

# A Tale of Two Hearts: Cardiac arrest post administration of misoprostol

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## Objectives

To report a case of cardiac arrest in the context of misoprostol administration and recent methamphetamine use.

## Summary of Patient Clinical Features

### Social History/ Demographics

- 39 year old Caucasian female
- Four children

### Previous Medical History

- Active substance abuse- routine methamphetamine use
- Nicotine dependence
- Previous alcohol abuse
- Anxiety and depression
- Previous terminations of pregnancy (TOP)

### Medication History

- Nil current prescription medications

## Case Description and Patient Progress

A 39-year-old Caucasian female presented 15 weeks pregnant to a local abortion clinic for surgical termination of pregnancy. In the hours following buccal administration of 800 micrograms of misoprostol she suffered ventricular fibrillation (VF) and a subsequent cardiac arrest. Following collapse, CPR was initiated by NSW paramedics and 4 shocks were delivered by an external manual defibrillator. The patient was intubated at the scene and further management was provided enroute to hospital. During transfer she received a further 4 shocks, 4mg IV adrenaline and 450mg IV amiodarone with no observable effect. On arrival to the local emergency department she suffered further episodes of VF and VF arrests.

Once stabilised, she was taken to the cardiac catheterisation lab (CCL) for investigation and management. Angiography revealed diffuse coronary artery vasospasm affecting all coronary arteries, and intracoronary glyceryl trinitrate was administered with good effect.

The patient was transferred to the Intensive Care unit for ongoing support and management. The patient remained in the Intensive Care Unit for several days and was then transferred to a general ward for further monitoring. Her 27 day admission was complicated by numerous clinical issues including:

- Sepsis
- Evacuation of uterus (termination process was not completed)
- Spinal infarct causing lower limb weakness
- Transient renal and hepatic dysfunction
- Mental health concerns and management of depression
- Management of illicit substance dependence

## Background

An Australian Public Assessment Report for misoprostol published in 2012 acknowledged an association with coronary artery vasospasm and other cardiac events.<sup>1</sup>

Through a preliminary literature search, at least 6 cases of coronary vasospasm have been reported post administration of misoprostol.<sup>2-6</sup> In 5 out of 6 of these cases, the women were above the age of 30 with misoprostol administration via different routes at varying doses. In all reported cases, onset of cardiac adverse events occurred within hours of misoprostol administration. Furthermore, an adverse drug reporting database from Europe revealed 143 reports of cardiac events following administration of misoprostol, accounting for 2% of the total reported adverse outcomes for misoprostol (4,700 of which were non-descript adverse events).<sup>7</sup>

In the setting of termination of pregnancy, misoprostol acts as a synthetic prostaglandin to induce uterine spasm. It is hypothesised that misoprostol induces coronary vasospasm through its action on E type prostanoid receptors, however the mechanism is not fully understood.<sup>2</sup>

## Clinical Considerations

### Risk factors for coronary vasospasm:

Coronary artery vasospasm is the transient narrowing of coronary arteries, inhibiting blood supply to the heart and often leading to myocardial infarction.<sup>8</sup> See figure 1.

The risk factors for cardiovascular disease are well known and researched, however, risk factors for coronary vasospasm specifically are not as well established. Recent research from 2017 concluded that smoking was the most significant factor contributing to vasospasm in patients without significant coronary narrowing.<sup>9</sup> The patient in the case presented did smoke.

Table 1- Risk factors for coronary vasospasm

Other risk factors for coronary Vasospasm <sup>8</sup>
• Chemotherapy medications (e.g. capecitabine)
• Migraine medications (e.g. sumatriptan)
• Being of Japanese decent
• Being a young female

With such indistinct precipitating factors, it presents as a challenge to screen or identify patients who may be a risk of coronary vasospasm.

Blood flow is constricted during an artery spasm

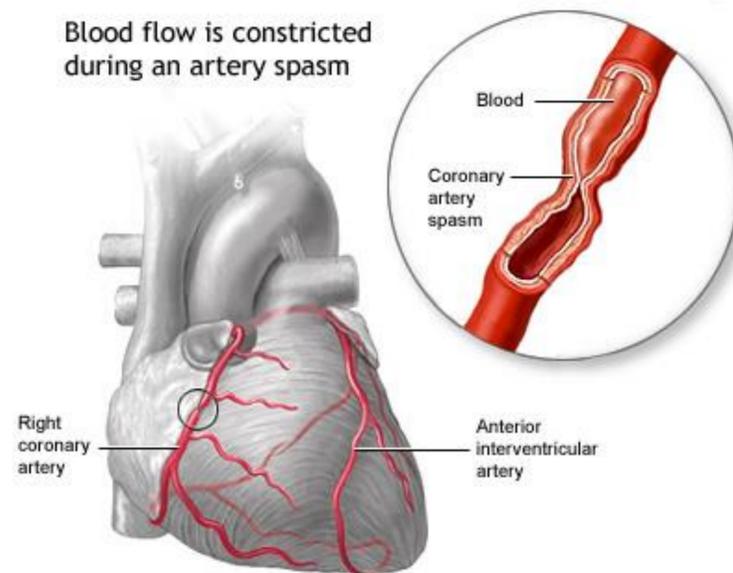


Figure 1- Picture of coronary artery vasospasm<sup>10</sup>

### Methamphetamine use:

A significant factor that must be taken into consideration for this case is the patient's recent and continuous use of intravenous methamphetamine. Methamphetamine use can contribute to poor cardiac outcomes in a number of ways. A study conducted in Finland found that cardiovascular adverse events were the fourth most common reason that intravenous drug users (IVDU) presented to hospital.<sup>11</sup>

Similar to misoprostol, the mechanism of methamphetamines causing vasospasm is not completely understood. It is proposed that induction of endogenous catecholamines causing upregulation of the sympathetic axis and impaired cellular metabolism may contribute. There is increased risk of this toxicity when methamphetamines are used in conjunction with other illicit substances such as cocaine.<sup>12</sup> However, it is unknown if methamphetamine use with misoprostol causes the same potentiating effects.

## Conclusion

This case presents a possible extremely rare side effect from a medication that is used every day. It is likely a number of factors contributed to this patient's coronary artery vasospasm, notably the recent use of both misoprostol and methamphetamine. Despite the uncertainty of the cause, cases similar to this need to be reported to governing bodies such as the Therapeutic Goods Administration. Such data and reports contribute to maintaining current and accurate information about medications which is integral to patient safety.

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