# A case of morphine toxicity in the setting of improper opioid rotation: A renewed call for prescriber vigilance

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### CASE

A man, aged 79 years, was brought in by ambulance to the emergency department (ED) after being found intermittently responsive by his spouse. This was on a background of a recent medication change of Jurnista® 20 mg (Janssen-Cilag Pty Ltd, Sydney, NSW, Australia; hydromorphone hydrochloride) once daily, which he was taking for chronic cancer pain, to MS Contin® (Mundipharma Pty Ltd, Sydney, NSW, Australia; morphine sulfate controlled release) 60 mg twice daily. This change was made by the patient's general practitioner (GP) because of the recent discontinuation of Jurnista® in Australia. It is a practice known as 'opioid rotation'.

### QUESTION 1

What is opioid rotation?

### QUESTION 2

How is opioid rotation performed?

### ANSWER 1

Opioid rotation (or switching) is a change in opioid drug or route of administration with the goal of improving outcomes.[1]

### ANSWER 2

Opioid rotation must be performed with consideration of individual patient characteristics, comorbidities and concurrent medications, using flexible dosing protocols that consider incomplete opioid cross-tolerance. Incomplete opioid cross-tolerance is the concept that the patient might have developed tolerance to one opioid without having developed full tolerance to another.[2] First, pick the new opioid based on their renal and hepatic function. Second, keep in mind any drug–drug interactions. Third, reduce the equivalent dose by 25–50%.[1]

### CASE CONTINUED

On examination in the ED, he had pinpoint pupils and was drowsy with evidence of an obstructive breathing pattern. He was intermittently desaturating and scoring 13–15 on the Glasgow Coma Scale (GCS). An electrocardiogram (ECG) showed a paced rhythm with no acute changes. Chest X-ray revealed no abnormalities. Venous blood gas detected an elevated potassium of 6.4 mmol/L but was otherwise normal. Routine bloods revealed an acute kidney injury (AKI) with a serum creatinine level of 339 μmol/L compared to the patient's baseline of approximately 159 μmol/L.

At this point, the following differential diagnoses were being considered: intracranial haemorrhage; opioid toxicity; electrolyte disturbance in the setting of multiple myeloma; and infection. Blood cultures were taken and the patient was started on empiric antibiotics (piperacillin/tazobactam) and intravenous (IV) fluids. Computed tomography of the brain showed that there was no acute intracranial haemorrhage.

The toxicology service was consulted and suggested an IV naloxone challenge of increasing doses targeting an improvement in respiratory effort rather than an improvement in GCS. The patient was then transferred to the intensive care unit (ICU) for ongoing monitoring of his IV naloxone infusion.

The patient's blood cultures returned positive for *Staphylococcus epidermidis* and antibiotic treatment with vancomycin was initiated. A subsequent toxicology review determined that although the patient received equianalgesic dosing, his MS Contin® was not renally adjusted.

### QUESTION 3

What opioids are safe to give to patients with renal impairment?

### ANSWER 3

Clinicians should always be vigilant when prescribing opioids to patients with renal impairment. The only opioids shown to have no clinically significant accumulation in older adults with chronic kidney disease are buprenorphine and fentanyl.[3] Hydromorphone is generally safe to use in renal impairment, but the lowest starting dose should always be prescribed as metabolites might accumulate.

### CASE CONTINUED

The patient progressed well on the naloxone infusion and was discharged from ICU to the ward. Palliative care input was sought for his ongoing pain management. The decision to cease MS Contin® and replace it with a fentanyl patch and hydromorphone prn was made, with follow-up at the chronic pain clinic arranged. Renal ultrasound revealed

no abnormalities, and it was determined that the patient's AKI was likely caused by dehydration. His serum creatinine level returned to baseline by the time of discharge. In the absence of any infective signs or symptoms, it was determined that the positive blood culture result was likely a contaminant. Antibiotics were ceased and weekly outpatient blood cultures were arranged for the three weeks following discharge. A retrospective review of the patient's SafeScript profile revealed that the patient had multiple red flag alerts on SafeScript, with the portal only having been accessed by dispensing pharmacists.

