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ORIGINAL RESEARCH

Cannabinoid hyperemesis syndrome: A 6-year audit of adult presentations to an urban district hospital

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Abstract

Objective: To describe the local experience of adult patients presenting with cannabinoid hyperemesis syndrome (CHS) to an urban ED in the outer northern suburbs of Melbourne.

Methods: Retrospective chart review of adult patients presenting to the ED with a documented history of CHS or equivalent terminology from January 2015 to January 2021. Age, sex, cannabis use, clinical features, pathology results, imaging and symptomatic management were examined as well as outcomes regarding disposition, representation, morbidity and mortality.

Results: One hundred and forty-two adult presentations were included. Sixty-seven were unique presentations and 29 were patients who represented during the study period. Most represented within 3 months (37.8%) and most represented at least twice. Males were overrepresented (68.7%). Patients were young (median age 31 years, interquartile range 23–35 years) and all had a history of regular cannabis use (usually daily). Cyclical nausea and/or vomiting was the most common clinical feature compared to others in previously reported diagnostic criteria. Patients typically had elevated white cell counts with associated neutrophilia (75.8%) and mild hypokalaemia (57.9%). Lipase was not elevated, and C-reactive protein was typically less than 50 mmol/L (98.2%). Imaging was not commonly performed but largely normal. Treatment was supportive with antiemetic use, intravenous fluids and analgesia. There were no deaths or admissions to intensive care.

Conclusions: Cyclical nausea and vomiting was the most common feature observed in this cohort compared to other clinical features reported in prior studies. Serum lipase was normal and C-reactive protein only mildly elevated. Prospective studies are required to further assess these findings.

Key words: *cannabinoid, cannabis, case series, hyperemesis, vomiting.*

Key findings

- CHS should be considered in patients presenting with nausea and/or vomiting aged 50 years and under, with a history of daily cannabis use, a serum lipase within normal limits and CRP of less than or equal to 50 mmol/L. Reduction in symptoms following droperidol or haloperidol is also supportive.
- While diagnostic criteria exist, there are limitations to their utility for the bedside clinician in the ED. The CHUNDER mnemonic offers an alternative means to assist in patient assessment.
- While droperidol is favoured, future prospective studies are required to best evaluate safety and efficacy in CHS.

Introduction

Cannabinoid hyperemesis syndrome (CHS) is a condition characterised by cyclical nausea, vomiting and in some cases, abdominal pain in the setting of regular cannabis use.[1] While its aetiology is not known, disruption of the endocannabinoid system from long-term use of cannabis has been postulated.[2] Treatment is supportive with administration of anti-emetics, analgesics, and replacement of fluid and electrolyte deficiencies.[1] Individuals can present multiple times to the ED and they may undergo repetitive investigations if the condition is not recognised.[3] Both patients and clinicians may underappreciate cannabis as a trigger for the presenting complaint because of the common belief that cannabis is 'anti-emetic' together with well-established stigma towards individuals who use drugs of abuse biasing the history taken.[4] Recently, a

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systematic review was proposed new diagnostic criteria for CHS as an alternative to criteria previously reported by Simonetto *et al.*[1,5] This has not been externally validated and thus its utility, particularly to the clinician at the bedside in the ED, has not been established.

Cannabis is the most commonly used drug of abuse in Australia and with recent epidemiological data showing increasing use in the community, it is possible that presentations of CHS may increase.[6] The prevalence in Australia is not known; however, authors in the USA have estimated that 2.75 million Americans may suffer from CHS.[7] ED clinicians should be aware of CHS as early recognition can direct patients to assistance with stopping cannabis use, which is the only known cure.[1] There is a paucity of reports regarding the Australian experience of CHS other than the original description of the condition.[8]

We sought to describe our local experience of CHS with respect to demographics, clinical features, investigation results, management and outcomes regarding disposition.

