

Cannabinoid Hyperemesis Syndrome

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### **Significance of the Problem**

Cannabinoid Hyperemesis Syndrome (CHS) is an unfamiliar clinical condition that has come to the forefront of diagnoses in the recent years. Problems have been associated with an increase in use of cannabis across the lifespan. In conjunction with this, medicinal marijuana use is on the rise as eighteen states have now legalized use of medical cannabis (Sun & Zimmerman, 2013). CHS can be characterized as intense hyperemesis in conjunction with frequent hot bathing associated with chronic cannabis use (Galli, Sawaya, & Friedenber, 2011). Generally, cannabis is known for its antiemetic properties, however in some cases over time paradoxical effects have been noticed with chronic usage. Also, paradoxical effects are thought to be associated with other additives mixed in with the cannabis. Typically, CHS has been diagnosed among a younger population in the twenty year old age range. However, with increasing use of cannabis, this syndrome may become more prevalent across the lifespan. In light of the increased use of cannabis around the United States, it is important that nurse practitioners are aware of this clinical condition to appropriately diagnose and treat patients affected. Thus, the purpose of this paper is to provide an overview of this new clinical syndrome in hopes to increase awareness among nurse practitioners, prevent miscellaneous testing, and provide appropriate evidence based treatment regimens.

### **Discussion of the Problem**

The issue at large is this confusing diagnosis that can often be overlooked and not treated properly leading to increased emergency room (ER) visits and diagnostic testing to rule out other potentially more life threatening illnesses. Often practitioners are misled by the initial presenting symptoms which can range from nausea, vomiting, abdominal pain, and signs of dehydration.

Without having knowledge of this syndrome, another path can be taken to attempt to identify a diagnosis. Frequently CHS is confused with cyclic vomiting syndrome, gastroparesis and small bowel dysmotility (Galli, Sawaya, & Friedenberg, 2011). Consequently, labs for a complete blood count (CBC), basic metabolic panel (BMP), hepatic panels (LFT's), and lipase levels are ordered to determine if there is another component that attributes to a potential diagnosis. Also, unnecessary abdominal x-rays, abdominal computerized tomography (CT) scans, esophagogastroduodenoscopy's, abdominal ultrasound, upper gastrointestinal work-ups, magnetic resonance cholangiopancreatography, and hepatobiliary iminodiacetic acid scans are ordered to rule out differential diagnoses. Therefore, increasing awareness of CHS is essential to eliminate accumulated ER visits and unnecessary costs associated with misdiagnosis and repeated abuse of cannabis as most individuals believe in the antiemetic properties of this drug thus contributing to the problem and cyclical pattern.

The effects of cannabinoid receptor activation on the gastrointestinal system include; altered intestinal motility, gastric acid secretion inhibition, relaxation of the lower esophageal sphincter, inflammation, and visceral pain (Galli, Sawaya, & Friedenberg, 2011). The activation of tetrahydrocannabinol (THC) in cannabis causes delayed gastric emptying and anti-emetic properties thus being counter intuitive preventing nausea and vomiting. Psychotropic effects are often the reason for abuse of this drug. The effects on the central nervous system include; short term memory loss, analgesia, stimulation of appetite and antiemetic properties (Galli, Sawaya, & Friedenberg, 2011).

Three phases of CHS have been proposed to help guide treatment modalities. The phases include; prodromal, hyperemetic, and recovery phase. In the prodromal phase the patient may experience abdominal discomfort, early morning nausea, and a fear of vomiting lasting possibly

months to years. The hyperemetic phase is characterized by intense nausea and vomiting, diffuse abdominal pain, weight loss, and dehydration with hemodynamic stability. During this phase is where patients learn the behavior of hot bathing to alleviate and control symptoms leading to a compulsive behavior. The compulsive hot bathing is thought to correct the imbalance of the hypothalamus thermoregulatory system induced by cannabis; however the mechanism of this learned act is not fully understood (Galli, Sawaya, & Friedenber, 2011). This phase is where most ER visits are noticed. The recovery phase can last days to months and is characterized by weight gain, normal bathing patterns, symptom cessation and return of wellness. Obtaining a thorough history plays a fundamental role in formulating any diagnosis and is not limited to CHS. Subsequently, asking appropriate questions can help the practitioner determine CHS. Key questions concerning long term cannabis use for more than one year, frequent or long hot showers/bathing, and improved symptoms with cannabis cessation all support diagnosis of CHS (Sun & Zimmerman, 2013).

