

# Misoprostol-induced seizures following self-abortion: a rare, but repeated occurrence

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## Abstract

Misoprostol is a synthetic prostaglandin E1 (PGE) analogue used for medical termination of pregnancy, managing miscarriage, inducing labour, cervical ripening, and treating postpartum haemorrhage. Generally, it is safe and well-tolerated, with dose-dependent adverse effects such as nausea, vomiting, diarrhoea, abdominal pain, fever, and headache that usually resolve within a few days. However, seizures are a rare complication, occurring primarily in patients with a history of epilepsy or a predisposition to seizures and is associated with high doses and rapid administration. This case report highlights the repercussions of a misoprostol overdose used for pregnancy termination, leading to seizures induced by hyperthermia. The first patient required temporary invasive ventilation and resuscitation but recovered, whereas the second patient receiving a lower dose, exhibited milder symptoms. Both patients received psychosocial counselling prior to discharge.

*Keywords:* early pregnancy, misoprostol, pregnancy termination, seizure

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## Introduction

There is an increasing trend of individuals turning to non-medical sources for abortifacients, which can lead to the misuse and abuse of medically approved drugs such as misoprostol. Despite being illegal in Malaysia, the widespread availability and affordability of the drug have contributed to its misuse, resulting in severe complications and morbidity in some cases. This report presents two cases of patients who presented with seizures after allegedly self-administering excessive amounts of misoprostol orally and vaginally. Treatment of such cases involves stabilising the patient's condition, monitoring vital signs, and addressing any complications that may arise.

## Case presentation

### Case 1

A 32-year-old lady, gravida 2 para 1 (with 1 set of twins), was brought to the emergency department by her husband with complaints of severe abdominal pain and behavioural changes after ingesting an unknown medication at midnight. The patient had no known medical illnesses; however, the husband claimed that she had postpartum depression following her first pregnancy, which required admission for 4 days. Subsequently, she was discharged home with psychoeducation and counselling. Upon further history, the husband revealed that the patient had self-administered misoprostol orally and vaginally, with a total dosage of 1400 mcg.

In the emergency room, the patient was delirious, agitated, and aggressive, prompting the emergency response team to initiate a red alert. The initial impression was meningoen­cephalitis, as the patient had a high-grade fever with a temperature of 42.5°C and exhibited bizarre behaviour. Clinically, she was tachycardic, with a heart rate of 140 beats per minute (bpm); tachypnoeic, with a respiratory rate of 30–40 breaths per minute; and hypotensive, with blood pressure (BP) of 80/40 mmHg. She was pale with minimal vaginal bleeding and premature uterine contractions. There were no other features of anaphylaxis. The patient suddenly developed unusual seizure symptoms, including spasmodic incurving of fingers resembling carpedal spasms of the hand in hypocalcaemia, lip-smacking phenomena, and blank staring eyes. This occurred approximately 6 times, with no regaining of postictal consciousness in between.

A decision was made to intubate her, with a rapid sequence intubation using intravenous (IV) fentanyl 100 mcg, IV midazolam 5 mg, and IV succinylcholine 100 mg to prevent impending collapse and airway protection. Following intubation, she received a fluid bolus of 30 ml/kg of crystalloid and 10 ml/kg of colloid. Low-dose inotropes were started, parenteral antipyretics were administered, and tepid sponging was performed to reduce fever. An urgent bedside ultrasound performed by the obstetric team revealed an estimated gestational age of 16 weeks with no foetal heartbeat present and no free fluid observed. At this point, the differential diagnosis included meningoencephalitis, septic shock due to septic abortion with disseminated features, electrolyte imbalance, anaphylactic shock, and possible misoprostol-induced seizure.

