ORIGINAL ARTICLE

GMJ. 2012;1(1):29-34
www.gmj.ir

Received: 06 July 2012
Revised: 21 July 2012
Accepted: 01 August 2012

Clinical Characteristics of Pediatric Patients with Cyclic Vomiting Syndrome in Southern Iran

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Abstract

Introduction: Cyclic vomiting syndrome (CVS) is characterized by recurrent episodes of intense nausea and vomiting interpreted with symptom free period. As data regarding the pattern of disease in our region is scarce, we performed this study to investigate the pattern of pediatric cyclic vomiting in Shiraz, southern Iran. **Methods and Patients:** This study was performed in Nemazee Hospital, territory health care center affiliated with Shiraz University of Medical Sciences from 2000 to 2010. Medical files were reviewed and data was collected by means of a checklist. Patients were divided into two groups including 1-13 years of age as children and those 13-18 years of age as adolescents. **Results**: Overall, 43 patients with CVS were included, among whom there were 26 (60.5%) females. The mean age at first attack was found to be 6.2 (3.7) years. Ten patients (23.3%) had a family history of migraine among which there were 8 females. The most common clinical complaint was found to be abdominal pain in 32 (74.4%) patients. GI (gastrointestinal) disorders were more common in the adolescent group rather than the children group (*p=0.007*).The most common trigger factor was upper respiratory tract infection (URI) detected in 13 patients (30.2%).The most associated disorder was abdominal migraine in 5 (11.6%) patients. Anemia was more common in the adolescent group (*p=0.009*) than in the children's group .There were no radiological and laboratory abnormalities among these patients. The most commonly used medications were anti-migraines in 31 (72.0%) patients.**Conclusion:** as there is no definite drug for CVS, knowing the common trigger factors which culminate in CVS in each region can be of great importance and can prevent attacks in the prodromal phase. **[GMJ. 2012;1(1):29-34]**

Keywords: Cyclic Vomiting Syndrome (CVS) – Migraine Disease – Epidemiology – Iran

Introduction

Cyclic vomiting syndrome (CVS) is a rare syndrome characterized by recurrent episodes of intense nausea and vomiting interrupted by symptom-free periods (1). The disease was first described in 1882 by Gee S, (2) and it is estimated that 1.9-2.3% of the pediatric population is affected. (3), 4The patients usually experience 4-12 episodes of vomiting per year and each episode lasts for two hours to three days.(3, 5, 6) The disease is usually (39-81%) accompanied by migraine and is sometimes referred to as abdominal migraine. 7Several trigger factors have been introduced so far, including stress, anticipatory anxiety, infection, exercise, trauma, menstruation, and foods; (6, 8) however, the exact pathophysiology of the disease is yet to be identified.

Presentations of the disease as well as the trigger factors differ in various ethnic groups and geographical regions. For instance, several studies have shown that the most com-

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mon trigger factor in European societies is considered to be food allergy, (9) while in south Asian and Turkish populations, school stress (10) and migraine headache (4) are, respectively, the most common trigger factors. Haghighat M. et al (11) described the pattern and the clinical entity of CVS in Iranian patients; however, they did not evaluate the trigger factors nor the detailed demographic, clinical, and laboratory entities of the disease. Thus, this study was performed in order to evaluate these parameters in Iranian pediatric patients with CVS.

Materials and Methods

This was a retrospective cross-sectional study of pediatric patients with CVS admitted to Nemazee hospital (a tertiary healthcare center affiliated with Shiraz University of Medical Sciences) between August 2000 and August 2010. The approval of the institutional review board (IRB) and ethics committee of the university was obtained before the study.

