Int J Basic Sci Med. 2016;1(2):63-66 Original Article

http://ijbsm.zbmu.ac.ir/ doi 10.15171/ijbsm.2016.14

A New Guideline for Using Erythromycin in Management of Childhood Cyclic Vomiting Syndrome

Mahmood Haghighat[1], Iraj Shahramian[2*], Seyed Mohsen Dehghani[1], Maryam Ataollahi[1], Maryam Bahmanyar[1]

[1]Department of Pediatric Gastroentrology, Shiraz University of Medical Sciences, Shiraz, Iran
[2]Department of Pediatric, Zabol University of Medical Sciences, Zabol, Iran

***Correspondence to**
Iraj Shahramian;
Email: ir_buper@yahoo.com

Received June 26, 2016
Revised August 14, 2016
Accepted August 21, 2016
Published online September 19, 2016

Abstract
Cyclic vomiting syndrome (CVS) is a functional disorder without any determined cause, though some motility disorders are considered in stream of this syndrome. There is no clear treatment for CVS and all treatments are borrowed from treatment of other similar diseases such as migraine. Clinical practice guideline instructs the pediatricians and pediatric gastroenterologists for treatment of CVS in both inpatient and outpatient settings. Since there is no practical guideline for the empirical management of CVS, this guideline was prepared for framing the treatments in a scientific and simple way for this disorder.

Keywords: CVS, Treatment, Guideline.

Please cite this article as follows: Haghighat M, Shahramian I, Dehghani SM, Ataollahi M, Bahmanyar M. A new guideline for using erythromycin in management of childhood cyclic vomiting syndrome. Int J Basic Sci Med. 2016;1(2):63-66. doi:10.15171/ijbms.2016.14.

Introduction

In 1882, Samuel Gee described cyclic vomiting syndrome (CVS) as a brain-gut disorder characterized by stereotypical severe intractable non-bilious vomiting lasting for hours or days, separated by symptom-free intervals lasting weeks or months.[1] The most common cause of recurrent vomiting in children after the gastroesophageal reflux disease is CVS and its estimated prevalence is 1.6% according to ROME III diagnostic criteria.[2]

In recent few years, it has been recognized that CVS is prevalent in children. There are as yet several empirical treatment regimens for CVS. Although in some studies female dominancy has been reported, there is no clear gender preponderance.[3-5] It is accepted that CVS is a self-limiting illness with documented relation to migraine headache and abdominal migraine.[6]

There are proven abnormal motilities in gastrointestinal tract during asymptomatic and symptomatic phases of CVS, such as gastric hypomotility, delayed gastric emptying, gastric dysrhythmia, and small bowel dysmotility.[7-9] This clinical practice guideline was prepared to instruct the pediatricians and pediatric gastroenterologists who take care of children in both inpatient and outpatient settings. It is desirable that the outcome of the guideline be defined as the resolution of CVS symptoms in children. This study amounts to the authorized endorsements of Shiraz on the treatment of CVS in children and safeguarding the patients from maltreatment that is common, can be present anywhere, and may co-exist with other health problems.

Erythromycin

Erythromycin is a macrolide antibiotic with the efficacy on motilin receptor in gastrointestinal tract and can improve the gastric motility as it is used as a motilin receptor stimulator.[2] Although gastric acid destroys the erythromycin, the erythromycin stratarate is more stable in acidic environment. Small intestine is the main route for its absorption, but it is rather slightly absorbed by stomach. Via oral route, near 50% of this drug is absorbed because in stomach and its acidic liquid, erythromycin is destroyed. The main part of erythromycin in plasma is as bound with plasma proteins and in vivo protein-binding erythromycin is more than 90%. Erythromycin tissue distribution is very high and it can cross the placenta about 10%. Additionally, its fetal plasma level is near 10%. Erythromycin is categorized in B pregnan-

cy risk category. It is metabolized by liver and primarily excreted from feces and urine.[10]

Patient-Centered Care

This guideline offers the best practical advice on the care of children aged 1-18 years old with CVS. Treatment and care should take individual needs and preferences into account. Patients should have the opportunity to make informed decisions about their care and treatment, in partnership with their healthcare professionals. If the patient is under 18, their family or caregiver should also be given information and support to help the child or young person to make decisions about his/her treatment.

Adult and pediatric healthcare teams should work closely to prepare assessment and services to young people with CVS. Diagnosis and management should be reviewed throughout the transition process, and there should be clarity about who is the leading clinician to ensure the continuity of care.

Key Priorities for Implantation

(1) Providing advice about CVS, that is common, usually begins in young age, may be frequent, and does not usually need further investigation.

(2) In children with cyclic vomiting, look out for the alarm signs which may suggest disorders other than CVS.

