CASE REPORT

How a Drug Shortage Contributed to a Medication Error Leading to Baclofen Toxicity in an Infant

Bonnie Lau, MD, PhD,^{1,2} Uma Khazanie, MD,¹ Emily Rowe, PharmD,¹ and Karen Fauman, MD¹

¹Department of Pediatrics, Floating Hospital for Children at Tufts Medical Center, Boston, Massachusetts; ²Department of Pediatric Hematology/Oncology, Johns Hopkins Hospital, Baltimore, Maryland

We report the case of a 4-month-old girl who developed encephalopathy, seizures, and respiratory compromise as a result of baclofen toxicity. After some investigation, the accidental ingestion of baclofen was caused by an error in compounding the patient's prescribed omeprazole with baclofen rather than sodium bicarbonate at a retail pharmacy. This error occurred because these two drugs, which were available as powders, were located side by side on the pharmacy shelf. The pharmacist further reported that their normal practice was to use injectable sodium bicarbonate rather than powder to compound an omeprazole suspension; however, the injectable form was not available due to a national shortage. This report demonstrates how a drug shortage contributed to severe clinical consequences and intensive care hospitalization of a patient. It also highlights the need for system improvement to minimize drug shortages.

INDEX TERMS: adverse drug effect, baclofen, drug shortage, encephalopathy, extemporaneous compounding, medication error, omeprazole, sodium bicarbonate

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INTRODUCTION

For the past decade, the United States has experienced an unprecedented increase in the frequency of drug shortages. These shortages have caused numerous difficulties for health care facilities, clinicians, and ultimately patients. Disturbances within the drug supply chain may increase the likelihood of medication errors. In fact, the Institute for Safe Medication Practices (ISMP) noted that 6% of adverse outcomes associated with drug shortages were related to “an error when a pharmacy attempted to compound a product or drug strength no longer available.”¹ We describe a case that exemplifies the association between a drug shortage and an error in extemporaneous compounding which resulted in harm to a patient.

CASE REPORT

A 4-month-old Caucasian female, who was tracheostomy- and gastrostomy (G-tube)-dependent due to Treacher Collins syndrome, was admitted to our pediatric intensive care unit

(PICU) with respiratory compromise and acute mental status change. Her parents describe her as having been in her normal state of health until the evening of admission when her mother gave the evening dose of omeprazole suspension through the G-tube. The mother then vented the G-tube by pressing on her abdomen to expel air according to their usual routine. While this process usually causes no distress, the infant began intermittent bouts of intense crying over the subsequent hour. Although the girl was consolable, her parents became increasingly concerned as she developed symptoms including pallor, irregular breathing pattern with periods of gasping, and episodes of apnea. During this period, she experienced 1 episode in which her eyes momentarily rolled upward without irregular movements of the extremities. Because the patient had a tracheostomy in place, her parents were able to provide positive pressure ventilation via bag valve mask while awaiting emergency medical services. The infant was stabilized and ventilated through the tracheostomy at a community hospital prior to transfer to the PICU at our tertiary care center.

On arrival in the PICU, the patient was ob-

tunded and opened her eyes only to deep painful stimulation. She had diffusely decreased tone, and pupils were 2 mm and sluggishly reactive. She was hypothermic with a temperature of 35.5°C and had no signs of infection or trauma on examination. Complete blood count results did not indicate an infectious process, but a blood culture was sent for analysis. Laboratory studies revealed hyperkalemic, hyperchloremic metabolic acidosis with the following abnormal serum values: potassium, 6.1 mEq/L; chloride, 113 mEq/L; bicarbonate, 18 mEq/L. Serum ammonia was also elevated at 90 mcg/dL, but liver and renal function results were unremarkable. Computed tomography scans of her head were negative for intracranial hemorrhage, infarct, space-occupying lesion, or midline shift. Chest and abdominal plain film results were also normal. Over the next few hours, the patient continued to have depressed mental status but remained otherwise clinically stable. Approximately 5 hours after she was admitted, she developed bicycling movements of her upper and lower extremities, which were thought to be consistent with seizure activity, and the pediatric neurology team was consulted.

On evaluation, the neurologists noted the patient had abnormal movements described as upper limb posturing with 1 arm stiffened and extended and the other flexed. The lower limb movements and eye movements were rhythmic. The episode ended after 2 intravenous doses of 0.1 mg/kg of lorazepam. Afterward the patient was less responsive and not breathing over the ventilator. Her extremities were minimally responsive to noxious stimuli, pupils were equal and minimally reactive, brainstem reflexes were intact, she was hypotonic and hyporeflexive, and Babinski was absent on the right foot and equivocal on the left foot.