CVS was diagnosed according to the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition consensus criteria: 1 all patients had at least 5 attacks in any interval, or a minimum of 3 attacks during a 6 month period; 2 episodic attacks of intense nausea and vomiting lasted 1 hour to10 days, occurring at least 1 week apart; 3 every patient had his or her stereotypical pattern and symptoms; 4 vomiting during attacks occurred at least 4 times for at least 1 hour; 5 all patients returned to the baseline health between the episodes; and 6 their symptoms were not attributed to another disorder. 12

The patients' records were used to obtain the data. Demographic data, past medical history, co-morbidities, family history, clinical presentation and findings, laboratory and paraclinical findings, and medications were all recorded in a checklist. A psychosocial history of the patient, family, and their related interactions were also obtained.

Patients 18 years of age and older and those and those whose medical files were incomplete were excluded from the study. The patients were divided into two groups; 1-13 and 13-18 year old patients were classified in children and adolescent groups, respectively. 13

Data were prospectively transferred into a computer database and further analyzed using SPSS for Windows; version 17.0 (SPSS Inc., Chicago, IL, USA). Independent t-test and Chi-square test ($\chi 2$) were used to determine the pattern of the disease according to age, sex, etc. Data are reported as the mean ± standard deviation. A two-sided P-value less than 0.05 was considered statistically significant.

Result

Overall, we included 43 patients with CVS, among whom there were 26 (60.5%) girls and 17 (39.5%) boys. The mean age of the patients was found to be 9.08(4.00)(range: 1–17) years. The mean age at the first attack was 6.2 (3.7) (range: 2 months – 15) years. The duration of attacks was 4.7 (2.4) (range: 1-10) days and the frequency of episodes in emetic phase ranged from 2 to 15 per day, with means of 5.5(4.1) and 5.0(2.00) times in boys and girls, respectively. 16 (37%) patients had intractable vomiting; 11 (25%) patients had bloody vomiting; 10 (23%) patients had postprandial vomiting; and only 4 (9.3%) patients showed projectile vomiting. Postprandial vomiting was more common in adolescents (50%) than children (15.1%) (p=0.022). The most common complication of the disease was dehydration, which was seen in 7 (16.3%) patients. 10 (23.3%) patients had a family history of migraine, while 3 (7%) patients had anxiety, and 2 (4.7%) patients had peptic ulcer.

The most common clinical symptoms were abdominal pain in 32 (74.4%), headache in 19 (44.2%), pallor in 14 (32.6%), and fever in 13 (30.2%) patients (Table1). Gastrointestinal (GI) disorder was more common in adolescents than children (p=0.007).

The trigger factors were URI (upper respiratory tract infection), UTI (urinary tract infections), food allergy, and anxiety. UTI was more common among girls than boys although this difference did not reach a significant cut-off (p=0.056) (Table1). Co-morbidities were anemia, motion sickness, abdominal migraine, and seizure. Anemia was more common in adolescents than children (p=0.009) (Table2).

Brain magnetic resonance imaging (MRI),

Table 1. complication, trigger factors and associated disorders among females and males in patients with cyclic vomiting

	Total (n=43)	Female (n=26)	Male (n=17)	P value
Complications				
Nausea	8(18.6%)	4(15.4%)	4(23.5%)	0.69
Pallor	14(32.6%)	8(30.8%)	6(35.3%)	1.00
Weakness	4 (9.3%)	2 (7.7%)	2(11.8%)	1.00
Headache	19(44.2%)	10 (38.5%)	9(52.9%)	0.35
Fever	13(30.2%)	9(34.6%)	4(23.5%)	0.44
Diarrhea	9(20.9%)	5(19.2%)	4(23.5%)	0.73
Constipation	7(16.3%)	3(11.5%)	4(23.5%)	0.41
Vertigo	4 (9.3%)	2 (7.7%)	2(11.8%)	1.00
Anorexia	14(32.6%)	10(38.5%)	4(23.5%)	0.31
Weight loss	4 (9.3%)	3(11.5%)	1 (5.8%)	1.00
Lethargy	7(16.3%)	4(15.4%)	3(17.6%)	0.84
Photophobia& phonophobia	8(18.6%	3(11.5%)	5(29.4%)	0.14
GI disorder*	6(13.9%)	4(15.4%)	2(11.8%)	0.74
Abdominal tenderness	9(20.9%)	8(30.8%)	1 (5.8%)	0.05
Electrolyte imbalance	7(16.3%)	4(15.4%)	3(17.6%)	0.84
Trigger factors				
URI	13(30.2%)	8(30.8%)	5(29.4%)	0.92
urinary infection	12(27.9%)	10(38.5%)	2(11.8%)	0.06
Food allergy	7(16.3%)	5(19.2%)	2(11.8%)	0.52
Anxiety	2(4.6%)	2(7.7%)	0(0%)	0.09
Associated disorders				
Abdominal migraine	5(11.6%)	4(15.3%)	1(5.8%)	0.34
Anemia	2 (4.6%)	2(7.7%)	0%	0.07
Seizure	3(6.9%)	1(3.8%)	2(11.7%)	0.32
Motion sickness	2(4.6%)	2(7.7%)	0(0%)	0.24