Methods

A retrospective chart review was undertaken of adult patients (defined as 16 years or older) presenting to the Northern Hospital ED with an ICD-10 diagnosis of vomiting (R11) or drug-cannabis use (F12). A free-text search of the cases identified using keywords including 'nausea', 'vomiting' (or equivalent terms such as emesis or hyperemesis), 'cannabis' (or equivalent terms such as cannabinoid, marijuana or THC) was undertaken to identify potentially eligible cases between 1 January 2015 and 1 January 2021. The Northern Hospital is an urban district centre and has a mixed adult and paediatric ED, which sees over 103 000 patients every year. The ED sees a culturally diverse population from three of Melbourne's fastest growing growth areas. A local audit of presentations in 2019 demonstrated that ~11% of presentations to the ED pertaining to mental health and/or substance abuse. Electronic and scanned clinical documentation was examined for both the original presentation and any relevant representations during the study period. Patients were included if they reported or had a documented history of cannabis use, had presented with nausea and/or vomiting and alternative diagnoses had been excluded. Four investigators (ER, HRS, OGF, and SS) reviewed patient records to determine eligibility and where there was uncertainty or lack of consensus, a clinical toxicologist (JAR) determined eligibility. Presentations with insufficient clinical data for analysis were excluded.

The investigators designed a standardised data collection tool to extract relevant clinical and demographic data including but not limited to the patient's age, sex, cannabis use history (amount, frequency, form used), presence of cyclical nausea and/or vomiting in addition to previously described diagnostic criteria proposed by both Simonetto *et al.* and Sorensen *et al.*[1,5] Data from pathology results, imaging, management provided, hospital length of stay (LOS), disposition, representation rate, morbidity and mortality were also extracted. Management was defined as administration of any medication, administration of intravenous (IV) fluids and any other invasive procedure.

Data were extracted from medical notes, nursing notes, medication administration charts, and flow sheets by four investigators (ER, HRS, OGF and SS). Doses of antiemetics given to treat CHS were recorded. Absence of any relevant data in the clinical record was assumed to be absent. Final data were checked and collated by the lead investigator (JAR) and analysed as either numerical or ordinal variables using Microsoft Excel™. Ethics approval was provided by the Northern Health Human Research Ethics Committee.

Results

One hundred and eighty-four presentations met inclusion criteria; however, only 142 presentations had sufficient clinical data for analysis. Of these, there were 67 individual patients who presented and of those, 29 presented more than once. The median number of representations was 2 (interquartile range [IQR] 2–3). Of note, one individual presented 24 times. Most represented within 3 months (38.0%, $n = 54$), 28.2% ($n = 40$) within 1 month and 12.0% ($n = 17$) represented within the week. Five patients presented after reporting having stopped cannabis. Two presented after 2 days of not using and one after 2 weeks. A further two patients denied cannabis use in ED but later confirmed ongoing use during their admission. No cases where cessation of symptoms after stopping cannabis were reported.

Patient and cannabis use demographics are summarised in Table 1. Males were more prevalent (68.7% *vs* 34.4%) and were young at first presentation (median age 31, IQR 23–35). The youngest patient was 17 years of age and the oldest 51 years. Most had a diagnosis of CHS (92.5%) or on assessing the clinical data were consistent with the diagnosis but had not been specifically documented. All patients had a history of cannabis use that was typically daily (92.5%). Twenty-three patients reported a median daily cannabis dose of 2 g. Just over 40% (40.2%) of patients used other drugs of abuse.

Cyclical nausea and/or vomiting was the most common feature (97.2%) followed by epigastric pain (28.9%) and abdominal pain described as cyclical (24.6%) (Table 2). Normal bowel habit was common (98.5%). Relief from hot showers/bathing was seldom report (11.2%). Umbilical pain and weight loss were not commonly documented. Morning predominance of symptoms was not reported.

Most patients had pathology investigations undertaken and findings are summarised in Table 3. Most patients had elevated white cell counts (WCC) with associated neutrophilia, with 75.8% having a WCC of greater than 11.0×10^9/L and neutrophils greater than 8.0×10^9/L. The highest WCC and neutrophil count was 23.7 and 20.9, respectively, in one case. Hypokalaemia was relatively common

TABLE 1. *Individual patient demographics and presentation characteristics*

Characteristics	*n* (%), *n* = 67
Sex	
Male	46 (68.7)
Female	23 (34.3)
Age	
Age at first presentation (years), median (IQR)	31 (23–35)
Age (years), range	17–51
Diagnosis	
Documented history of CHS	62 (92.5)
CHS not documented as diagnosis but clinically consistent	5 (7.5)
Cannabis use	
Daily use reported	62/67 (92.5)
Cannabis documented without frequency	5/67 (7.5)
Quantity of cannabis used (g)	
Daily (*n* = 23), median (IQR)	2 (1–2.75)
Weekly (*n* = 14), median (IQR)	12.3 (7–21)
Other drug of abuse history	27 (40.2)

CHS, cannabinoid hyperemesis syndrome; IQR, interquartile range.

