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

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 hemodialysis 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
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 hyper-
biaurinemia was visited by a pediatrician at 4th day of
life and he was given erroneously Phenobarbital to treat
hyperbilirurinemia. 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 pharma-
cokinetic 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 \((5 \times 325 = 1625 \text{ mg})\), 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 States 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 (0.2%) 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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References