CLINICAL

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THE THERAPEUTIC EFFICACY OF PRM MEDICINE GUNA-BOWEL IN PAEDIATRIC CYCLIC VOMITING SYNDROME

SUMMARY

The cyclic vomiting syndrome (CVS) diagnosis is based on the Rome III diagnostic criteria (Los Angeles, 2006).
The data by Li *and* Balin (2000) and Scarcia (2000) estimate that in 68% of the cases the most frequent trigger factors include:

- **Infectious diseases in 41%, especially chronic sinusitis;**
- **Mental stress (34%);**
- **Food, including chocolate, cheese and other;**
- **Physical exhaustion or sleep deprivation (18%);**
- **Atopy (13%);**
- **Menstrual periods (13%) and other.**

- Patients with CVS aged from 2 up to 7 years old were divided into 2 study groups: the control group included 16 children who received standard therapy; the second group included patients with CVS (35 children) who received standard therapy and Guna Bowel for a period of 10 days.
All the examined patients were hospitalized immediately: in 52% of cases it was the second episode in the disease history, 48% of children had relapsing course.
The supplementation of the basic treatment with the PRM preparation Guna Bowel markedly improved the clinical picture in children with CVS: during the first three days all children reported decrease of pain syndrome (in the control group this was noticed in 87%), toxic syndrome reduced in 86% of the patients and 67% of the controls, vomiting episodes in the first two days ended in 87% of the children who received Guna Bowel and in 74% of the controls.

KEY WORDS **CYCLIC VOMITING SYNDROME, PAEDIATRICS, GUNA-BOWEL**

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INTRODUCTION

The **cyclic vomiting syndrome** (CVS) diagnosis is based on the Rome III diagnostic criteria (Los Angeles, 2006) that include the following:

1. Two or more periods of intense nausea and unremitting vomiting or retching, lasting from several hours to several days.
2. Return to usual state of health that lasts from several weeks to several months.

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- Mental stress (34%)
- Food, including chocolate, cheese, and other
- Physical exhaustion or sleep deprivation (18%)
- Atopy (13%)
- Menstrual periods (13%) and other.

The pathophysiology in CVS is unknown. Two different functional structures in the brain are responsible for the act of vomiting: the vomiting centre situated in the lateral reticular formation and a chemoreceptor trigger zone on the floor of the IV ventricle, known as *area postrema*.
The main role is played by the vomiting centre which represents a collector of afferent impulses.
The chemoreceptor trigger zone initiates the act of vomiting by sending the impulses to the vomiting centre.

- Two mechanisms of vomiting and eructation are known: the first mechanism is related to the initial activation of the vomiting centre.
Afferent vagal and sympathic nerves send impulses to the vomiting centre from the biliary tract and digestive organs, larynx, peritoneum, coronary arteries, the vestibular apparatus, thalamus, hypothalamus, and cortex.
The motor impulses are transmitted to the vomiting centre from the diaphragm through the diaphragmatic nerves, to intercostal and abdominal muscles through the spinal nerves, and to the pharynx, larynx, oesophagus and stomach through the vagal nerve.
The second mechanism is based on the chemoreceptor trigger zone stimulation, in which impulses are directed to activate the vomiting centre. The trigger factors of the chemoreceptor zone are: *serotonin, angiotensin, neurotensin, VIP, gastrin, substance P, dopamine,* drugs, uremia, hypoxia, diabetic ketoacidosis, endotoxin Gram-positive bacteria, radiations, and others.

The CVS involves disturbances of the hypothalamic-pituitary-adrenal axis (with secretion increase of the Corticotropin-Releasing Factor) as well as vegetative dysregulation (sympathicotonia).

It is known that the stress activation of the hypothalamic-pituitary-adrenal axis causes bouts of vomiting.
The core nucleus in the central nervous system that takes part in the regulation of the hypothalamic-pituitary-adrenal axis is the paraventricular nucleus (PVN) of hypothalamus.
The PVN is the source of the corticotropin-releasing factor which is the main physiological regulator of the pituitary adrenocorticotropic hormone (Tache *and* Bonaz, 2007).

The following conditions play an important role in the development and course of the CVS:
- Disorders of the autonomous nervous system;
- Excessive production of IL-6 which is a marked activator of the hypothalamic-pituitary-adrenal axis.

The CVS is considered as a mitochondrial disease because of the DNA mutations in the mitochondria which are the "electric power suppliers" of the cell.
Any mitochondrial enzyme defect (there are around 80 active enzymes operating in the mitochondria) disturbs the proper functioning of the "energy station", which affects, first of all, the energy-dependent tissues and organs – the Central Nervous System, cardiac and skeletal muscles, kidney, liver, and endocrine glands.