TABLE 2. *Clinical features attributed to cannabinoid hyperemesis syndrome and their prevalence*

Clinical features	*n* (%), *n* = 142
Cyclical nausea and/or vomiting	138 (97.2)
Cyclical abdominal pain	35 (24.6)
Epigastric pain	41 (28.9)
Umbilical pain	7 (4.9)
Relief from hot showers	16 (11.2)
Normal bowel habit	140 (98.5)
Diarrhoea	1 (1.5)
Morning predominance of symptoms	0 (0)
Weight loss	
Weight loss documented, no amount stated	5 (3.5)
Weight loss less than 5 kg	1 (0.7)
Weight loss greater than 5 kg	3 (2.1)

(57.9%) but mild, with only 1.6% being less than 3.0 mmol/L. Serum magnesium, while not ordered frequently, was abnormal in one-fifth of patients (21.6%). Renal injury was mild and uncommon. C-reactive protein (CRP) was not markedly elevated and less than 50 mmol/L in 98.2% of cases. Lactate on venous blood gas analysis was raised in about half of the samples taken (47.1%) but 92.2% were less than 5.0 mmol/L. Lipase was within normal parameters.

Nineteen patients had an X-ray, of which three were abnormal – two showing faecal loading and one showing right lung basal atelectasis. Seven presentations underwent computed tomography (CT) imaging but only one was abnormal demonstrating a 'markedly distended stomach with fluid and gas suggesting gastroparesis or gastric outlet obstruction'. The same patient had several presentations prior and after this with repeated episodes of vomiting and no other cause found. Endoscopy was performed in five presentations and only one was abnormal showing gastritis.

Treatment was supportive and is summarised in Table 4. Patients often received more than one type of anti-emetic agent during their admission. Only 10 patients received droperidol on its own and 20 patients received ondansetron only. Ondansetron was used more often compared to droperidol (63.4% *vs* 38% of presentations). More than one dose of ondansetron was given compared to droperidol (60.4% *vs* 20.4%). Only one adverse event was documented with droperidol causing dystonia requiring benztropine. Other anti-emetics included metoclopramide, promethazine, prochlorperazine, pyridoxine and cyclizine. Furthermore, IV fluids, paracetamol and oral opioids were most commonly administered other than anti-emetics.

The median hospital LOS was 212 min (IQR 157.0–319.0). Disposition for most presentations was a Short-Stay type ward (78 presentations, 54.9%). Patients were discharged home from ED on 50 occasions (35.2%). Fourteen patients discharged against medical advice prior to reaching their intended disposition (9.9%). There were no admissions to intensive care and no deaths.

Discussion

While awareness is increasing, knowledge of CHS is still limited to case-based evidence. Our case series is the largest to date with respect to total presentations and supports the

TABLE 3. *Frequency of investigations and analysis of results obtained*

Investigation	*n* (%), *n* = 142	Median (IQR)
Haematology		
White cell count ($\times 10^9$/L)	132 (92.3)	14.1 (11.2–16.8)
Greater than 11.0	100 (75.8)	
Neutrophils ($\times 10^9$/L)	132 (92.3)	11.5 (8.4–13.8)
Greater than 8.0	100 (75.8)	
Biochemistry		
Potassium (mmol/L)	126 (88.7)	3.9 (3.6–4.2)
Less than 4.0	73 (57.9)	
Less than 3.0	2 (1.6)	
Urea (mmol/L)	131 (92.3)	4.7 (3.8–6.4)
Greater than 7.0	22 (16.8)	
Creatinine (μmol/L)	132 (93.0)	71 (62–81.5)
Greater than 110	7 (5.3)	
Magnesium (mmol/L)	37 (26.6)	0.82 (0.75–0.8)
Less than 0.70	8 (21.6)	
Lipase (mmol/L, normal <60)	95 (66.9)	23 (12.0–28.0)
Greater than 60	3 (3.2)	
Greater than 180	0 (0)	
CRP (mmol/L, normal <8)	109 (76.8)	3.15 (1.0–9.3)
Greater than 8	33 (30.3)	
Greater than 50	2 (1.8)	
Lactate (mmol/L)	51 (35.9)	1.95 (1.4–2.9)
Greater than 2.0	24 (47.1)	