**QUESTION 4**

What is SafeScript?

**ANSWER 4**

SafeScript is a real-time prescription monitoring (RTPM) system. An RTPM is a clinical tool that provides access to a patient's prescription history for high-risk medicines to enable safer clinical decisions.[4] As of April 2020, it is mandatory (in the state of Victoria) to check SafeScript prior to writing or dispensing a prescription for a medicine monitored through the system. Red flag alerts pertain to multiple provider episodes, high-risk drug combinations and opioid dose threshold breach. RTPM systems are different in each state (Table 1). There are plans to implement a national RTPM system.

**Table 1. Real-time prescription monitoring (RTPM) systems and requirements by jurisdiction**

| State/Territory | RTPM name | Link |
|---|---|---|
| Australian Capital Territory (ACT) | Canberra Script | www.act.gov.au/health/providing-health-care-in-the-act/pharmaceutical-services/canberra-script/about-canberra-script#:~:text=The%20use%20of%20Canberra%20Script,patient%20information%20in%20Canberra%20Script |
| New South Wales (NSW) | SafeScript NSW | www.health.nsw.gov.au/pharmaceutical/safescript/practitioners/Pages/faqs.aspx#:~:text=Is%20the%20use%20of%20SafeScript,encouraged%20to%20use%20the%20system |
| Northern Territory (NT) | NTScript | https://health.nt.gov.au/professionals/medicines-and-poisons-control2/medical-practitioners-schedule-8-medicines |
| Queensland (Qld) | QScript | www.health.qld.gov.au/clinical-practice/guidelines-procedures/medicines/compliance-monitoring-enforcement/regulatory-approach |
| South Australia (SA) | ScriptCheckSA | www.sahealth.sa.gov.au/wps/wcm/connect/public+content/sa+health+internet/clinical+resources/clinical+programs+and+practice+guidelines/medicines+and+drugs/drugs+of+dependence/scriptchecksa+real+time+prescription+monitoring+in+south+australia/scriptchecksa+for+prescribers+and+pharmacists |
| Tasmania (Tas) | TasScript | www.health.tas.gov.au/health-topics/medicines-and-poisons-regulation/medicines-and-poisons-regulation-information-health-professionals/real-time-prescription-monitoring/tasscript-health-practitioners |
| Victoria (Vic) | SafeScript | www.health.vic.gov.au/safescript/safescript-for-prescribers-and-pharmacists |
| Western Australia (WA) | ScriptCheckWA | www.health.wa.gov.au/Articles/N_R/Prescription-monitoring-in-Western-Australia |

**CASE CONTINUED**

By day six, the patient had made a full recovery and was discharged, with follow-up arranged for ongoing chemotherapy, haematology outpatient clinic, chronic pain clinic and a GP appointment.

**QUESTION 5**

When should advice be sought for opioid rotation?

**ANSWER 5**

Clinicians who are not frequently undertaking opioid rotation, who feel uncomfortable with a particular situation or might be prescribing opioids that require enhanced knowledge (such as methadone and buprenorphine), should consider seeking advice.[1] Options include pain specialists, palliative care physicians or experienced GP colleagues.

## Key points

- Use a validated opioid dose conversion calculator to calculate the equianalgesic dose of the new opioid (we suggest the Australian and New Zealand College of Anaesthetists Faculty of Pain Medicine Opioid Calculator[5] or the eviQ Opioid Conversion Calculator[6]).
- Identify an automatic dose-reduction window of 25–50% lower than the calculated equianalgesic dose.
- Therapeutic Guidelines advises that morphine is not appropriate for patients with renal impairment; however, buprenorphine and fentanyl are okay.[7]
- Know the requirements for RTPM in your jurisdiction (Table 1).

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