Three phases are distinguished in the evolution of the CVS:

I. Nausea-free interval between episodes when the child feels well;

II. A prodrome starting when the patient begins to feel the symptoms signalling the approach of an episode of headache, nausea and general weakness; it may be prevented by taking the necessary treatment. If it develops, it may last from several minutes to several days, but in 25% of the children it may not occur at all;

III. A vomiting phase is characterized by intense nausea and vomiting and is manifested in all children with CVS.

CVS prophylaxis treatment is administered in the 1st and 2nd phase of the disease, and monotherapy or bitherapy is used:
- Antihistamines: *cyproheptadine* and *pizotifen* (cyproheptadine 0.25–0.5 mg/kg/day);*pizotifen* 0.5-1.0 mg once at night
- β-Blockers: *propranolol* 0.25–1.0 mg/kg/day
- Tricyclic antidepressants: *amitriptyline* 0.25-0.5 mg/kg, *phenobarbital* 2 mg/kg
- Alternatives: *topiramate, valproic acid, gabapentin, levetiracetam, L-carnitine* 50–100 mg/kg/day, *Coenzyme Q10* 10 mg/kg/day.

Acute management is performed in hospital settings and includes the following medications:
- 10% glucose concentration, 4%

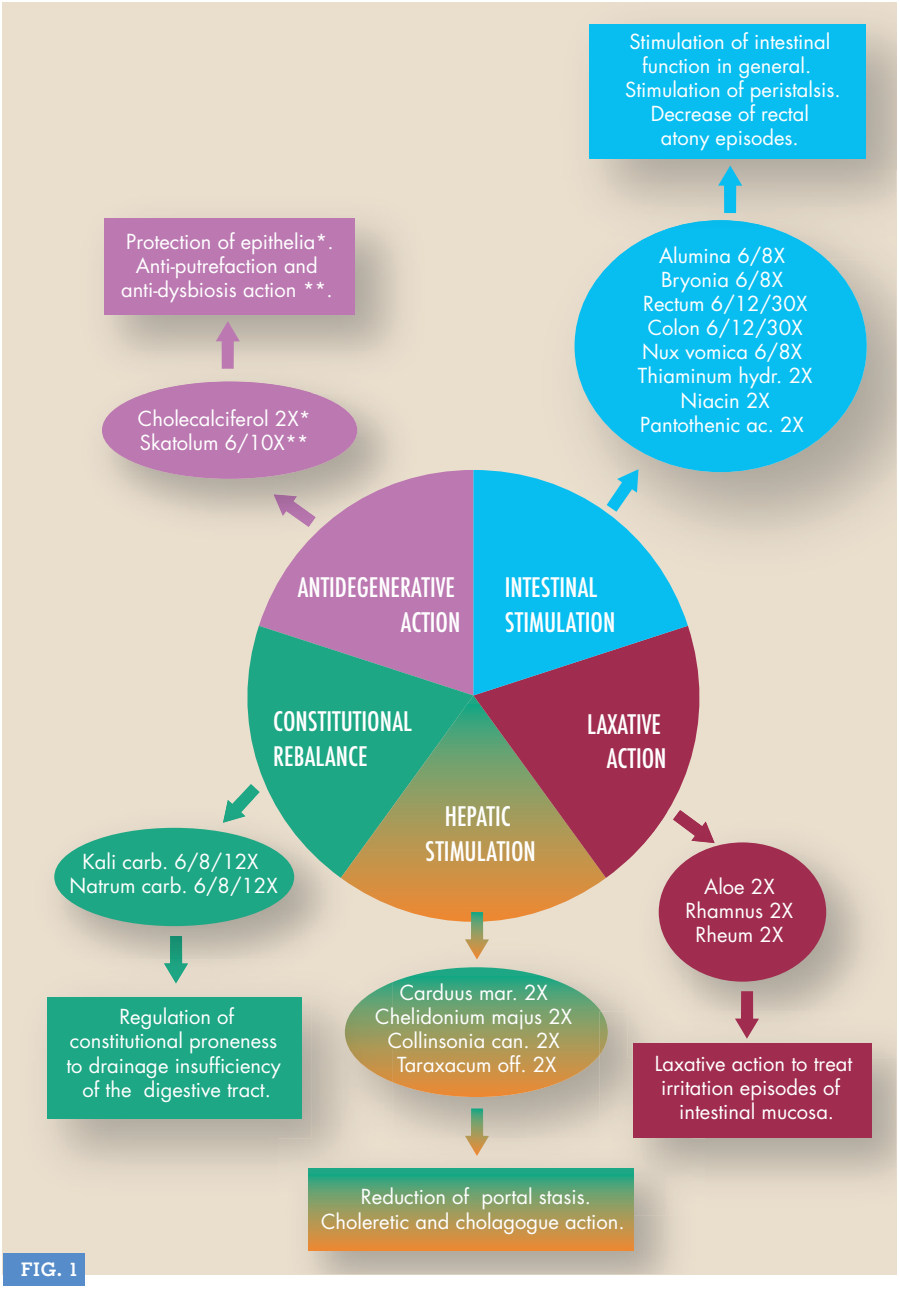

FIG. 1

Mechanisms of action of Guna Bowel.

potassium chloride, 10% NaCl
- *Ondansetron* 0.3-0.4 mg/kg/hour and in a second stage 0,1 mg/kg/hour
- *Omeprazol* 1 mg/kg/day two times a day or *Lorazepam* 0.05-0.1 mg/kg
- *Chlorpromazine* 0.15–0.3 mg/kg two or three times a day.

