Cannabinoid hyperemesis: cyclical hyperemesis in association with chronic cannabis abuse

J H Allen, G M de Moore, R Heddle, J C Twartz

Background and aims: To explore the association between chronic cannabis abuse and a cyclical vomiting illness that presented in a series of cases in South Australia.

Methods: Nineteen patients were identified with chronic cannabis abuse and a cyclical vomiting illness. For legal and ethical reasons, all patients were counselled to cease all cannabis abuse. Follow up was provided with serial urine drug screen analysis and regular clinical consultation to chart the clinical course. Of the 19 patients, five refused consent and were lost to follow up and five were excluded on the basis of confounders. The remaining nine cases are presented here and compared with a published case of psychogenic vomiting.

Results: In all cases, including the published case, chronic cannabis abuse predated the onset of the cyclical vomiting illness. Cessation of cannabis abuse led to cessation of the cyclical vomiting illness in seven cases. Three cases, including the published case, did not abstain and continued to have recurrent episodes of vomiting. Three cases rechallenged themselves after a period of abstinence and suffered a return to illness. Two of these cases abstained again, and became and remain well. The third case did not and remains ill. A novel finding was that nine of the 10 patients, including the previously published case, displayed an abnormal washing behaviour during episodes of active illness.

Conclusions: We conclude that chronic cannabis abuse was the cause of the cyclical vomiting illness in all cases, including the previously described case of psychogenic vomiting.

METHODS

Nineteen patients were identified following an original clinical observation by Allen linking chronic cannabis abuse to a cyclical vomiting illness in several cases in South Australia in 2001. Patients were either referred by doctors (12 cases), self referred (two cases), or identified on the ward by the nursing staff (five cases) during acute admission for profuse vomiting. Of these 19 patients, five refused consent and were lost to follow up and 14 fully consented for publication and presentation. Each patient was allotted a letter of the alphabet to preserve anonymity. Patients were followed up with serial urine drug screens and regular clinical consultations to chart their clinical course.

Inpatients were observed with particular reference to autonomic changes in body temperature (measured tympanically), blood pressure, heart rate, fluid intake, skin flushing, and perspiration. However, patient anxiety, compounded by the severity of the hyperemesis, made formal autonomic testing impossible.

All reasonable efforts were made to exclude confounding causes for their cyclical vomiting given the resources at hand. As a result, five patients were excluded from the study for the following reasons:

- Polydrug use (patients O and C).
- Porphryia cutanea tarda (patient Z).
- Acute pancreatitis (patient B).
- Schizophrenia (patient T).

The remaining nine cases are presented in tables 1–4. They were compared with a case of psychogenic vomiting described in 1996 by de Moore and colleagues. In their article, de Moore and colleagues described in detail a man (Mr G), who had smoked marijuana as a teenager, developed a cyclical vomiting syndrome in his twenties, and was noted to have multiple showers on the ward. Marijuana was not proposed as a cause of his illness.

RESULTS

The results of the study are presented in tables 1–4. The findings were as follows:

(a) there was a delay of several years in the onset of the vomiting illness in all cases against a background of ongoing cannabis abuse. In all cases, chronic marijuana abuse predated the cyclical vomiting syndrome;

(b) cessation of cannabis abuse led to cessation of the cyclical vomiting illness in seven patients (X, Y, A, Q, J, K, and L);

(c) three patients (R, E, and G) did not abstain and continued to have episodes of vomiting;
three patients (X, Y, and K) rechallenged themselves after a period of abstinence and all suffered a return to illness and hospital admission. Two of these patients (X and Y) subsequently abstained again from cannabis and got better and remain well. Miss K, however, has not, and remains ill.

Collateral features included a prodromal illness in four cases (Y, A, L, and G) of episodic early morning nausea or vomiting on one or more days per week. This predated the cyclical hyperemesis by months or years. The cyclical hyperemesis occurred in all cases. The severity of illness was reflected by the frequency of hospital admissions and necessity for intravenous fluids.

A novel finding was a “compulsive bathing” or washing behaviour noted in nine of 10 patients (X, Y, A, Q, R, J, K, E, and G). These patients would have multiple hot showers or baths on the ward. This ritual became the patients primary preoccupation, with them often waking at night to perform it.

A number of cases had marked weight loss in the range of 5–10 kg during their illness (Y, X, A, R, K, E, and G), with marked weight gain of approximately 5 kg following 3–6 months of abstinence (Y, X, A, J, K). Neither anorexia nervosa nor bulimia was a noted feature of the disease process. None of the patients exhibited abnormal fear of weight gain or body image distortion.

