

Oxycodone/naloxone: An unusual adverse drug reaction

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Case

A woman, 52 years of age, presented with a complex medical history, including chronic liver disease, transjugular intrahepatic portosystemic shunting, stage 1 oesophageal varices and depression. The relevant medications were slow-release and immediate-release oxycodone, and a selective serotonin reuptake inhibitor (SSRI), which she had been taking for more than one month.

On the day of presentation, the patient's regular oxycodone was switched to fixed-ratio combination oxycodone/naloxone, to limit her propensity to constipation and resultant hepatic encephalopathy. She remained on oxycodone as needed for breakthrough pain.

Within approximately one hour of a single dose of oxycodone/naloxone (20 mg/10 mg), the patient developed significant psychomotor agitation with rigors, myoclonic jerks, tachycardia, diaphoresis, malar flushing, hyperaesthesia, hyperosmia and frequent yawning. She remained lucid.

Question 1

What is the most likely diagnosis?

Question 2

How would you manage this patient?

Question 3

What are the differential diagnoses?

Question 4

What is the mechanism for this patient's presentation?

Answer 1

The most likely diagnosis was acute narcotic withdrawal, secondary to the naloxone component of the combination oxycodone/naloxone entering the systemic circulation and competing for the μ -opioid, κ -opioid and δ -opioid receptor sites in the central nervous system.¹

Answer 2

The fixed-ratio combination oxycodone/naloxone was ceased and the patient was given a stat dose of oxycodone and diazepam 5 mg. Her condition improved markedly after approximately 45 minutes.

The patient was closely monitored for any signs of further clinical deterioration, including encephalopathy. There has been no recurrence of her symptoms. The Naranjo score was 6, indicating a probable adverse drug reaction.² Additionally, it is most important to record such adverse drug reactions as an alert in the patient's medical record and inform the patient, family, general practitioner (GP) and community pharmacist.

Answer 3

Possible differential diagnoses considered for this acute episode included delirium, sepsis, serotonin

syndrome, acute decompensated liver failure or an acute psychiatric presentation.

Answer 4

Naloxone is well absorbed orally; however, it usually undergoes extensive first-pass hepatic metabolism (approximately 97–98%), resulting in low systemic bioavailability, but with antagonism of intestinal opioid receptors, thus reducing constipation when co-administered with an opioid such as oxycodone.³

However, as this patient had an iatrogenic portosystemic shunt, the oral naloxone was able to bypass the liver and directly bind with opioid receptors in the central nervous system, akin to parenteral dosing.

Fixed-ratio oxycodone/naloxone is a commonly prescribed analgesic drug combination because of its reduced side effect profile (eg constipation).⁴ However, caution must be exercised when prescribing combination oxycodone/naloxone in patients with portal hypertension and pathological dilatation of existing anastomoses between the portal and systemic venous systems (eg oesophageal varices), or iatrogenic portosystemic shunting.

Key points

- Fixed-ratio combination oxycodone/naloxone is a commonly prescribed analgesic.

- Caution must be exercised when prescribing oxycodone/naloxone in patients with portosystemic shunting.

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