Treatment methods for CHS can be complicated as normal antiemetic medications often do not work confounding the problem of intense nausea and vomiting. Also, opioids thought to improve abdominal pain can actually contribute to nausea and vomiting thus worsening abdominal pain associated with profuse retching. Treatment recommendations include the use of proton pump inhibitors to suppress acid production, intravenous fluid replacement (0.9% sodium chloride) of one to two liters for dehydration, and short term use of lorazepam for anticipated nausea and vomiting has been shown to help in some case reports (Sun & Zimmerman, 2013) (Galli, Sawaya, & Friedenber, 2011). Because of the limited research done on this syndrome, there is no real evidence based regimens to guide treatment. Accordingly suggestions for treatments are based off of case reports. Further research and clinical trials are needed for CHS

to determine best practice regimens. As a result of case reports reviewed, cannabis cessation appears to be the one true cure for this syndrome.

### **Literature Review**

An extensive literature review revealed several case series reports and literature reviews. No randomized control trials or systematic reviews were located. The first article reviewed was the original study performed in 2004 bringing attention to this new syndrome. This case series identified nineteen patients that had cyclical vomiting associated with chronic cannabinoid use through referrals from other physician practices, nurses on the ward and two volunteers. Out of the nineteen patients only ten were actually studied due to confounding variables and patient consent. Eight of the patients were male and two were female. All of the patients were assigned a letter to provide anonymity for the study results. The data studied included; cannabis use age of onset, cyclical vomiting onset, illness duration, cannabis dose, compulsive hot bathing, and hospital admissions (Allen, De Moore, Heddle, & Twartz, 2004). Once cannabis cessation took place, data was obtained looking at resolution of symptoms and any additional treatment modalities that took place during that time period. Of all of the ten participants, seven remained abstinent from cannabis use, while the other three relapsed thus causing symptoms of cyclical vomiting and excessive hot bathing to resume. The thought behind the relapse of symptoms is explained by the authors regarding the metabolism properties of cannabis. Cannabis is extremely lipophilic and has a long half-life of 24 to 48 hours thus increasing the likelihood of toxicity with repetitive use of cannabis (Allen, De Moore, Heddle, & Twartz, 2004). A limitation with this study was the small sample size potentially leading to a lack of reproducibility. This case series showed the need for further research in this topic area to provide evidence based treatment regimens.

Another article referred to the 2004 article and furthered the research in the United States using eight cases to characterize CHS. This case series report was a quantitative study that used a retrospective chart review with subsequent patient interviews to gather and analyze data (Soriano, Batke, & Cappell, 2009). The three investigators gathered the cases from a gastroenterology clinic and inpatient units at a hospital that fit the symptomology of CHS. Among the eight cases, five were male and three were female with a mean age range of thirty two years old. There was an average of seven ER visits, five clinic visits, and three hospital admissions between all eight cases studied (Soriano, Batke, & Cappell, 2009). Vomiting episodes occurred between two to three times an hour during the hyperemesis phase of CHS along with an average of five hot baths/showers a day. Antiemetic medications promethazine and ondansetron were given for nausea and vomiting without any reports of relief with either medication. Proton pump inhibitors were also given for abdominal pain without relief in seven of the eight patients. Seven of the eight patients all had normal laboratory values that included a CBC, BMP, LFT's, and lipase level. Diagnostic studies performed to rule out other diagnoses included; abdominal x-ray, abdominal CT, abdominal ultrasound, and six patients had an esophagogastroduodenoscopy. After the eight patients received counseling on cannabis cessation, only four actually ceased use of cannabis with one relapse. The other four continued repetitive use of cannabis thus had several relapses of CHS. The patient who reverted back to using cannabis redeveloped CHS. A limitation of this study is the small sample size utilized and the lack of a control group.

A case series of ninety eight patients was studied to reveal more information about CHS. Inclusion criteria in this study included; the lack of other major illnesses explaining CHS symptomology, long term cannabis use prior to appearance of symptoms, and a history of