observations of prior reports in some respects but diverges in others. Observations made from this cohort offer some further insights. Firstly, male sex was more common in this cohort as previously described in other case series.[1,5,9,10] Patients were young as previously observed but some individuals had an onset of symptoms prior to the age of 30, which is highlighted in both the Sorensen and Simonetto criteria.[1,5] CHS in paediatric and adolescent patients is an emerging phenomenon and prompts further thought regarding aetiology of the condition.[11] A combination of increasing use patterns and prevalence of high tetrahydrocannabinol (THC)-containing strains may contribute to onset at a younger age.[11] Polysubstance use may also be influential and in our cohort, 40% reported use of other drugs of abuse. While our findings support younger age as a risk factor, there is no support for using decade of cannabis use or symptom onset as part of diagnosis.

Cyclical nausea and/or vomiting and regular cannabis use were the most common clinical features among in our cohort. Similarly, when reported, daily use was the most common pattern of use. Diagnostic criteria pertaining to cannabis use patterns vary widely among previously proposed diagnostic criteria ranging from 'long term cannabis use' to 'daily cannabis use'.[1,5,12]

Many of the other 'major' features proposed by both Sorensen *et al.* and Simonetto *et al.* were not well-represented in our cohort. Relief from hot showers/bathing was only mentioned in a tenth of cases. This may be due to variance in documentation or impracticalities in obtaining detailed information from an unwell patient with severe vomiting. Interestingly, there were instances where only nursing documentation reported relief from hot showers adding to the possibility that clinical awareness varies among clinicians. Abatement of symptoms following cannabis cessation was not observed in our cohort. Practically, patients may not have had a period of abstinence making this feature less useful. A few patients presented with CHS symptoms up to 2 weeks after last reported use of cannabis. This may be due to the long half-life of THC and its metabolites. Delta-9-tetrahydrocannabinol (Δ9-THC) concentrations are still detectable in whole blood up to 7 days after last use of cannabis.[13]

Normal bowel habit was a common feature in our cohort although diarrhoea has been reported in prior case series.[5] Weight loss was reported in a small group of participants; however, there were insufficient data to determine whether this was secondary to dehydration from hyperemesis or loss of weight because of malnutrition.

Investigation results were detailed in this cohort, which is a novel aspect beyond prior literature where medical work-up is often globally reported as normal.[5,14] While some findings were expected such as raised WCC and neutrophils, hypokalemia and mild renal impairment, others suggest possible benefit. A CRP greater than 50 mmol/L and/or an abnormal lipase should prompt clinicians to consider alternative diagnoses. Similarly, hypomagnesaemia was noted in a fifth of those in whom it was measured. Assessment in a larger cohort is needed to better ascertain clinical significance but could be due to poor nutritional intake as seen in people with a history of chronic alcohol use.[15] Dietary intake and nutritional quality are poorly described among individuals who regularly use cannabis.

Imaging was not often utilised and may be due to consensus opinion that plain abdominal X-rays have limited clinical utility and CT imaging should be avoided in younger non-trauma patients. Utility of CT imaging is likely to vary from country to country as well as institution

TABLE 4. *Summary of management provided*

Treatment	*n* (%, *n* = 142)	Median (IQR)
Ondansetron	90 (63.4)	
Patients only given ondansetron	20 (14.1)	
Number of doses per presentation		1 (1–3)
More than one dose administered	54 (38.8)	
Greater than 8 mg given	26 (18.3)	
Adverse effects reported	0	
Droperidol	54 (38.0)	
Patients only given droperidol	10 (7.0)	
Number of doses per presentation		1 (1–1)
More than one dose administered	11 (20.4)	
Greater than 2.5 mg given	7 (4.9)	
Adverse effects reported	1 (dystonia)	
Metoclopramide	66 (46.4)	
Other	39 (27.5)	
Analgesics		
Paracetamol	35 (24.6)	
NSAIDs	16 (11.3)	
Oral opioids	29 (20.4)	
Intravenous opioids	14 (9.9)	
Intravenous fluids	93 (65.5)	

NSAIDs, non-steroidal anti-inflammatory drugs.