**GI disorder is consisting of reflux, gastritis, peptic ulcer etc.*

Table 2. complications, trigger factors and associated disorders among children and adolescents

	Children (n=33)	Adolescents (n=10)	P value
Complications			
Nausea	6(18.2%)	2(20%)	0.90
Pallor	9(27.3%)	5(50%)	0.18
Weakness	2(6.1%)	2(20%)	0.18
Headache	15(45.5%)	4(40%)	0.76
Fever	11(33.3%)	2 (20%)	0.42
Diarrhea	7(21.2%)	2(20%)	0.93
Constipation	5(15.2%)	2(20%)	0.72
Vertigo	3(9.1%)	1(10%)	0.93
Anorexia	11(33.3%)	3(30%)	0.84
Weight loss	4(12.1%)	0(0%)	0.25
Lethargy	5(15.2%)	2(20%)	0.72
Photophobia and phonophobia	5(15.2%)	3(30%)	0.29
GI disorder*	2(6.1%)	4(40%)	0.01
Abdominal tenderness	6(18.2%)	3(30%)	0.42
Electrolyte imbalance	6(18.2%)	1(10%)	0.54
Trigger factors			
URI	11(33.3%)	2(20%)	0.421
Urinary infection	8(24.2%)	4(40%)	0.180
Food allergy	4(12.1%)	3(30%)	0.36
Anxiety	1(3.0%)	1(3.0%)	0.93
Associated disorders			
Abdominal migraine	3(9.1%)	2(20%)	0.35
Anemia	0	2(20%)	0.01
Seizure	2(6.1%)	1(10%)	0.67
Motion sickness	2(6.1%)	0(0%)	0.42

**GI disorder is consisting of reflux, gastritis, peptic ulcer* etc.

Table 3. Medications used in pediatrics with CVS in southern Iran

Medications	Total (n=43)	Female (n=26)	Male (n=17)	Children (n=33)	Adolescents (n=10)
Anti migraine	31(72%)	20(76.9%)	11(64.7%)	22(66.6%)	4(40%)
Anti peptic ulcer	26(60.5%)	16(61.5%)	10(58.8%)	19(57.5%)	7(70%)
Erythromycin	23(53.5%)	14(53.8%)	9(53%)	17(51.5%)	6(60%)
Antiemetic	19(44.2%)	13(50%)	6(35.3%)	14(42.4%)	5(50%)
Anti convulse	11(25.6%)	6(23.7%)	5(29.4%)	11(33.3%)	5(50%)

Electroencephalography (EEG), Electrocardiography (ECG), sonography, and audiometry outcomes were all normal in the patients' files. Two (4.6%) patients showed bleeding; one patient showed gastritis; and another one showed peptic ulcer in their upper GI series.
The medicines used for these cases were Cyproheptidine, Impiramin, Pizotifen, Amitriptrine, and Propranol as anti-migraine, Omeprazole, Ranitidine, Famotidin, Cemetidine, Pantaprazolas as anti-peptic acid, Erythromycin as kinetic drug, Ondansetron, and Metoclopramideas as anti-emetic, Phenobarbital, Sodium volporate, Lorazepam, and Diazepam as an anti-convulse drug (Table 3).