Based on the properties of the Physiological Regulating Medicine (PRM) drug **Guna Bowel** (FIG. 1) (detoxification, decreased flatulence and increase of the intestinal motility), we have included it in the therapeutic scheme during the 3rd phase – the period of acute manifestations.

- **The aim of this study** was to evaluate **Guna Bowel** therapeutic effectiveness in children with CVS.

PATIENTS AND METHODS

Patients with CVS aged from 2 up to 7 years old were divided into **2** study groups: the **control group** included **16 children** who received standard therapy; the second group included patients with CVS (**35 children**) who received standard therapy and **Guna Bowel** for a period of 10 days.

In both groups the following main symptoms were observed: pain, vomiting, dehydration, and toxicity.

All the patients underwent comprehensive clinical, biological and instrumental examinations: electrocardiography, ultrasonography, esophagogastro-duodenoscopy and chest radiography when it was necessary. General analysis of the blood and urine, biochemical and enzyme immunoassay tests to assess serum amylase, ALT, AST, general bilirubin and its fractions, total protein, urea, glucose, and cholesterol were performed. Ionogram and anion balance (*Gas Easy Blood* device - Medica) were also performed. Ketones in urine were assessed by using the biochemical method with sodium nitroprusside.

Children were examined by the following specialists: neurologist, gastroenterologist, nephrologist, and others.
- Biological tests have been collected to assess biochemical indicators in both groups (lactate, sodium, potassium, HPL, SAO, metabolic molecules, ketones, necrotic substances in serum, amylase concentration in serum and urine).

RESULTS AND DISCUSSION

All the examined patients were hospitalized immediately: in **52%** of cases it was the second episode in the disease history, **48%** of children had relapsing course.
A seasonal character was noticed with a higher prevalence of the episodes in spring and summer; this can be explained with an increased risk caused by food triggering the disease.
It is necessary to mention that in **45.8%** of patients there was a positive history of chronic ENT disorders (pharyngitis, sinusitis), and in **73%** of the children neurological disorders were found (residual encephalopathy and epilepsy syndrome).

The general condition was considered severe in **82.3%** of the cases and very severe in **17.7%** of the patients. Nausea, repeated vomiting (six and more episodes), sometimes with undigested food, bilious emesis in **14%**, acetone halitosis, severe abdominal pain were the major complaints. Moderate dehydration syndrome (**6-9%** of weight loss) was assessed in **92.7%** of the children, severe dehydration (acute weight loss up to more than 10%) in **7.3%** of the cases.
Signs of airways disorders included a mostly mild compensatory metabolic tachypnea in children. Acute bronchitis was noticed in **5.6%** of the cases and in **1.2%** of the patients acute focal bronchopneumonia was diagnosed.
Ketoacidosis levels in children with CVS (assessed by acetone concentration in urine) increased markedly in **85.72%** of the children and moderately in **14.28%**. In **64.32%** of the patients metabolic acidosis was determined and mixed acid-base disorder in **35.68%** of the cases.
In **43.6%** of the children hypoglycemia was revealed, in **10.9%** - hyperglycemia thus pancreatic lesions being confirmed in **53.7%** of the patients with CVS.
Therapeutic management was focused on the toxic syndrome and dehydration, and included measures for rehydration, electrolyte and acid-base re-balancing, restoration of peripheral circulation disorders, treatment of the main disease which triggered CVS development. To correct hemodynamic and metabolic crisis an infusional 5% dextrose solution was initially applied, 0.9% NaCl and Ringer, but the infusion volume varied depending on the severity of the dehydration and toxic syndrome.
When an improvement of the clinical condition was obtained and the vomiting episodes had become less frequent, the therapy continued with oral rehydration (5% dextrose, oral rehydration solutions).

The supplementation of the basic treatment with the PRM preparation **Guna Bowel** markedly improved the clinical picture in children with CVS: during the first three days **all** children reported decrease of pain syndrome (in the control group this was noticed in **87%**), toxic syndrome reduced in **86%** of the patients and **67%** of the controls, vomiting episodes in the first two days ended in **87%** of the children who received **Guna Bowel** and in **74%** of the controls.
Metabolic acidosis was corrected in the first day of treatment in **68%** of the patients in the study group and in **45%** of the children who received only the basic treatment.

Therefore, the use of Guna Bowel in addition to the therapeutic scheme has contributed to the clinical improvement in children with CVS, with a twofold decrease of the pain and 1.3 fold of toxic syndrome, a decrease of vomiting episodes frequency, a 1.5 fold recovery rate of fluid and electrolyte balance compared with the control group.

The administration of **Guna Bowel** to children with CVS reduced the duration of episodes by one day (24 hours).

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