Blood tests showed mild hypomagnesaemia. Cultures from blood and vaginal swabs were negative and the brain CT scan was normal. She received a loading dose of IV phenytoin 1 g over 1 hour and was transferred to the ICU for monitoring and ventilatory support. She had no further convulsions and was extubated the same day. The medically induced delivery of the non-viable foetus was uneventful. She was given IV ceftriaxone for 3 days, followed by IV ampicillin-sulbactam for a week. Based on the evidence, the final diagnosis was misoprostol-induced convulsions. The patient completed her antibiotic regimen and was referred to the psychiatric team for assessment. She received non-pharmacological treatments such as relaxation therapy and behavioural therapy, along with coping therapy. She was administered intramuscular etonogestrel 68 mg as contraception and was discharged after a week of observation in the ward.

## Case 2

A previously healthy 15-year-old mother with an unintended and undesired pregnancy, in her second trimester was brought to casualty with a generalised tonic-clonic seizure after a self-induced abortion attempt by self-administering 3 oral doses and 2 vaginal doses of misoprostol with a total dosage of 1000 mg.

The patient's vital signs were BP 110/80 mmHg, heart rate of 125 bpm and a high-grade fever of 40°C. Otherwise, she was saturating well and not tachypnoeic, with a respiratory rate of 18 breaths per minute. The seizure she experienced was of modest intensity and lasted for 3 minutes. It exhibited a similar semiology to that of our initial patient but was successfully aborted with a single dose of IV diazepam 5 mg. Her vitals and presentation were less severe than those of the first patient, likely due to a lower cumulative dosage of misoprostol. However, the drugs were taken all at once, which led to hyperthermia and seizures.

Her vital signs improved within 4 hours, and she was closely monitored using a fit chart, remaining seizure-free. The induced infant weighed about 200 g, which was not viable. She stayed physically well for the next 24 hours under observation. Like the first patient, her septic workup, CT brain, and serum electrolytes were normal, leading to a diagnosis of misoprostol-induced seizure. Despite symptoms like acute kidney injury and mild transaminitis, she recovered quickly, managed her grief, and was discharged. She was referred for counselling on adolescent pregnancy and psychoeducation was provided to both her and her partner. Contraception was also offered, and the patient was reviewed in the nearest health clinic for further follow up.

## Discussion

Misoprostol is a synthetic PGE analogue that is converted into the active metabolite misoprostol acid after desulfation, and it replaces protective prostaglandins consumed during therapies that inhibit prostaglandin synthesis. It inhibits gastric acid secretion and protects the gastric mucosa. Initially used to treat peptic ulcers induced by non-steroidal anti-inflammatories, it has become widely used in obstetric practice for medical termination of pregnancy in the first and second trimesters, management of missed abortion, medical management of incomplete abortion, and treatment of postpartum haemorrhage due to its uterotonic and cervical ripening effects.<sup>1</sup>

The World Health Organization recommends a dose of 800 mcg via buccal, vaginal, or sublingual route for patients less than 13 weeks of gestation, while patients with gestational age greater than 13 weeks are recommended to take 400 mcg every 3 hours until abortion occurs, up to 5 doses in 24 hours. The toxic dose in humans has not yet been determined, but studies have shown that the maximum cumulative dose tolerated is 1600 mcg.<sup>2</sup> Though both of our patients took less than the maximum tolerated dose, they experienced severe adverse effects, likely due to the drugs being taken excessively at once. Misoprostol can cause side effects such as fever, chills, nausea, vomiting, and diarrhoea. Uncommon side effects include delirium and confusion. In this case report, our first patient presented with compensated shock likely due to hypotension caused by peripheral vasodilatation as a result of circulating prostaglandin, leading to compensatory tachycardia that was further exacerbated by high-grade fever. Patients are typically not very responsive to fluid therapy, and early initiation of vasopressors is recommended to meet the transiently increased metabolic demand state.