BOX 1. *The CHUNDER mnemonic for cannabinoid hyperemesis syndrome*

*C*yclical nausea and/or vomiting
*H*istory of regular (usually daily) cannabis use
*U*nder 50 years of age
*N*ormal lipase
*D*iagnosis of exclusion, i.e. other pathology excluded
*E*levation of CRP less than 50 mmol/L
*R*eduction in symptoms after droperidol (or haloperidol)

to institution potentially explaining this occurrence in our cohort.

Documentation of management was variable but typically consistent of an anti-emetic, analgesia and intravenous fluids. Topical capsaicin has been shown to be beneficial in CHS but it is not part of our hospital's formulary so was not examined.[16] A recent Australian study showed that droperidol reduced LOS and the overall amount of anti-emetics required in CHS patients.[17] Due to the nature of documentation and use of multiple anti-emetics concurrently, it was not possible to undertake meaningful statistical analysis of antiemetic effects in this cohort although it appeared that less droperidol was required to be given compared to ondansetron. Response to droperidol (or haloperidol) as previously reported may also guide clinicians in their determination as to whether CHS should be considered.[17,18] A prospective study is required to determine both the efficacy and safety of droperidol for CHS as well as comparing it to other agents shown to have efficacy in mitigating vomiting in CHS such as haloperidol and olanzapine.[18,19]

Our study has several strengths as well as the common limitations associated with retrospective studies. This was a large study of patients with CHS or presentations consistent with CHS. The initial search for presentations was broad and intended to capture as many presentations as possible. Data extracted were comprehensive and endeavoured to include clinical features including components of two diagnostic criteria together with pathology, imaging and endoscopy results, management and disposition outcomes. Our study has provided some new insights into the condition — namely that white cell count is often elevated (and can be >20 cells $\times$ 10^9), serum lipase is not elevated in these presentations, serum CRP is rarely elevated more than 50 mmol/L, hot showers did not appear to be pathognomonic as prior authors have stated, and abstinence for cannabis use for a few weeks is not sufficient to alleviate the condition suggesting a longer effect of cannabis on the gut and mechanisms pertaining to emesis.

Like other retrospective series, ours was subject to the same challenges from documentation quantity, quality and contribution from varying clinical awareness of a condition by treating clinicians. Investigations were not uniform among out cohort meaning strength of association is limited. Our cohort did not correlate well with either the Simonetto or Sorensen criteria. As it was assumed in our study that if a particular outcome was not documented, it was therefore absent, this may have affected reporting. A formal external validation sample for both or either set of criteria should comprise of at least 100 patients with CHS and 100 patients without CHS in order to be statically robust so this analysis was not undertaken with this cohort.[20]

Based on our findings, a simple, practical and mischievously Australian mnemonic (CHUNDER) is detailed in Box 1 to help ED clinicians increase or decrease the likelihood of CHS as a diagnosis based on our study. It is critical to emphasise that CHS is a diagnosis of exclusion.

The present study provides additional insights into CHS. While

diagnostic criteria exist, there are impracticalities that reduce their utility in a single presentation to the ED. The CHUNDER mnemonic is offered to increase or decrease clinical suspicion at the bedside and will be validated both in future retrospective and prospective studies as part of the CHESS (Cannabinoid Hyper-Emesis Syndrome Study) initiative. In addition, further prospective evaluation of droperidol and other agents will assist with rationalising therapeutic options for CHS.

Conclusions

Cannabinoid hyperemesis syndrome should be considered in patients under 50 years of age presenting to the ED with a history of regular cannabis use and presentations consisting of cyclical nausea and/or vomiting. Findings such as a normal lipase and CRP less than 50 mmol/L may increase the likelihood of CHS as a diagnosis, but ultimately it remains a diagnosis of exclusion. Treatment is supportive but further higher-quality studies are needed to better delineate diagnostic features and therapeutic options.

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Author contributions

All authors made a substantial contribution to the concept, design, data collection, data analysis and drafting of the article. All authors have revised the submitted article and have approved it for publication.

Competing interests

None declared.

Data availability statement

The data that support the findings of the present study are available on request from the corresponding author. The data are not publicly available because of privacy or ethical restrictions.

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