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Case Report

Acute convulsions following sublingual misoprostol administration for postpartum hemorrhage: a report of two cases

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ABSTRACT

Misoprostol is widely used for the prevention and treatment of postpartum hemorrhage (PPH) because of its efficacy, affordability, and ease of administration. However, the sublingual route is associated with rapid absorption and higher peak plasma concentrations, which may increase the risk of systemic adverse effects. We report two cases of primigravida women who developed acute altered mental status, hallucinations, and generalized tonic-clonic seizures following administration of 800 µg sublingual misoprostol after vaginal delivery. Extensive evaluation excluded common obstetric and neurological causes of postpartum seizures. Both patients recovered completely with supportive management and anticonvulsant therapy. These cases highlight the possibility of severe neurotoxicity associated with high-dose sublingual misoprostol and emphasize the need for cautious use and careful monitoring in the postpartum period.

Keywords: Misoprostol, Postpartum hemorrhage, Seizures, Sublingual route, Neurotoxicity

INTRODUCTION

Misoprostol, a synthetic prostaglandin E1 analogue, is widely used in obstetrics for cervical ripening, induction of labor, and prevention and treatment of postpartum hemorrhage (PPH) because of its proven efficacy, low cost, and stability at room temperature.¹

Among the available routes of administration, the sublingual route offers rapid absorption, higher bioavailability, and higher peak plasma concentrations, making it particularly effective in the management of PPH.²

However, this pharmacokinetic advantage is also associated with a higher incidence of dose-related adverse effects such as shivering, fever, nausea, vomiting, and diarrhea.^{1,3} Rare but serious complications including hyperthermia, altered mental status, seizures, and

rhabdomyolysis have been reported, particularly with high doses (≥ 800 µg) administered via the sublingual route.^{4,6}

These neurological manifestations can closely mimic obstetric emergencies such as eclampsia, sepsis, amniotic fluid embolism, or cerebral venous thrombosis, often leading to extensive investigations and diagnostic uncertainty in the immediate postpartum period.⁷ We report two cases of primigravida women who developed acute altered sensorium, hallucinations, and generalized tonic-clonic seizures shortly after receiving 800 µg sublingual misoprostol following vaginal delivery, in whom other possible etiologies were excluded, suggesting misoprostol-induced acute neurotoxicity.

CASE REPORTS

Case 1

A primigravida at 39 weeks of gestation with deranged liver function tests was admitted for induction of labor.

The intrapartum course remained uneventful. Vacuum-assisted vaginal delivery was performed at full cervical dilatation and station +4, resulting in the birth of a 3.8-kg female neonate.

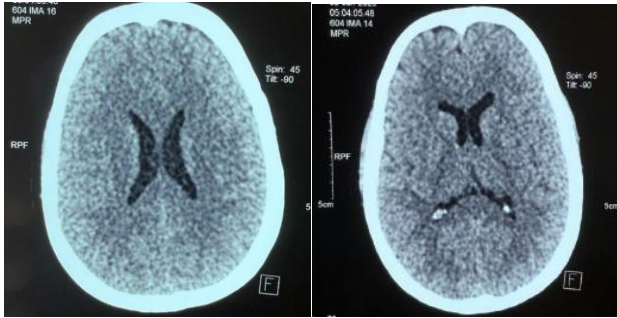


Figure 1: Normal NCCT head findings of case 1.

Following delivery, the patient received 800 µg sublingual misoprostol along with intravenous tranexamic acid. She subsequently developed massive postpartum hemorrhage, which was managed with carboprost (three doses), methylergometrine (three doses), and intrauterine balloon tamponade, after which hemostasis was achieved.

Approximately three hours postpartum, clinical examination revealed a soft abdomen, well-contracted uterus, and minimal vaginal bleeding. However, the patient developed acute disorientation and visual hallucinations. Her vital parameters showed blood pressure of 112/74 mmHg, pulse rate of 170/min, and oxygen saturation of 94%. Laboratory investigations revealed hemoglobin of 6.8 g/dl and total leukocyte count of 16,000/mm³. Two units of packed red blood cells were transfused.

Subsequently, the patient developed generalized tonic-clonic seizures. She was treated with a magnesium sulfate loading dose and intravenous levetiracetam 750 mg. Non-contrast CT scan of the brain was normal. With supportive management, the patient gradually improved and achieved complete neurological recovery.

Case 2

A primigravida with an IVF-conceived pregnancy at 40 weeks of gestation had an uneventful antenatal course. Labor was induced at term. Vacuum-assisted vaginal delivery was performed at full cervical dilatation and station +3, resulting in the birth of a 3.2-kg male neonate.

For prophylaxis against postpartum hemorrhage, 800 µg sublingual misoprostol and intravenous tranexamic acid were administered. Approximately two hours postpartum, uterine tone was adequate and vaginal bleeding was within normal limits. However, the patient developed acute altered sensorium and hallucinations. Vital signs revealed blood pressure of 112/74 mmHg, pulse rate of 160/min, and oxygen saturation of 90%.

