well baby circumcised by a general surgeon at 7th day of life. He was given acetaminophen 325 mg adult suppository every 2 hours and was discharged to home. When he was brought to our hospital, he was taken 5 suppositories of adult acetaminophen. He was admitted to NICU because of vomiting and decrease of neonatal reflexes and level of consciousness. Treatment with intravenous infusion of N-Acetylcystein began. Apnea and recurrent seizure occurred in first day of admission. Ultimately, he intonated and the respiratory support with ventilator started. Finally, he was discharged with Phenobarbital as a maintenance therapy for his seizure. He is now alive as a spastic cerebral palsy patient.

Case 4:

A 28-day-old neonate was admitted to NICU because of seizure. He was circumcised by a general physician 2 hours ago. For local anesthesia and dorsal penile nerve block (DPNB) he received lidocaine 2% five milliliters, three times more than the usual dosage. Twenty minutes after injection of lidocaine, he developed convulsion and wrongly treated with rectal diazepam. Apnea after treatment with diazepam occurred. Apnea recovered with mouth-to-mouth ventilation and then patient was brought to our hospital. He was conservatively treated and discharged with a good general condition after recovery.

Case 5 & 6:

A full term and 20-day-old male neonate was admitted to NICU with apnea and cyanosis. On physical exam, his pupil was miotic and there were the decrease of neonatal reflexes and bradypnea. The detailed history revealed that his parents give him opium extract to relieve his crying and colic. The patient was treated with naloxone HCL and after recovery; he was discharged with a good condition.

In addition, a six-day-old neonate was visited in emergency room with drossiness, cyanosis and respiratory distress. Her parents gave opiate to her because of her restlessness. After admission to NICU and treatment with naloxone her respiratory condition and drossiness responded to therapy and the sign and symptom of opium toxicity was disappeared.

Discussion

In these case series of study, we reported several neonatal drug toxicities which were occurred because of high toxic dose administration and the most of drugs were prescribed by a physician, but two of them were given opium by their parents as home folk remedy.

Drug therapy in neonate has not been totally safe and effective, even by a physician. The drug pharmacokinetic like absorption, distribution, metabolism and excretion in neonatal period differs significantly from other age groups. The knowledge about the right drug selection and the right dose administration together with the serum level monitoring is required [5] to improve the safety and avoid toxicity in neonatal period. Most of digoxin toxicities in neonates are due to wrong dose administration and/or renal failure, because it has a narrow margin of safety. Although the drug of choice for the treatment of digoxin toxicity is the digoxin-specific Fab antibody fragment [6], but because of its unavailability, we have successfully treated our severely sick baby with blood exchange transfusion, although because of large extravascular volume of distribution, digoxin is not effectively removed by exchange transfusion [7].

Rectal acetaminophen toxicity in our cases highlights the need for better education of medical professionals including general surgeon regarding the appropriate use and dose of acetaminophen in newborns. In our case report, he received an adult acetaminophen suppository 325 mg every two hours up to five times (5×325=1625 mg), so the total dose is near 11.6 times higher than the toxic dose. Acute intake of more than 140 mg/kg of acetaminophen establishes potential risk for acetaminophen toxicity and requires urgent evaluation [8]. He was vigorously treated with intravenous N-acetylcysteine (NAC) infusion protocol without any adverse effects, but he developed severe seizure and encephalopathy. A similar case of acetaminophen toxicity with encephalopathy and

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oliguric renal failure was reported in a term neonate after circumcision in the United State of America [9]. Although the treatment of choice is NAC infusion, one case of acetaminophen toxicity reported by Lederman in an infant of 29 weeks' gestation who was exposed to the drug when his mother ingested 32.5 g, 16 hours before delivery and the infant was treated with exchange transfusions [10].

Circumcision is the most common surgical procedure performed in the neonatal period in our community. The most widely used pharmacological agent for pain management during circumcision is dorsal penile nerve block (DPNB) by injected lidocaine [11]. Maximum safe doses of lidocaine are 5 mg/kg without epinephrine. Concentrated preparation (e.g., 2%) should not be used because diluted solutions (0.3%) are equally effective as concentrated solution (1-2%). Diluted solutions also causes less burning discomfort on injection and permit use of larger volumes without achieving toxic doses. For example, a 5 kg infant for suturing may safely receive up to 5×5= 25 mg of lidocaine. This maximum dose would be given with either 1.25 mL of lidocaine 2%, 2.5 mL of lidocaine 1%, or 5 mL of lidocaine 0.5% [12].

The diagnosis of neonatal drug toxicities requires a high index of suspicion. One of the limitations in our cases was the lack of confirmation of the diagnosis by serum level determination because of its unavailability and the admission of the patient on holiday to the private laboratory which was closed and responsible to check the serum level. Although the net diagnosis required serum level determination, we could not postpone the immediate therapeutic measures in the presence of a reliable history of drug exposure and a wrong written dose on a prescription, accompanied with the typical clinical sign and symptoms, for most offending agent, qualitative measurement is not possible or likely to change the decision for treatment [13].

In conclusion, the better education of medical professional and parents are required to avoid neonatal drug toxicities.

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