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Toxic Ingestion of Acetaminophen and Acetylsalicylic Acid in a Parturient at 33 Weeks Gestation: A Case Report

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Abstract

The anesthetic management of toxic ingestion during pregnancy requires concomitant concerns for both mother and fetus. We describe the management of a parturient at 33 weeks of gestation after a suicide attempt by ingestion of acetaminophen (APAP) and acetylsalicylic acid (ASA). Timing of toxin ingestion must be determined, prompt antidote administration prioritized, and hepatotoxicity-induced hematologic impairment anticipated. Fetal exposure to toxins must also be minimized. The use of point-of-care rotational thromboelastometry in conjunction with standard coagulation testing in such cases facilitates consideration of neuraxial anesthesia and determination of risk for postpartum hemorrhage.

We report the presentation and delivery of a parturient who ingested toxic levels of APAP and ASA in a suicide attempt. Written consent to use and existing protected health information was obtained.

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DISCLOSURES

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CASE DESCRIPTION

The patient was a 28-year-old primigravida at 33 weeks of gestation with a medical history of pseudotumor cerebri and type 2 diabetes mellitus. She presented at an outside institution reporting ingestion of APAP 50 g and ASA 5 g within the hour. The patient received 2 doses of activated charcoal 1 hour after the reported time of toxin ingestion. The APAP level at 4 hours was 26 µg/mL. Although this is well below toxic levels on nomogram, *N*-acetylcysteine (NAC) was administered for fetal protective effects. A loading dose of 140 mg/kg of intravenous (IV) NAC was administered, followed by an infusion of 50 mg/kg over 4 hours, then 100 mg/kg over 16 hours. The salicylate concentration at 4 hours was 0.7 mg/dL, a nontoxic level.

The patient was transferred to our labor and delivery unit 14 hours after toxin ingestion. On arrival, the patient was alert, oriented, and in no acute distress. Vital signs included a blood pressure of 125/71 mm Hg, heart rate of 117 beats per minute, and respiratory rate of 25 breaths per minute. The baseline fetal heart rate was 180–200 beats per minute, and there were no uterine contractions. Admission laboratory studies included a platelet count of 301 K/µL, INR of 1.2, and normal liver function tests. A point-of-care coagulation test, rotational thromboelastometry (ROTEM), was performed to evaluate global hemostasis. ROTEM EXTEM clotting time was mildly prolonged at 73 seconds (normal range in pregnancy, 31–63 seconds), but all other ROTEM parameters were within the normal range.

Approximately 24 hours after toxin ingestion, the patient reported new-onset muffled hearing. A salicylate concentration drawn at this time had increased to 14.3 mg/dL, and the anion gap had increased from 13 to 20 mmol/L with a bicarbonate level of 15 mmol/L. Maternal venous blood gases were drawn based on symptoms and were significant for a mixed respiratory alkalosis and metabolic acidosis with a pH of 7.42. Fetal tachycardia (>160 beats per minute) persisted. Toxicology was consulted for concern of greater fetal than maternal toxicity from ASA overdose. It was only then discovered that the patient had taken ASA that was enteric coated, leading to a delayed peak ASA level. Shortly thereafter, repetitive fetal heart rate decelerations prompted urgent cesarean delivery.

Based on reassuring ROTEM and standard coagulation tests 3 hours prior, a single-shot spinal was performed, and the patient underwent cesarean delivery without complication. Apgar scores were 5 at 1 minute and 8 at 5 minutes. Venous and arterial umbilical cord blood gases were pH, 7.15/Pco₂, 45/Po₂, 11/HCO₃, 15.7 and pH, 7.11/Pco₂, 49/Po₂, 13/HCO₃, 15.6, respectively, reflecting fetal acidosis. The maternal postpartum period was unremarkable. All maternal laboratory studies normalized within 48 hours of delivery.

The newborn was transferred to the neonatal intensive care unit (NICU) for management of prematurity and toxin exposure. Respiratory distress developed 4 hours after birth, requiring endotracheal intubation for 6 hours. Three hours after birth, arterial blood gas analysis revealed metabolic acidosis (pH, 7.33/Pco₂, 40/Po₂, 22.3/HCO₃, 21.1), which normalized by 10 hours of life. Neonatal salicylate level was 12.6 mg/dL 24 hours after birth, while maternal salicylate level drawn 6 hours prior was 5.4 mg/dL. Neonatal liver function testing revealed a mild transaminitis on day 1 of life with normalization by day 3 of life. The

neonate was discharged from the NICU 3 weeks after birth. The neonate's NICU requirement was largely for sequelae of prematurity and not residual toxic effects from APAP or ASA exposure.

DISCUSSION

While previous case reports have detailed outcomes after APAP or ASA overdose in pregnancy, there are no reports to our knowledge that describe anesthetic management after overdose of combined toxic ingestion of APAP and ASA during pregnancy or the safety of neuraxial anesthesia in this situation.

