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Cannabinoid hyperemesis syndrome

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Cannabis is an antiemetic - but paradoxically, chronic use can cause intermittent debilitating vomiting known as cannabis (or cannabinoid) hyperemesis syndrome (CHS). Since the legalization of cannabis in several states in the USA, hospital visits for persistent or cyclic vomiting have increased.^{1,2} With cannabis use in Canada increasing,³ pharmacists should be aware of CHS in order to help patients and other health care professionals avoid delay in diagnosis and effective treatment.

What is cannabinoid hyperemesis syndrome (CHS)?

Cannabinoid hyperemesis syndrome (CHS) is similar to cyclic vomiting syndrome. The association of CHS with chronic cannabis use was first reported in 2004, although the authors had noticed cases of hyperemesis with cannabis use for years.⁴ CHS typically occurs in younger patients who began using cannabis at an early age. It manifests after one to five years (though the range can be between four months to 27 years) of daily or at least weekly use.⁴⁻⁷ Between episodes patients with CHS may be relatively symptom-free or experience morning nausea and occasional vomiting, anorexia, and abdominal pain lasting for weeks to months. Then severe vomiting and retching begin suddenly.

Hot showers or baths provide temporary relief. A history of compulsive bathing or showering suggests the diagnosis of CHS. Vomiting may last hours to days (typically 48 hours) and then

stops.

Complications include acute dehydration, renal failure,⁸ erosive esophagitis,⁹ weight loss,⁶ and scalding from hot showers. Patients may also experience social distress, impaired job performance and absenteeism. CHS may go undiagnosed for years,⁶ resulting in repeated hospital and physician visits, fruitless investigations and ineffective treatment.

Pathophysiology

The pathophysiology is poorly understood and many chronic cannabis users do not develop it, although CHS is likely under-reported. CHS may result from an imbalance of the antiemetic effects of cannabinoids on the central nervous system and the pro-emetic effects on the digestive tract, cannabinoid receptor down-regulation, individual patient factors such as genetic polymorphisms, differing chemical composition of cannabis strains, or toxins and pesticides in cannabis from the growing and harvesting process.^{4-7,10}

Whether the causation of CHS relates to tetrahydrocannabinol (THC) or cannabidiol (CBD) is uncertain.^{9,11} Most published cases involve smoking natural cannabis,¹² but there are several cases of CHS caused by synthetic cannabinoids.^{13,14} Anecdotally, cannabis concentrates (e.g. dabs and shatter) may also cause CHS.

Treatment

Patients may need supportive care including rehydration to correct fluid and electrolyte imbalance, and analgesics with the caution that opioid analgesics may worsen nausea and vomiting. Almost all patients in published case reports report temporary relief with hot showers or baths,⁶ but this may not be practical.

There are no randomised controlled trials of pharmacologic treatments for vomiting in CHS. A recent systematic review found that in case reports and case series, antiemetics including diphenhydramine, phenothiazines, metoclopramide, and ondansetron are usually ineffective.¹⁵ However, there is limited evidence of benefit from intravenous benzodiazepines, intravenous haloperidol, and topical capsaicin. In case reports, a single intravenous dose of haloperidol 1 to 5 mg improved vomiting within one to two hours when other treatments have failed,^{16,17} and a controlled trial comparing intravenous haloperidol to ondansetron is underway.¹⁸ A single topical capsaicin application (usually 0.075%) to the abdomen, back or chest may provide relief;^{15,19} in one series relief was achieved within 45 minutes.²⁰ Lower strength capsaicin (0.025%) has also been reported.¹⁰

Abstaining from cannabis leads to sustained resolution of CHS in almost all patients, while

resuming regular cannabis use results in return of hyperemesis within weeks to months.⁶ Tricyclic antidepressants (TCAs) have been reported to reduce and possibly prevent symptoms in patients with cyclical vomiting who were also chronic cannabis users, but it is unclear whether this is a direct effect, or due to a reduction in cannabis use due to TCAs.¹⁵ Oral haloperidol (5 mg/d) for three weeks was reported to abolish CHS within one day but the long-term effectiveness is unknown.²¹

The pharmacist's role

The differential diagnoses of severe nausea and vomiting is long and patients may need to see their family doctor or even go to emergency for treatment of severe dehydration or prolonged vomiting.^{9,22} However, the diagnosis of CHS is likely for patients with repeated intermittent hyperemesis, a history of chronic cannabis use, and relief of their symptoms with hot baths or showers.⁹

The pharmacist should alert other health care professionals involved in the patient's care if they suspect CHS.

Treatment should include rehydration, warming, and reducing or stopping cannabis use.⁹ Haloperidol or topical capsaicin may be considered for acute treatment.

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