cyclical vomiting (Simonetto, Oxentenko, Herman, & Szostek, 2012). A retrospective chart review was completed by two investigators between June 2005 and June 2010 to determine eligibility. From this search ninety eight patients met the inclusion criteria for this study. Results of the chart review revealed a mean age of thirty two years old, 67% of patients were male, and 33% female. The average use of cannabis before symptom onset was two to five years with the highest daily average of 59%. Characteristics of the patients studied revealed all participants had nausea and vomiting, 86% had abdominal pain that ranged from epigastric, periumbilical, diffuse and other, and 91% had relief with hot showers (Simonetto, Oxentenko, Herman, & Szostek, 2012). Other symptoms included diaphoresis, bloating, flushing and chills. Diagnostic studies performed ranged from laboratory tests including CBC, BMP, LFT's, pancreatic enzyme levels to more exclusive tests such as abdominal CT, upper endoscopy's, colonoscopy's, and gastric emptying studies. All diagnostic studies except the gastric emptying studies revealed insignificant results. The gastric emptying studies showed 48% of the patients had normal gastric emptying, 30% had delayed emptying, and 25% had rapid gastric emptying (Simonetto, Oxentenko, Herman, & Szostek, 2012). Follow up lacked among the ninety eight patients studied with only ten participants being available. Among the ten patients followed up, only six patients abstained from cannabis use with complete resolution of symptoms within one to three months. This study's end result identified essential diagnosis characteristics associated with CHS. The characteristic features include; severe cyclic nausea and vomiting, resolution of symptoms with cannabis cessation, symptom relief with hot showers/baths, abdominal pain, weekly use of cannabis, weight loss greater than five pounds, normal bowel habits, morning prevalence of symptoms, negative laboratory, radiographic and endoscopic test results followed by long term cannabis use (Simonetto, Oxentenko, Herman, & Szostek, 2012). Limitations of this study

include recall bias from the retrospective quality of this study and the lack of a control group. Also, this study was performed in a tertiary care center and may be difficult to replicate data if performed in another environment. This study however did have a much larger sample size to begin with, but needed better follow up.

### **Summary**

All of these case series reviewed bring forth awareness of this syndrome to the forefront for practitioners to include with differential diagnoses. Research on CHS is lacking especially with higher levels of research guiding evidence based practice for treatment of this syndrome. Therefore, CHS remains difficult to treat during the hyperemesis phase based on evidence. Throughout research reviewed the one consistent method of treatment is encouraging cessation of cannabis use among those individuals with suspected CHS. CHS remains a new diagnosis that many are unaware of and is commonly mistaken for other diagnoses.

With the ever growing cannabis use among individuals important considerations must be taken when treating vulnerable populations such as elderly individuals. As disease states rise in this population such as cancer, medicinal marijuana may be prescribed to these individuals to increase appetite and limit nausea episodes. Marijuana use is forecasted to increase among people fifty years and older from 1% to 2.9 % by the year 2020 (Colliver, Compton, Gfoerer, & Condon, 2006). The significance of this increase may result in adverse effects from cannabis abuse and may lead to CHS. Thus, CHS should not be overlooked in this population as it could have devastating effects if unnoticed. Dehydration is a major factor with cyclical vomiting episodes that occurs with the hyperemesis phase of CHS. Appropriate rehydration and possible hospitalization with this population specifically may need to take place. Age related changes can affect fluid shifts among the elderly increasing the likelihood of dehydration. Changes included



are a blunted thirst response that occurs with aging and a decrease in total body fluid (Mentes, 2006). Electrolyte abnormalities such as increased creatinine levels from baseline, hypokalemia, and hypomagnesaemia should not be ignored and treated promptly. As discussed previously, cannabis is highly lipophilic and elderly individuals have increase fat stores leading to an increase in volume of distribution for lipophilic drugs. Therefore, the metabolic pathway of cannabis would fall under the oxidation and hydroxylation phase I converting the drug to metabolites that may be harmful with accumulation (Katzung, Masters, & Trevor, 2012). Cannabis also has a long half-life of 24 to 48 hours contributing to potential harmful effects among the elderly.

### **Role of the Adult Gerontological-Acute Care Nurse Practitioner (AG-ACNP)**

The AG-ACNP has a critical role in diagnosing and managing a patient with CHS. The awareness of this syndrome encourages appropriate questions to be asked while obtaining a thorough history. The AG-ACNP can help promote understanding of this syndrome with other practitioners as well as educating patients diagnosed with CHS. In planning the treatment options, the AG-ACNP must use the principle of beneficence. This principle will assist with educating cessation of cannabis use and explaining this in a way that the patient understands. The AG-ACNP can also play a significant role with furthering the research on CHS to improve an evidence based approach with treatment regimens. Since CHS is relatively new, additional research is needed to foster best practices.

### **Conclusion**

Due to the lack of evidence on this subject matter, it is difficult to ascertain evidence based treatment regimens. Therefore the purpose of this paper was not fully attainable as the hierarchy of evidence was limited. The case series reported in the literature review were helpful

in sharing information regarding diagnosis of CHS, however little was noted about initial treatments during hyperemesis phase of this syndrome. CHS is an interesting phenomenon that warrants further research to facilitate best practices.

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