(3) Do not routinely evaluate or treat CVS.

(4) Do not offer treatment without specialist's advice and take their potential to cause adverse events into account.

Terms Used in This Guideline

(1) Children: 1 to under 18 years old

(2) CVS: is the cyclic vomiting with fulfilling the ROME III criteria

(3) Frequent episode: episodes that happen more than one time per month

(4) Severe attack: lasts more than 2 to 3 days

Who to Treat?

Patients fulfilling ROME III criteria and having characteristic clinical manifestations in the absence of alarm signs could be treated by empiric therapy and invasive tests are not essential for diagnosis of CVS.[2] CVS diagnostic criteria are:

(1) Stereotypical episodes of vomiting regarding the onset (acute) and duration

(2) Three or more discrete episodes in the previous year

(3) Absence of nausea and vomiting between episodes

Self-limiting nausea, abdominal pain, headache, motion sickness, photophobia and lethargy, as well as 2-accompanying signs of fever, pallor, diarrhea, dehydration, excess salivation, and social withdrawal are supporting criteria of CVS. Moreover, in the patients' point of view, nausea is considered as the most persistent and distressing symptom.[2]

Alarm signs in CVS fall into some categories including abdominal (bilious vomiting, abdominal tenderness, severe pain), the events occurring later are associated with metabolic disorders such as: fasting and high protein diet, and rapid progression and conversion to chronic pattern.[10]

For patients with alarm symptoms and signs, further evaluation before treating is indicated.[2,10]

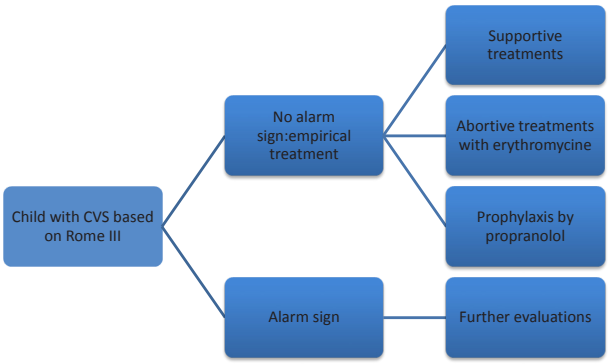

Figure 1. The Algorithm of Cyclic Vomiting Syndrome Treatment

How to Treat CVS?

Considering four phases of CVS treatment, CVS could be divided into four categories: lifestyle modification, supportive management, 3-prophylactic therapy, and 4-abortive therapy. The goals for prophylactic and abortive therapy are daily treatment for preventing episodes and preventing progression of vomiting. These managements are based on four phases of CVS[3,11]:

(1) The inter-episodic phase is symptom-free period for patients.

(2) The prodromal phase with nausea but without vomiting and preserved ability for oral intake.

(3) The vomiting phase which is characterized by severe, persistent nausea, and vomiting.

(4) In recovery phase nausea subsides and terminates; the patient's appetite and oral tolerance return.

Phase I

Prevention of episodes is the goal of the inter-episodic phase that could be achieved by life-style changes, avoidance of commencing factors, and physiological manipulations for reduction of stress.[11]

Phase II

Although the prodromal starts with feeling symptoms, the patient is still able to intake oral drugs. Termination of this part is with the beginning of vomiting. The prodromal phase could last from minutes to days. To treat it, we should determine its constituent symptoms. Supportive managements include intravenous fluids as 10% dextrose for reduction of catabolism and the least stimulation with a combination of antiemetics and sedation. For nausea, try high dose 5-ht3 antagonist antiemetics (ondansetron [Zofran] at 0.3 –0.4 mg/kg/dose). Sedation is offered by: diphenhydramine, lorazepam, or chlorpromazine.[3,11-13]

The abortive therapy is indicated for those who have sporadic episodes (less than once per month), short episodes (duration less than 24 hours) or breakthrough attacks in spite of prophylaxis.[10] We recommend the use of erythro-

mycin in a dose of 3-5 mg/kg for 7 days as abortive treatment in prodromal phase if abortive therapy is indicated.[10] Other drugs used for abortion include sumatriptan and zolmitriptan.[14]

Phase III

Intense nausea and vomiting are characterizing factors of attack phase; hence termination of the nausea and vomiting is the therapeutic goal in this phase. Severe symptoms could be extremely distressing or life threatening in some patients. Therefore, treatment of attacks must take place promptly. In this phase, lorazepam (0.05- 0.1 mg/kg, maximum 3 mg/dose) and ondansetron (Zofran) at 0.3-0.4 mg/kg/dose by IV piggyback over 15 minutes, chlorpromazine (0.5–1 mg/kg/dose), and diphenhydramine (0.5–1 mg/kg/dose) are used for treatment.[3,11-13]

