

Therapeutic error: Carboprost Tromethamine Given to a Newborn Intramuscularly

R Robinson, M Mujumdar, J Griffith, M Casavant, S Baker

Citation

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Abstract

Carboprost tromethamine is given intramuscularly (IM) to postpartum women for control of uterine bleeding. We are describing a case of apnea due to accidental administration of this drug to a newborn. In the delivery room, he accidentally received carboprost tromethamine IM instead of hepatitis B vaccine. Within four hours the child was intubated. Intermittent ventilation continued for approximately 26 hours. Blood pressure and heart rate remained stable over this time period. Delaying routine newborn medication therapy until infants are in the newborn nursery may reduce medication errors in the delivery room. Carboprost tromethamine can cause life-threatening adverse events.

INTRODUCTION

Adverse drug reactions (ADRs) are unintended events related to medication therapy that may occur with prophylaxis, diagnosis, and/or therapy. Medical errors including ADRs are the eighth leading cause of morbidity and mortality in the United States.¹ The true incidence is controversial, but one out of five injuries or deaths per year to hospitalized patients may be as a result of ADRs.² Epidemiological studies indicate that they may occur in 6.7 percent of hospitalized patients.³ As compared to a control group of hospitalized patients who did not experience an ADR, hospitalized patients who did had a two-fold greater mean length of stay and incurred double the expense.⁴ The cost to society has been estimated to be \$ 136 billion annually.⁵

Postpartum hemorrhage (PPH) is a potentially life-threatening blood loss during either vaginal (>500 mL) or cesarean (>1,000 mL) deliveries. Carboprost tromethamine (Hemabate®) is a synthetic prostaglandin analogue (15-methyl prostaglandin F₂-alpha tromethamine salt) given intramuscularly for the treatment of PPH unresponsive to

conventional management methods [e.g., intravenous oxytocin, uterine massage, intramuscular ergot preparations] during both vaginal and cesarean delivery.⁶ Carboprost tromethamine given intramuscularly, stimulates gravid myometrial contractions similar to those experienced during labor to evacuate post-conception materials from the uterus. Post partum, the resultant contractions provide hemostasis at the site of placentation.⁶

CASE REPORT

A 2.7 kilogram, 37-week gestation male was born to a 35-year old, gravida-two, para-one female via repeat cesarean section. Cesarean section was uncomplicated and the preterm infant did well post-partum. APGAR scores were eight at one minute and nine at five minutes. In the delivery room the infant received 125 mcg carboprost / 41.5 mcg tromethamine intramuscularly instead of hepatitis B vaccine. Approximately 12 minutes post injection, the infant became acrocyanotic, discoloration starting in the lower extremities and working upwards. He was initially given blow-by oxygen until the infant developed apneic spells, requiring bag and mask ventilation. Within 4 ½ hours the infant became hyperthermic (101°F - axillary), hypotonic and required intubation. Initial ABG was pH 7.26, pCO₂ 57.2, pO₂ 25.4, and a base deficit of -2.7. Though the normal pH for newborns reaches 7.37 at 24 hours, shortly after birth 7.26 - 7.29 is the normal range for arterial blood gas pH.⁷ CBC showed a white count of 32.9, hemoglobin 16.3, hematocrit 49.3, platelets 164, neutrophils 52 percent, lymphocytes 40 percent, and monocytes six percent. Blood cultures were drawn and the patient was started on intravenous ampicillin and gentamicin for possible sepsis and was subsequently transferred to a pediatric facility.

The infant continued to have brief apneic episodes over the following 24 hours and required approximately 26 hours of

intermittent ventilatory support. Blood pressure and heart rate remained stable throughout admission. An echocardiogram post-exposure showed a widely dilated patent ductus arteriosus that closed on its own by 36-hours and very mild tricuspid and mitral valve incompetence. Metabolic acidosis continued to worsen with a final base deficit of -11.6 which resolved by 84 hours. The infant remained quiet but responsive. No sedation was required.

DISCUSSION

Carboprost tromethamine is a prostaglandin similar to prostaglandin F₂-alpha dinoprost, except for the addition of a methyl group at the C-15 position resulting in its longer duration of activity. It is indicated only when other medicines more commonly used to treat PPH (e.g., oxytocin and ergometrine) are ineffective at stopping the bleeding. Carboprost tromethamine mimics the action of naturally-occurring prostaglandins in the body, causing contraction of the muscles of the uterus to stop postpartum uterine bleeding.

Carboprost tromethamine also stimulates the smooth muscle of the gastrointestinal tract commonly producing vomiting, diarrhea or both. Elevated blood pressure is also a side effect and is felt to be due to vascular smooth muscle stimulation. Some patients experience transient bronchoconstriction. A number of patients also experience fever as carboprost tromethamine is known to elevate body temperature. Adverse effects associated with the standard treatment of PPH in the mother include gastrointestinal effects, moderate increases in blood pressure, flushing, fever and headache. In our patient, the usual adverse effects seen in the treatment of PPH due to either vaginal or cesarean delivery were not observed.

Three cases of accidental neonatal carboprost tromethamine intramuscular injection have been reported previously.⁸ Two infants who received the standard dose (125 mcg carboprost / 41.5 mcg trimethamine) remained asymptomatic 24 hours after intramuscular exposure. One infant who received twice the standard dose experienced bronchospasms, tachypnea, dystonia, seizure, hyperthermia, and diarrhea; all signs that resolved within 18 hours. Our patient experienced significant respiratory compromise and bronchospasm at the standard carboprost tromethamine dose to treat PPH. The respiratory

compromise may be related to the prostaglandin activity described above or the may be due in part to the preservatives in the preparation. Carboprost tromethamine does contain benzyl alcohol, which has been associated with "gasping syndrome" in premature infants. After inadvertent injection of carboprost tromethamine, to an infant, we advise that the child receive close observation and aggressive supportive care, including mechanical ventilation as needed. In any event, four cases of accidental infant administration of a medication used to treat PPH within a maternity ward warrants concern. If routine neonatal medications were administered only outside of the birthing unit, all four episodes could have been avoided and potential pulmonary, cardiovascular and neurologic risks to the infants avoided.

CORRESPONDENCE TO

Dr. Jill R.K. Griffith
Central Ohio Poison Center
Columbus Children's Hospital
700 Children's Drive
Columbus, Ohio 43210
(614) 722-2636
(fax) (614) 221-2672
griffitj@chi.osu.edu

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Author Information

Renee D. Robinson, Pharm.D., MPH

Assistant Professor, Department of Pediatrics, The Ohio State University College of Medicine and Public Health and Children's Hospital

Mamta A. Mujumdar, B.S

Research Assistant, The Ohio State University College of Medicine and Public Health and Children's Hospital

Jill R.K. Griffith, B.S. Pharm.D.

Central Ohio Poison Center, Columbus Children's Hospital

Marcel J. Casavant, M.D.

Medical Director, Central Ohio Poison Center, The Ohio State University College of Medicine and Public Health and Children's Hospital

Stephen D. Baker, Pharm.D.

Director, Central Ohio Poison Center, Columbus Children's Hospital