Discussion

This study reveals the pattern of the disease in pediatric patients with CVS in the southern part of Iran. CVS is a rare phenomenon 1 with unknown etiology (11). Knowing the pattern of the disease helps us diagnose and treat it more effectively. Clinical characteristics of the disease vary in different ethnic groups and countries, such as the United States of America, Scotland, Ireland, Australia, Turkey, and Taiwan. As sufficient literature on CVS features among Iranian populations does not exist, an attempt was made to conduct this research on CVS features among Iranian populations; there was an attempt to conduct this research.
In our study, the girl to boy ratio was found to be 1.5:1, which is consistent with studies from Turkey (2/1) Southeast Asia(1.6/1); however, it is contrary to that of Taiwan (1/2) and the USA (1/1.7). The gender ratio in studies from Scotland and Ireland was equal (1/1).
The previous studies indicated the mean age of the 1st attack to be between 4.6-6.9 years. 1 It was 6.9 in the USA, 14 5.3 in Scotland, 3 3.5 in Austria, 15 5.2 in Thailand, 16and 6.8 in Taiwan17, while our study suggested 6.2(3.7) as the mean age.
In our study, duration of attacks ranged from 1 to 10 days, with a median of 4.7 days and the frequency of attacks ranged from 2 to 15 times per year. Other published data showed almost similar consequences. (3, 4, 10, 14)
Postprandial vomiting and GI disorder were more common in the adolescents, moreover, anemia was only seen in two adolescent girls; so avoiding these factors is recommended in the adolescents group to prevent the attacks.
The most important trigger factor was URI in comparison to previous studies where it was reported to be a psychiatric problem (5, 14) so we suggest pediatricians mention this factor, especially, especially in our region.
In some studies nausea and abdominal pain were the most common complaints. (14, 18, 19) In a Turkish study, all the patients showed pallor and anorexia. (4) In Ireland and Taiwan, 71% of patients had abdominal pain. (17, 20) in the present series, abdominal pain and headaches were the chief complaints the patients had.
Studies in Scotland (3) and Turkey 4found the prevalence of migraine in children with CVS to be 21% and 25% respectively, however, 44.2% of our patients had headache and 11.6% had abdominal migraine.
Most of the patients had taken anti-migraine drugs (72%). Similarly a study in Taiwan found cyproheptadine and/or amitriptyline offers greater improvement in duration and frequency of episodes. (17) Although some studies suggested Cyproheptadine, anti- histamine and serotonin receptor antagonist as the first choice in children 5 years old or less. (7, 12), and β-blocker propranolol as the second choice p drug in children with CVS of all ages, 12 another study suggested that, as there is no approved 1st choice drug for CVS, using a combination of drugs can be a good policy. (19)
The previous study in southern Iran by Haghighat M. et al which was conducted between 1994 and 2005 included 181 patients with CVS. Mean age of onset of symptoms and duration of attacks were 5 (3.3) and 4.25, respectively, which were a bit less than those we found (6.2 (3.7) and 4.7 (2.4) respectively). 11 In that study 25% of patients had a history of motion sickness and 5% had seizures, while in our results only 4.6% of patients had motion sickness and 6.9% had seizures. The study did not report any other accompanied illness and they did not explain the trigger factors. The Haghighat study recommended propranolol as the best drug for CVS.

In conclusion, as there is no definite drug for CVS, knowing the common trigger factors which culminate in CVS in each region can be of great importance and can prevent attacks in the prodromal phase. The present study investigated the trigger factors as well as demographic, clinical, and laboratory data in pediatric patients with CVS. It was found that some differences in patterns of the disease exist between girls and boys, and also between children adolescents, but because our population was insufficient, more studies with greater populations are needed in order to identify differences of the syndrome patterns in different ages and sexes.

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