Several patients displayed a dose related response to increased cannabis use (Y, Q, J, E, G) where cannabis was employed as either an anxiolytic or analgesic. Low grade pyrexia was noted after bathing in two cases (X and R), with marked thirst and polydipsia in five cases (Y, X, A, Q, and R). An occasional neutrophilia was noted in six cases (Y, X, A, R, K, and G). A positive cannabinoid urine drug screen was present in all cases (detected at levels $50 \mu l$). Significant oesophagitis was diagnosed in five of the cases (modified Table 1).
Savary-Miller criteria: Y (grade 4), A (grade 2), R (grade 2), K (grade 2), and G). Y was the only patient to have gastric emptying studies performed acutely, displaying severely delayed gastric emptying for solids and liquids. X and A had normal studies but these were performed between episodes of illness. There was a past medical history of severe hyperemesis gravidarum (requiring hospital admission and IV fluids) for both of the women in the study (X, K).

**DISCUSSION**

We found that vomiting may present in a prodromal form initially or may proceed directly to the hyperemetic stage. The phenomenon of compulsive bathing behaviour is discussed, as is a differential diagnosis, clinical management, and possible pathophysiological pathways.

**Prodromal illness**

Chronic cannabis abuse predated the onset of the prodromal illness. For some months or years, prior to the onset of cyclical hyperemesis, several patients (Y, A, L, and G) described the onset of early morning nausea and vomiting on one or more days a week. These patients reported nausea at the sight or smell of food and “fear of vomiting”. However, unlike patients with anorexia nervosa or bulimia, they maintained normal eating patterns. Appetite was normal. Weight loss was a common feature at this stage in the presentation. Compulsive bathing was minimal or absent.

**Hyperemetic presentation**

This component of the illness was relatively stereotyped. The patients would start to profusely vomit, often without warning. Nausea, sweating, colicky abdominal pain, and polydipsia often accompanied these events. Patients would take multiple hot baths or showers in an attempt to quell the hyperemesis. Most attempted to cope at home unless they exhausted their hot water supply or became debilitated by severe vomiting. At this point they would present to hospital for intravenous fluid replacement. Vomiting tended to be intractable and refractory to the spectrum of antiemetic medication. The bathing behaviour was often commented on by the ward staff and noted in the case notes. Body temperature, in two cases, charted immediately following the bathing behaviour.

**Compulsive bathing behaviour**

The compulsion to have multiple hot showers or baths was not part of a psychosis or obsessive-compulsive disorder. This was a learned behaviour which often did not present with the first few episodes of illness (as in L) but once established rapidly became a compulsion. The symptoms of nausea, vomiting, and abdominal pain would all settle within minutes in a hot bath or shower. Symptomatic relief was temperature dependent. The hotter the water, the better the effect. As the water cooled the symptoms returned. Two patients (X, Y) even scalded themselves in an attempt to have the water as hot as possible. These patients did not exhibit delusions or hallucinations which drove this behaviour, nor did they regard the showering as irrational and did not appear to resent it. Cessation of cannabis lead to cessation of the washing behaviour.

**Differential diagnosis**

Cyclical vomiting syndromes fall into two distinct categories: those with a physical basis and those of unknown aetiology. Hyperemesis gravidarum and some variants of porphyria are typical toxicities, with Addison’s disease and hypothyroidism. Recent research has focused on it being a variant of migraine headache or abdominal migraine. We see this disorder as a separate entity from both of these. It is a diagnosis of exclusion. The compulsion to have multiple hot showers or baths is not part of a psychosis or obsessive-compulsive disorder. This behaviour was a learned behaviour which seemed to be dependent on the patient’s physical state. It was not part of a psychosis or obsessive-compulsive disorder. This behaviour was a learned behaviour which seemed to be dependent on the patient’s physical state.