Phase IV

After the termination of vomiting, the recovery phase commences. The purpose of the recovery phase is oral intake resumption without relapsing of nausea and vomiting.[14] Deciding for prophylaxis is made as soon as recovery is complete. Daily prophylaxis is indicated in patients with[3,11]:

(1) Frequent episodes that happen more than once per month

(2) Children with severe attacks (lasting more than 2 to 3 days)

(3) Failure of abortive and supportive therapies

We recommend the propranolol 1 mg/kg as drug of choice in all age categories for prophylaxis although previous consensus recommended cyproheptadine for children 5 years or less and amitriptyline for patients older than 5.[2,10] In spite of others, we recommend a period of 9 months rather than long term or lifelong prophylactic treatment.

Ethical Approval

Not applicable.

Competing Interests

Authors declare that they have no competing interests.

Acknowledgements

The authors would like to thank Center for Development of Clinical Research of Nemazee Hospital. The editorial assistance of Dr. Nasrin Shokrpour is also highly appreciated.

References

1. Gee S. On fitful or recurrent vomiting. Saint Bartholomew's Hospital Reports 1882;18:1-6.
2. Haghighat M, Rafie SM, Dehghani SM, Fallahi G, Nejabat M. Cyclic vomiting syndrome in hildren: experience with 181 cases from southern Iran. World J of Gastroenterol. 2007;13:1833-1886. doi:10.3748/wjg.v13.i12.1833.
3. Li BU, Lefevre F, Chelimsky GG, et al. North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition consensus statement on the diagnosis and management of cyclic vomiting syndrome. J Pediatr Gastroenterol Nutr 2008;47:379. doi:10.1097/mpg.0b013e318173ed39.
4. Lucarelli S, Corrado G, Pelliccia A, et al. Cyclic vomiting syndrome and food allergy/intolerance in seven children: a possible association. Eur J Pediatr 2000;159:360. doi:10.1007/s004310051287.
5. Lee WS, Kaur P, Boey CC, Chan KC. Cyclic vomiting syndrome in South-East Asian children. J Paediatr Child Health. 1998;34:568.
6. Welch KM. Scientific basis of migraine: speculation on the relationship to cyclic vomiting. Dig Dis Sci. 1999;44:26S.
7. Boles RG, Adams K, Ito M, Li BU. Maternal inheritance in cyclic vomiting syndrome with neuromuscular disease. Am J Med Genet A. 2003;120A:474. doi:10.1002/ajmg.a.20126
8. Li BU, Misiewicz L. Cyclic vomiting syndrome: a brain-gut disorder. Gastroenterol Clin North Am. 2003;32(3):997-1019. doi:10.1016/s0889-8553(03)00045-1
9. Dong M, Li ZH, Li G. Clinical characteristics of 41 children with cyclic vomiting syndrome. Zhonghua Er Ke Za Zhi. 2008;46(6):450-453.
10. Haghighat M, Dehghani SM, Shahramian I, Imanieh MH, Teimouri A, Noori NM. Combination of erythromycin and propranolol for treatment of childhood cyclic vomiting syndrome: a novel regimen. Gastroenterol Hepatol Bed Bench. 2015;8(4):270-277.
11. Lee LY, Abbott L, Mahlangu B, Moodie SJ, Anderson S. The management of cyclic vomiting syndrome: a systematic review. Eur J Gastroenterol Hepatol. 2012;24(9):1001-1006.
12. Boles RG. High degree of efficacy in the treatment of cyclic vomiting syndrome with combined co-enzyme Q10, L-carnitine and amitriptyline, a case series. BMC Neurol. 2011;11:102. doi:10.1186/1471-2377-11-102.
13. Pareek N, Fleisher DR, Abell T. Cyclic vomiting syndrome: what a gastroenterologist needs to know. Am J Gastroenterol. 2007;102:2832. doi:10.1186/1471-2377-11-102
14. Evans RW, Whyte C. Cyclic vomiting syndrome and abdominal migraine in adults and children. Headache. 2013;53(6):984-993. doi:10.1111/head.12124

Appendix 1

How Did This Guideline Develop?

Shiraz University of Medical Sciences commissioned Dr Haghighat and Dr Shahramian to prepare this guideline. Dr Shahramian reviewed the evidence and developed the recommendations.

Implementation

Shiraz University of Medical Sciences has evolved tools to help pediatric gastroenterologists and pediatricians to implement this guideline.

Updating the Guideline

This clinical guideline is updated so that the recommendations take important new information into account. New evidence is checked after publication, and pediatric gastroenterologists and pediatricians are asked for their views; we use this information to decide whether all or part of a guideline needs updating. If important new evidence is published at other times, we may decide to do a more rapid update of some recommendations.