Hyperpyrexia in both of these patients was likely due to PGE<sub>2</sub>, which is a primary mediator of fever induction by binding to PGE receptors and shifting hypothalamic set points upwards, triggering temperature elevation.<sup>3</sup> Durocher *et al.* found that 35.6% of patients who received misoprostol for post-partum haemorrhage developed a fever of  $\geq 40.0^{\circ}\text{C}$ .<sup>3</sup> Our patients' temperatures on arrival ranged from 40–42°C, consistent with these findings. Regular antipyretics and aggressive cooling therapy are essential. Few studies examine prostaglandin E analogues' seizure pathophysiology, but one study on mice reveals Misoprostol lowers seizure threshold.<sup>4</sup>

It is crucial not to overlook other potential causes of recurrent seizures and status epilepticus. Epilepsy can be ruled out, given that this is a provoked, first-episode seizure with no previous history. A diagnosis of meningoencephalitis is supported by fever, altered mental state, and seizures; this condition is also characterised by neck rigidity, photophobia, and indications of elevated intracranial pressure. Contrast-enhanced CT (CECT) of both patients' brains were normal, ruling out this possibility. Conversely, leptomeningeal enhancement would have been detected if meningoencephalitis were the probable diagnosis. Lumbar puncture was not performed because the patients and spouse had declined.

Septic shock secondary to septic abortion was also considered but ruled out due to the absence of specific signs such as foul-smelling vaginal discharge and growth of organisms from high vaginal, placental and foetal swab culture. Despite presenting with features of sepsis such as fever, tachycardia, and hypotension, further investigations did not support this diagnosis. Electrolyte imbalances such as hyponatremia, hypernatremia, hypocalcaemia, and hypomagnesemia can potentially cause seizures. Therefore, it is essential to rule out these imbalances before further evaluation.

A seizure is an abrupt and transient surge of electrical activity in the brain, while epilepsy is a neurological disorder marked by the occurrence of 2 or more unprovoked seizures. After the initial evaluation at the emergency department, a thorough medical and neurological examination is conducted, along with blood tests. It is crucial to position the head in a way that opens the airway. If there are problems with oxygenation or ventilation, intubation with rapid sequence induction should be performed. Supplemental oxygen therapy should be administered for those not requiring intubation. Seizure control can be achieved by administering benzodiazepines, such as lorazepam 2 mg or diazepam 5 mg, at 5-minute intervals.<sup>5</sup> If the seizure is reoccurring, it is recommended to administer a bolus of an anti-epileptic drug (AED) together with benzodiazepines. One option is to administer phenytoin at a dose of 15–20 mg/kg for 25–50 minutes.<sup>5</sup> In cases where phenytoin is contraindicated, IV levetiracetam of 40–60 mg/kg over 15 minutes is preferred.

Recovery times for both cases described in this report were within 4 to 6 hours, which is consistent with the results of a pharmacokinetic study conducted by Zieman *et al.*<sup>6</sup> Plasma concentration of misoprostol gradually increases after vaginal administration, reaching its maximum level after 70–80 minutes, before slowly declining after 6 hours.<sup>6</sup> Therefore, it is essential to provide aggressive and optimal resuscitative and supportive therapy in the early stages to prevent further morbidity and mortality, as this condition is easily reversible if well managed. The ultimate goal of treating these patients is to refer to a psychiatric team for assessment, psychoeducation, and psychotherapy to address their concerns and issues. Proper contraception advice should also be given until they are ready for conception.

## Conclusion

Despite its widespread off-label use in obstetrics and gynaecology, it is crucial to consider misoprostol's potential adverse effects, including rare events like hyperpyrexia and convulsions, as observed in our cases. Misuse of misoprostol for self-induced abortion can have severe consequences and should be strongly discouraged. Ensuring access to safe, legal abortion services, alongside education and awareness campaigns, can mitigate such incidents. Healthcare professionals must remain vigilant about medication misuse, educate patients on the risks, and ensure early recognition and optimal supportive care to reduce morbidity and mortality.

## Declarations

### Informed consent for publication

The patients provided informed consent for the use of the clinical data contained in this case report.

### Competing interests

None to declare.

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