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Original Article

Relapse Rate of Clinical Symptoms After Stopping Treatment in Children with Cyclic Vomiting Syndrome

Mahmoud Haghighat[1], Maryam Gholami Shahrebabak[1], Seyed Mohsen Dehghani[1], Maryam Ataollahi[1], Nazanin Amin Farzaneh[1], Samaneh Hamzeloo Hoseinabadi[1], Hazhir Javaherizadeh[2*]

[1]Gastroenterohepatology Research Center, Nemazee Teaching Hospital, Shiraz University of Medical Sciences, Shiraz, Iran
[2]Clinical Sciences Research Institute, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

Abstract

Background: Cyclic vomiting syndrome (CVS) is a chronic functional gastrointestinal disorder. It is characterized by recurrent episodes of vomiting typically separated by periods of symptom-free or baseline health. The present study aimed at evaluating the effectiveness of propranolol and the relapse rate of clinical symptoms after stopping treatment in children suffering from CVS.

Methods: Records of 504 patients below the age of 18 years with CVS who were treated with propranolol from March 2008 to March 2018 were reviewed. The duration of follow-up was 10 years.

Results: The average age of CVS affliction was 4.3 years and the average age at the diagnosis was 5.8 years. All subjects were treated with propranolol (for an average of 10 months). 92% of treated subjects were cured, causing a dramatic decrease in the rate of vomiting ($P<0.001$). Only an average of 10.5% of the studied subjects (53 people) showed a relapse of symptoms after stopping the treatment. The results of a 10-year follow-up period of the patients showed that 24 had abdominal migraine and 6 had migraine headaches, all of whom lacked the symptoms of disease relapse (prognostic evaluation).

Conclusion: The findings of this investigation show that the duration of treating CVS with propranolol could be shortened to 10 months with a low percent of symptoms relapse and this shortening may be effective in preventing the undesirable side effects of the drug. The presence of abdominal migraine and migraine headaches in patients after treatment accomplishment and the lack of disease relapse can be prognostic measures for this disease, which require intensive attention.

Keywords: Cyclic vomiting syndrome, Children, Propranolol, Duration of treatment period

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Introduction

Cyclic vomiting syndrome (CVS) is a chronic functional gastrointestinal disorder with sudden and relapsing episodes of severe emesis and vomiting, followed by asymptomatic episodes.[1-6]

At the present, CVS diagnosis is based on clinical criteria and there is no available specific diagnostic test or biomarker. The strategy of the North American Society for Gastroenterology, Hepatology, and Nutrition (NASPGHAN) was designed for CVS diagnosis in children, which insisted on a stereotypic pattern and an asymptomatic inter-episodic period. Diagnostic criteria for CVS, based on NASPGHAN strategies include at least five attacks during any time interval or at least three attacks during six months; disease attacks appear as sudden vomiting with high severity, lasting from one hour to 10 days and at least a one-week interval, unique stereotypical symptoms for each patient; occurrence of vomiting in each attack at least four times in an hour and lasting at least for one hour; patient's baseline level between attacks, and lack of symptoms compatibility with other disorders.[7,8]

CVS is a disorder with unknown etiology and pathophysiology and its acute symptoms are disabling and often require medical care. If acute CVS symptoms are not prevented, it can negatively affect patients' lives. However, the types of different treatments and treatment duration are very controversial.[9] It is thought that CVS is a type of abdominal migraine [10] and often leads to migraine headaches since a familial history of migraine headaches has been usually observed.[11,12] Therefore, anti-migraine drugs could prevent CVS.[13] Propranolol is usually administered to avoid CVS attacks.[14] Previous studies with propranolol have proven that this drug should be considered a prophylactic agent to control the symptoms and prevent attacks.[15] On the other hand, this drug is mostly used in children, and comparison with the other treatment available has shown a moderate response rate in several studies including high numbers of patients treated. No patient stopped the treatment because of unwanted side effects.[15,16] Meanwhile, efficiency rate, lack of disease symptoms relapse after stopping treatment, and treatment duration (especially in children) are among important and unclear problems in previous reports and studies, which are the focus of the present study. Duration of the treatment period in children with CVS can also

*Corresponding Author: Hazhir Javaherizadeh, Email: hazhirja@yahoo.com

months (minimum of 6 and maximum of 24 months) with no drug-originated side effects. Follow-ups of patients indicated an 87% positive response to 1 mg/kg of propranolol. Drug dosage was then elevated to 2 mg/kg with a total curative rate of 92% in the subjects. The ratio of patients with vomiting decreased significantly after drug therapy. Based on NASPGHAN's guidelines, propranolol is a second-line agent for preventing CVS.[8] However, the efficiency of this drug was very high in the present study. It is while in our other study on 181 CVS patients, 94% of patients had an acceptable response after propranolol administration.[19] Our previous studies on 206 patients with CVS in 2017 also established that as a prophylactic agent, propranolol had an acceptable response in 92.2% of such patients.[17] These results are comparable with those of other studies. In NASPGHAN Announcement it has been stated that propranolol has a moderate efficiency (35-75%) for CVS treatment in children.[8] Sunku also reported an efficiency rate of 52-65% in 2009.[30] In an investigation by Sezer and Sezer in 2016, 82% of the propranolol group showed a positive response to the treatment.[15]

Analysis of data gathered in the present work showed that only an average of 10.5% of the subjects (53 subjects) showed disease symptoms relapse after stopping the treatment and the sex had no effect on the drug's effect on these symptoms. Long-term follow-ups of patients in a 1- to 10-year time interval indicated that 24 subjects had abdominal migraine and 6 had migraine headaches of whom, all lacked symptoms of disease relapse. In another report, we followed up on 31% of patients with at least five years of drug withdrawal, and symptomatic relapses were observed in only 3.8% of subjects.[19] In another study, we also showed that during 9 months of treatment with propranolol, only 7.8% of subjects suffering from CVS had symptomatic relapses.[17] Therefore, noticing the successful treatment results with propranolol in our study and the lack of reports about effective remediation with propranolol, it is suggested that this drug can be administered for 8 to 10 months.

Our results recommend that the highest frequency of disease incidence and diagnosis was in the age group under 6 years old and preschool ages. CVS treatment period could also shorten via propranolol administration, which would be along with helpfulness in preventing from drug's side effects. The occurrence of abdominal migraine and migraine headache symptoms in patients after full healing and lack of disease relapse can act as a prognostic agent for this disease, which requires paying more attention.

Our data about relapse need further studies. The recent guidelines recommend other drugs for the prophylaxis of CVS, but the availability and low cost of propranolol and experiences with propranolol can be beneficial in some cases with CVS.

Study limitations

Single center study, patents incompliance, and loss of some data during follow up.

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Competing Interests

The authors declare no conflict of interest related to this work.

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