Laboratory investigations showed hemoglobin of 10.8 g/dl, total leukocyte count of 30,000/mm³, and elevated D-dimer levels (1882 ng/ml). Differential diagnoses including septic encephalopathy, amniotic fluid embolism, and cerebral venous thrombosis were considered. The patient was started on broad-spectrum antibiotics, aggressive intravenous hydration, and intravenous dexamethasone.

Non-contrast CT scan of the brain and CT pulmonary angiography were normal. Shortly after imaging, the patient developed generalized tonic-clonic seizures, which were treated with magnesium sulfate loading dose and intravenous levetiracetam 750 mg. MRI brain with MR venography was subsequently performed and revealed no abnormalities. The patient recovered completely within 48 hours without any residual neurological deficits.

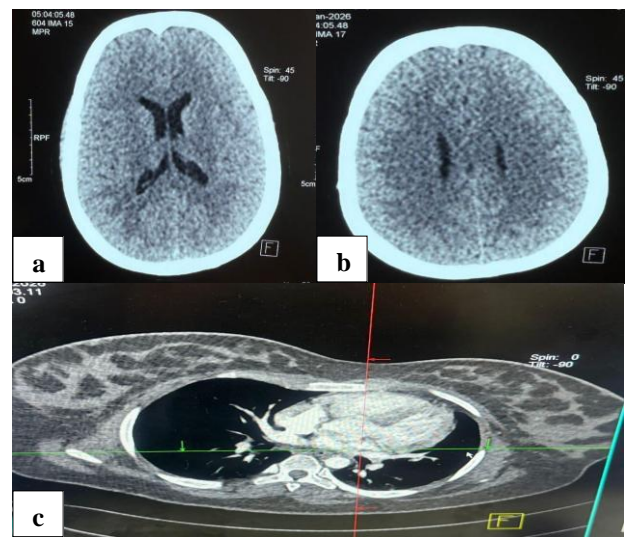


Figure 2: (a and b) Normal NCCT head findings, and (c) normal CTPA findings of case 2.

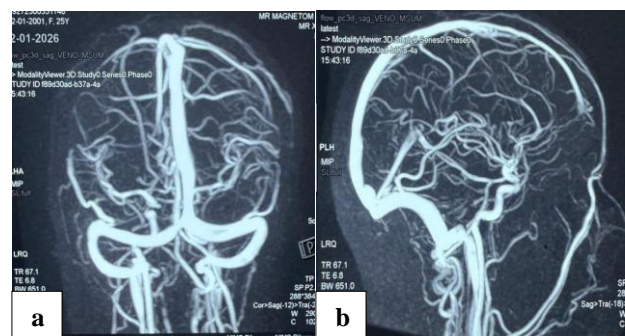


Figure 3 (a and b): Normal MR venogram findings of case 2.

DISCUSSION

In both cases, neurological symptoms developed within a few hours after administration of 800 µg sublingual misoprostol, suggesting a strong temporal association. Sublingual misoprostol is known to produce rapid

systemic absorption and significantly higher peak plasma concentrations compared with oral or vaginal administration, which may contribute to dose-related systemic and neurological adverse effects.^{2,8}

Prostaglandin E1 analogues may influence central thermoregulation and neuronal excitability, potentially leading to hyperthermia, altered mental status, seizures, and rhabdomyolysis.^{4,5} Similar cases of severe hyperthermia and seizures following high-dose sublingual misoprostol administration for postpartum hemorrhage have been described in the literature.^{6,7}

In the present cases, alternative causes of postpartum seizures such as eclampsia, intracranial hemorrhage, cerebral venous thrombosis, amniotic fluid embolism, and sepsis were systematically excluded through clinical assessment, laboratory investigations, and neuroimaging. The absence of hypertension, proteinuria, focal neurological deficits, and normal neuroimaging findings further supported a drug-related etiology.

Additionally, both patients demonstrated rapid and complete neurological recovery with supportive treatment and anticonvulsant therapy, which is consistent with previously reported cases of misoprostol-induced neurotoxicity. Such reactions are typically self-limiting once circulating drug levels decline.^{6,8}

Recognition of this rare adverse effect is important for obstetricians, as it may mimic life-threatening postpartum complications and lead to unnecessary investigations or delays in appropriate management.

CONCLUSION

Misoprostol remains an effective and widely used uterotonic agent for the prevention and treatment of postpartum hemorrhage. However, high-dose sublingual administration may rarely lead to severe neurological adverse effects, including altered mental status and seizures. Increased awareness among obstetricians and vigilant postpartum monitoring are essential for early

recognition and timely management of this uncommon but potentially serious complication.

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Ethical approval: Not required

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