**Table 3: Clinical characteristics of the first five study subjects**

<table>
<thead>
<tr>
<th>Cannabis</th>
<th>Mr Y</th>
<th>Mr X</th>
<th>Mr A</th>
<th>Mr Q</th>
<th>Mr R</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haematology (10×9/l)</td>
<td>Hb: 161 g/l</td>
<td>Hb: 156 g/l</td>
<td>Hb: 165 g/l</td>
<td>Hb: 146 g/l</td>
<td>Hb: 153 g/l</td>
</tr>
<tr>
<td>WCC: 16.9</td>
<td>WCC: 11.5</td>
<td>WCC: 15.2</td>
<td>WCC: 14.0</td>
<td>WCC: 12.2</td>
<td></td>
</tr>
<tr>
<td>Neut: 15.2</td>
<td>Neut: 9.7</td>
<td>Neut: 13.0</td>
<td>Neut: 11.9</td>
<td>Neut: 10.6</td>
<td></td>
</tr>
<tr>
<td>Plat: 277</td>
<td>Plat: 261</td>
<td>Plat: 237</td>
<td>Plat: 239</td>
<td>Plat: 225</td>
<td></td>
</tr>
<tr>
<td>Amylase</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
<td></td>
</tr>
<tr>
<td>Hep/IV</td>
<td>Neg</td>
<td>Neg</td>
<td>Neg</td>
<td>Neg</td>
<td></td>
</tr>
<tr>
<td>HbCG</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
<td></td>
</tr>
<tr>
<td>C2H5OH</td>
<td>Neg</td>
<td>Neg</td>
<td>Neg</td>
<td>Neg</td>
<td></td>
</tr>
<tr>
<td>Urine drug screen (µg/l)</td>
<td>Cannabis only</td>
<td>Cannabis only</td>
<td>Cannabis only</td>
<td>Cannabis only</td>
<td></td>
</tr>
<tr>
<td>Endoscopy (modified Savary-Miller criteria)</td>
<td>Grade 4 erosions</td>
<td>Normal</td>
<td>Grade 2 erosions</td>
<td>Normal</td>
<td></td>
</tr>
<tr>
<td>Colonoscopy</td>
<td>Neg</td>
<td>Neg</td>
<td>Neg</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>Abdominal ultrasound</td>
<td>Neg</td>
<td>Neg</td>
<td>Neg</td>
<td>Neg</td>
<td></td>
</tr>
<tr>
<td>Barium studies</td>
<td>Neg</td>
<td>Neg</td>
<td>Neg</td>
<td>Neg</td>
<td></td>
</tr>
<tr>
<td>Gastric emptying study</td>
<td>Gravely delayed</td>
<td>Normal</td>
<td>Normal</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>Multiple other investigations</td>
<td>Neg</td>
<td>Neg</td>
<td>Neg</td>
<td>Neg</td>
<td></td>
</tr>
</tbody>
</table>

Hb, haemoglobin; WCC, white cell count; Neut, neutrophils; Plat, platelets; Sod, sodium; Hep/IV, hepatitis/human immunodeficiency virus; HbCG, beta human chorionic gonadotrophin (pregnancy test); C2H5OH, alcohol.
marijuana consumption at the time of illness in an attempt to avoid its well documented antiemetic properties.

Psychogenic vomiting, first described by Hill in 1968, as a separate entity to bulimia and anorexia nervosa, is a cyclical vomiting illness resurfacing in adult life from a tendency to vomit in childhood. Such patients commonly use illicit drugs or alcohol to control their illness. The uncanny resemblance of our cases to a documented case of psychogenic vomiting is remarkable. The triad of chronic cannabis, cyclical vomiting, and compulsive bathing is indicative of a new syndrome with cannabis toxicity as a cause.

**Clinical management**

Patients tended to fall into two categories: those that scorned the idea that cannabis was the cause of their vomiting and those that accepted the concept. The former group often refused consent to treatment and follow up. The latter group was well motivated, happy to be consented, and punctually attended appointments. All patients, for legal and ethical reasons, were counselled to cease all cannabis abuse. Benzodiazepines, used for a maximum of two weeks at the time of initial presentation, were offered to patients to avert a reaction to cannabis following several years of exposure. One logical explanation for this might lie with marijuana’s effect on the limbic system of the brain, particularly at the hippocampal-hypothalamic-pituitary level. Cannabinoids have a long half life. They are extremely lipophilic and bind to cerebral fat. Regular use is accumulative and this might give rise to toxicity in the sensitive patient. Cannabis is known to delay gastric emptying and, interestingly, one of our patients (Y) had a severely delayed gastric emptying study at acute presentation while two others (X, A) had normal studies when investigated between bouts of illness.

Patients exhibited odd behaviour: they repeatedly bathed in hot water to abate their illness; they vomited severely and uncontrollably; they lost and gained kilos of weight in the presence and absence of cannabis, respectively; and they displayed a spectrum of autonomic symptoms from sweating, flushing, thirst, and alteration in body temperature to colicky abdominal pain.