Lumbar puncture was performed with an opening pressure of 20 mm Hg, and cerebrospinal fluid had 520 red blood cells, 2 nucleated cells, 57 mg/dL protein, and 61 mg/dL glucose, and culture was negative. Brain magnetic resonance imaging was negative except for known choanal atresia. Electroencephalography showed significant generalized slow background activity (1-2 Hz) with intermittent, rare sharp waves in the left frontal and temporal regions with no obvious epileptic activity, suggestive of moderate to severe encephalopathy.

The differential diagnosis for the patient's encephalopathy included infection, infarction, intoxication/ingestion, or metabolic abnormality. All test results for infection were negative, and the computed tomography and magnetic resonance images were inconsistent with an infarct.

The neurology team determined that the symptoms began moments after receiving the first dose from a newly refilled bottle of omeprazole. Given the relationship between the onset of symptoms and administration of the newly compounded omeprazole suspension, neurology recommended toxicology studies for opiates, alcohol, THC, cocaine, amphetamines, and benzodiazepines, which were negative. The patient maintained normal vital signs and returned to her baseline with supportive care and was discharged late on hospital day 2.

At the request of the medical staff, the parents brought the bottle of omeprazole suspension to the hospital where it was noted to have dark-colored precipitate and a metallic odor. The hospital medical and pharmacy staff contacted the retail pharmacy that compounded the omeprazole prescription. Initially the retail pharmacy reported that the omeprazole was made following a published recipe using omeprazole capsules and sodium bicarbonate but, upon further investigation, realized that an error had been made. Normally, the retail pharmacy used injectable sodium bicarbonate to prepare the omeprazole suspension, but due to a national shortage of injectable sodium bicarbonate, the retail pharmacy used sodium bicarbonate powder. Unfortunately, the powders in the pharmacy were arranged alphabetically on the shelf. Instead of using the sodium bicarbonate powder, the pharmacist mistakenly used baclofen powder; therefore, the omeprazole suspension was compounded with baclofen powder, which resulted in a medication error and patient hospitalization.

The calculated dose of baclofen the patient received (480 mg) was approximately 160 times the dose recommended (3-6 mg) for spasticity in a 4-month-old. Baclofen toxicity explained the constellation of signs and symptoms that occurred in the patient, including flaccid paralysis, seizure, respiratory changes, minimally reactive pupils, metabolic acidosis, and slow-wave electroencephalography findings.² The timeline of acute presentation and recovery with supportive care was also consistent with oral baclofen toxicity

and pharmacokinetics, although pediatric infant cases have not been described to date.

DISCUSSION

Multiple reports of baclofen toxicity have been published; however, this is the first case report of baclofen toxicity related to a drug shortage. The increase in drug shortages is more than an inconvenience to patient care. There are a multitude of reports of near misses, errors, and adverse outcomes associated with drug shortages.¹ Most of the reports were related to shortages of sedatives, paralytics, chemotherapies, opioids, and antibiotics.

In the ISMP 2010 survey, there was 1 report of a shortage of ondansetron that led to the use of a new vial that looked like vials of hydralazine. This led to administration of the wrong drug to patients.² This example is similar to our case report, where the shortage of sodium bicarbonate injection required the use of an alternative dosage form, which contributed to a medication error.

In 2011, the ISMP asked hospital pharmacy staff if the drug shortage problem in the United States resulted in harmful outcomes for hospitalized patients.¹ The responses fell into 4 categories: 1) provision of an alternative medication that was not the drug of choice, and which led to inadequate treatment (35%); 2) an error with an alternative drug or form/strength of a drug used as a substitution for the drug in short supply (27%); 3) an omission of vital medication leading to non-treatment of the patient (27%); and 4) an error when a hospital pharmacy attempted to compound a product or drug strength no longer available (6%). Our case is an example of the forth category. Although it is the least common reason

for adverse outcomes related to drug shortages, these types of errors often result in the most severe outcomes, including death.

Ours may be the first case of an error resulting from an extemporaneously prepared compound for enteral use caused by a drug shortage. Our patient presented with symptoms warranting admission to a PICU. Fortunately the infant recovered from a baclofen overdose related to a drug shortage and pharmacy error. It is imperative to change the current system to decrease drug shortages, and therefore improve patient safety.

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Abbreviations G-tube, gastrostomy tube; ISMP, Institute for Safe Medication Practices; PICU, pediatric intensive care unit.

Correspondence Bonnie Lau, MD, PhD, 1800 Orleans Street, Room 11379, Baltimore MD 21287; email: blau1998@gmail.com

REFERENCES

1. Institute for Safe Medication Practices. ISMP survey on drug shortages. *ISMP Medication Safety Alert!* [newsletter] April 19, 2012.
2. Caron E, Morgan R, Wheless JW. An unusual cause of flaccid paralysis and coma: baclofen overdose. *J Child Neurol.* 2014; 29(4):555-559.
3. Institute for Safe Medication Practices. ISMP survey on drug shortages. *ISMP Medication Safety Alert!* [newsletter] 2010;15(15):4.