APAP toxicity presents most commonly with nausea, vomiting, and abdominal pain, followed by potential progression to elevated hepatic transaminases, encephalopathy, coagulopathy, jaundice, and death from liver failure within 4–7 days.¹ The Rumack–Matthew nomogram evaluates the timing of serum APAP concentration after ingestion to help predict hepatotoxicity risk.² The antidote for APAP toxicity is NAC, which prevents the formation of hepatotoxic APAP metabolites. NAC protocols vary, including 20- and 48-hour IV regimens and 72-hour oral regimens. A typical 20-hour IV regimen consists of an initial 150 mg/kg bolus dose followed by a maintenance dosing of 50 mg/kg given over 4 hours, then 100 mg/kg over 16 hours.³ Early administration of NAC in APAP toxicity in pregnancy may be warranted, as APAP can cross the placenta and result in an accumulation of fetal toxic metabolites.⁴ There are limited data about fetal evaluation in the context of maternal APAP overdose. Two reports of APAP overdose describe fetal heart rate decelerations in utero without neonatal compromise after delivery.^{5,6} However, APAP overdose with fulminant maternal hepatic failure and liver transplant after daily ingestion of 6 g of APAP for 2 weeks resulted in fetal demise.⁷ Premature neonates may be affected to a greater extent.⁸

ASA toxicity can present with a wide range of symptoms, including tachycardia, tinnitus, vomiting, and seizures. Bleeding occurs because of irreversible inhibition of COX-1 and COX-2 enzymes with platelet dysfunction despite a normal platelet count.¹ Hemodialysis in severe cases of salicylate poisoning decreases mortality.⁹ Thresholds for hemodialysis initiation are primarily clinical. Because treatment takes time and involves the administration of high volumes of bicarbonate solutions to alkalinize the urine, indications for hemodialysis focus on a rapid correction of severe symptoms or response to fluid overload. Indications for hemodialysis, therefore, include pulmonary edema (either noncardiogenic or from congestive heart failure), fever, seizure, increasing ASA concentrations despite apparently adequate therapy, hypoxemia, or salicylate concentrations >100 mg/dL.¹⁰ ASA freely crosses the placenta, and elimination is slow due to immature fetal renal function. The preferential distribution of ASA into the fetal brain is due to pH differences across the fetal blood–brain barrier and can exacerbate the risk for intracranial hemorrhage.^{11,12} For these physiologic reasons, fetal effects of maternal ASA toxicity can also be extremely detrimental, with reports ranging from nonreassuring fetal heart rate tracing requiring emergency cesarean delivery to fetal demise.^{13–15}

The patient's salicylate and APAP concentrations measured shortly after ingestion suggest that she may have consumed a lower dose of toxins than reported. Although the patient's only apparent symptom of acute ASA overdose was a change in hearing, the fetal effects of these ingestions appeared to be much more significant, with fetal tachycardia and decelerations on fetal heart monitoring. The residual effects of ASA on the neonate after delivery were significant and included metabolic acidosis and salicylate concentrations that exceeded maternal salicylate levels. This may have implications for cases of chronic high-dose ASA ingestion in addition to large-volume acute ingestions. Fetal effects of maternal APAP overdose appeared milder in comparison to effects from ASA overdose and may be related to subtoxic ingested levels of APAP or early administration of NAC to reduce toxic metabolite formation.³

Consideration of toxicity-related coagulopathy is paramount before performing a neuraxial anesthetic. In this case, we evaluated for APAP-mediated hepatotoxicity and impaired liver synthetic function. This patient's toxicity nomogram, stable physical presentation, and normal liver function testing were reassuring. We also considered the risk of impaired platelet function from ASA toxicity, which can occur despite a normal platelet number. ROTEM testing revealed a normal maximum clot formation, suggestive of retained platelet function and normal global coagulation. However, ROTEM for this purpose must be interpreted with caution. Therapeutic (subtoxic) doses of APAP and ASA have not been found to impart any detectable alterations in ROTEM parameters.^{16–18} While the threshold for ROTEM to detect coagulopathy from APAP or ASA toxicity in pregnancy has not been demonstrated, the absence of gross coagulopathy on ROTEM in this case was clinically reassuring.

In summary, prompt management of APAP and ASA toxic ingestion with antidote therapy (charcoal and NAC) may have enhanced maternal and newborn outcomes. A delivery plan for the parturient after toxic ingestion should be defined and reevaluated as the course of toxicity evolves, with the understanding that worsening maternal morbidity imparts a higher risk to the fetus as well. Furthermore, ion trapping and immature metabolism may impart higher vulnerability of the fetus to toxic metabolite accumulation, especially with excess ASA ingestion. Vigilance for higher risk of bleeding from a neuraxial anesthetic technique or from delivery is important when toxins ingested can impact hemostasis. Spinal anesthesia was an option for this patient due to reassuring maternal status, subtoxic serum drug levels, absence of significant transaminitis, and reassuring global coagulation on ROTEM testing. The evolution of maternal and newborn status in such circumstances must be dynamically monitored at every decision point.

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