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**Pathophysiologically considerations**

Cannabis has traditionally been associated with an antiemetic action following acute ingestion. Here, however, we are presented with the paradoxical effect of hyperemesis in susceptible chronic cannabis smokers. Such a paradoxical response has only previously been demonstrated with acute toxicity to intravenous injection of crude marijuana extract.14 We suspect that susceptible individuals may develop a reaction to cannabis following several years of exposure. The reasons for this are obscure. We also have difficulty explaining why, while this disease takes years to develop, it resurfaces within weeks of cannabis resumption, even after considerable periods of abstinence.

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| Table 4 | Clinical characteristics of the remaining four study subjects and the case of psychogenic vomiting described in 1996 by de Moore and colleagues (Mr G*) |
|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|
| Cannabis          | Mr J              | Miss K            | Mr L              | Mr E              | Mr G*             |
| Haematology (10x9/1) | Hb: 143 g/l  | Hb: 144 g/l  | Hb: 169 g/l  | Hb: 156 g/l  | WCC: raised     |
|                   | WCC: 7.7          | WCC: 16.8         | WCC: 6.7          | WCC: 9.0          | Neut: raised     |
|                   | Neut: 3.9          | Neut: 14.4         | Neut: 3.2          | Neut: 5.1          |                 |
|                   | Plate: 234        | Plate: 280        | Plate: 233        | Plate: 288        |                 |
| Amylase           | Normal            | Normal            | Normal            | Normal            |                 |
| Hep/HIV           | Neg               | Neg               | Neg               | Neg               |                 |
| BCG               | Neg               | Neg               | Neg               | Neg               |                 |
| Ch2OH             | Nil               | Nil               | Nil               | Nil               |                 |
| Porphyria         | Neg               | Neg               | Neg               | Neg               |                 |
| Urine drug screen (µg/l) | Cannabis only | Cannabis only | Cannabis only | Cannabis only | Cannabis only |
| Endoscopy (modified Savary-Miller criteria) | Grade 2 erosions | Grade 2 erosions | Grade 2 erosions | Grade 2 erosions | Grade 2 erosions |
| Colonoscopy       | Neg               | Neg               | Neg               | Neg               |                 |
| Abdominal ultrasound | Neg               | Neg               | Neg               | Neg               |                 |
| Barium studies    | Neg               | Neg               | Neg               | Neg               |                 |
| Gastric emptying study | Neg               | Neg               | Neg               | Neg               |                 |
| Multiple other investigations | Neg               | Neg               | Neg               | Neg               | Neg               |

Hb, haemoglobin; WCC, white cell count; Neut, neutrophils; Plate, platelets; Sod, sodium; Hep/HIV, hepatitis/human immunodeficiency virus; BCG, beta human chorionic gonadotrophin (pregnancy test); Ch2OH, alcohol.
CONCLUSION
All 10 patients described in this paper were cyclical vomitters and chronic cannabis users. All long term sufferers (nine of 10) also exhibited an abnormal bathing behaviour during the acute phase of their illness. Symptoms resolved in seven patients with cannabis abstention, confirmed by urine drug screening. Three patients relapsed due to resumption of urinary drug screening. Two of these three abstained again and got better, while the third did not, and remains sick. These observations suggest a causative role for chronic cannabis abuse. Simultaneous induction of cyclical hyperemesis and compulsive bathing behaviour suggests a toxic response to one or more of the active ingredients of cannabis, presumably acting, at least in part, on the limbic system of the brain. Elucidation of the responsible pathways will require further research.

The compulsion to have multiple hot showers or baths exhibited by these chronic cases is not trivial. It is clinically important to both nurse and doctor as it “flags” these patients on the ward. Their ready identification should lead to a reduction in morbidity for the patient and cost to the health service. The consequences of this discovery bear further consideration. The paradoxical effect of its action must raise concerns about the long term tolerability of marijuana. Furthermore, it would also appear clinically prudent to exclude cannabis as an underlying cause in other cyclical illnesses, such as atypical abdominal and pelvic pain. Cannabis abstention, with urine drug screen monitoring, can be titrated against a clinical course. Finally, we feel that this disorder is an important differential diagnosis for unexplained vomiting, particularly in communities tolerant of cannabis. The diagnosis can be considered or discounted with the aid of an inexpensive consented drug screen.

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