INFLUENCE OF PHARMACOLOGICAL CORRECTION ON THE QUALITY OF LIFE OF CHILDREN WITH FUNCTIONAL DYSPEPSIA

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Abstract

Objective: To study the influence of pharmacological psychocorrection with drugs derived from GABA on the quality of life of primary school-aged children with functional dyspepsia.

Materials and methods. 80 children aged 6–12 years with FD have been examined. Children were divided into 4 groups: Group 1 – 20 patients who received γ-amino-β-phenylbutyric acid hydrochloride along with baseline therapy, Group 2 – 20 patients who received comprehensive treatment and calcium hopantenate, Group 3 – 20 children who received vitamin-mineral complex and protocol treatment, and Control Group – 20 children who received baseline treatment. Study Design: general clinical, instrumental, psychodiagnostic, statistical.

Results. Using the PedsQL questionnaire, physical functioning disorders were found in children with FD – 97.5 ± 1.2 % (78/80) of children, emotional functioning disorders – 91.3 ± 1.6 % (73/80) of cases, functioning at school disorders – 88.8 ± 2.7 % (71/80) of patients. During one-month case monitoring, children who took GABA drugs reported an improvement in the quality of life compared with baseline treatment and a group of children, who took a mineral-vitamin complex: physical functioning – ($p_1 = 0.016$), ($p_2 = 0.03$), emotional functioning – ($p_1 < 0.001$), ($p_2 < 0.001$), functioning in school – ($p_1 = 0.005$), ($p_2 = 0.004$).

Conclusion. The use of γ-aminobutyric acid drugs is safe and effective and they significantly improve the quality of life of children with FD.

Keywords: functional gastrointestinal disorders, functional dyspepsia, quality of life, treatment.

DOI: 10.21303/2504-5679.2020.001518

1. Introduction

Functional dyspepsia (FD) is a functional gastrointestinal disorder (FGID), which is one of the dominants in the Rome classifications from the beginning of their creation. FD is manifested by constant or recurrent abdominal pain upper and, according to the Rome IV criteria, is assigned to group B – gastroduodenal disorders [1, 2]. The prevalence of FD according to various studies varies from 1.4 % to 30 % [3, 4].

The authors believe that the FGID significantly affects the quality of life of children [5, 6], modulates the nature and intensity of clinical symptomatology, patient behaviour, his/her emotional state and social functioning [7, 8].

The issue of the advisability of long-term administration of drugs to such patients that affect the function of the central nervous system is being constantly debated in the scientific literature [4, 7]. Therapy with tricyclic antidepressants (amitriptyline, imipramine) has proven its effectiveness in complex cases, but its common use is limited by a significant number of side effects [4, 9]. The advisability of psychotherapeutic correction in case of functional dyspepsia, like other forms of FGID, is considered, which requires active training of relevant specialists in Ukraine and the development of the psychotherapeutic care system in general [10, 11].

So, the issue of finding effective means and correcting psychoemotional disorders and quality of life in children with functional gastrointestinal disorders and, in particular, functional dyspepsia continues to be relevant.

Since several studies have shown an increase in the activity of excitatory amino acids in children with FGID [12, 13] special attention in the aspect of psychocorrection shall be paid to ɣ-aminobutyric acid (GABA) drugs [14, 15]. GABA is a natural metabolite with the functions of an inhibitory neurotransmitter, which favourably affects the energy of the neuron, neurodynamics, and cerebral circulation [16, 17]. Thus, a combination of soothing and mild psychostimulating effects is achieved. In its pure form, exogenously introduced GABA does not penetrate the blood-brain barrier (BBB) [18], which intensified the need for the creation of several complex compounds [9, 12]. In our opinion, γ-amino-β-phenylbutyric acid hydrochloride (Phenibut) and calcium hopantenate are of great interest to the FD treatment [11].

Objective. To study the influence of pharmacological psychocorrection with drugs derived from GABA on the quality of life of primary school-aged children with functional dyspepsia.

2. Materials and methods

During 2016–2017 80 children aged 6–12 years (38 boys and 42 girls) who sought help from the Kyiv City Children's Clinical Hospital No. 1 with complaints which, according to the Rome IV criteria, met the diagnosis of functional dyspepsia, have been examined. The study was approved by the committee on bioethics of the Shupyk National Medical Academy of Postgraduate Education (protocol No. 2 of 10.01.2017) and was carried out in accordance with the guidelines of the Helsinki Convention, 1975. All participants and their parents were fully informed about the methods and scope of the study and gave written informed consent for participation.

The inclusion criteria in the study were: the presence of voluntary informed consent of the child parents to participate in clinical trials; the age of patients varies from 6 to 12 years; the presence of a functional dyspepsia diagnosis; the absence of clinical and laboratory signs of organic lesion of GIT. The exclusion criteria from the study were: refusal of the patient's parents to participate in a clinical trial; the presence of anxiety symptoms; detection of signs of an inflammatory, metabolic, neoplastic process, anatomical defects that could explain the onset of dyspepsia symptoms during the examination; the presence of chronic diseases of the gastrointestinal tract; the presence of mental illnesses; the presence of severe diseases of the child of any localization; taking drugs that affect the functional activity of the central and autonomic nervous system; failure to comply with study requirements.

All children underwent a set of diagnostic procedures in accordance with the Unified Clinical Protocol of Medical Aid for Children with FD (Order of the Ministry of Health of Ukraine No. 59 dated January 29, 2013) and the local protocol: general work-up, EGD, determination of H. pylori antigen in feces, Ultrasonography of the abdominal organs to exclude concomitant pathology [10].

Quality of life assessment was carried out using the «Paediatric Quality of Life Inventory», «PedsQL»), which consists of 23 statements, grouped on 4 scales: health, emotional and physical well-being, labour productivity, relationships with others. The rate of disorders was assessed in points: 1 – «I never feel», 2 – «almost never», 3 – «sometimes», 4 – «often», 5 – «almost always» [8].

To assess the quality of life in the comprehensive treatment of FD, children were divided into 4 groups by simple randomization: 3 experimental and 1 control group with 20 patients each. The groups were comparable by sex, age, clinical options for FD, and the morbidity. All children received treatment according to the Unified Clinical Protocol of Medical Aid for Children with FD (Order of the Ministry of Health of Ukraine No. 59 dated January 29, 2013) and the local protocol (correction of the day regimen and diet, antacid, antisecretory drugs, prokinetics) [4]. Children of the first group received γ-amino-β-phenylbutyric acid hydrochloride as part of a comprehensive treatment at a dose of 100 mg t.i.d. for 1 month; children of the second group received a calcium salt of hopantenic acid as part of a comprehensive treatment at a dose of 125 mg (1/2 tablet) t.i.d. for 1 week; at a dose of 250 mg t.i.d. for 45 days; at a dose of 125 mg (1/2 tablet) t.i.d. for 1 week (total 2 months); at a dose of 250 mg q.i.d. for a month; children of group 3 received a complex of organic compounds of magnesium and B6 vitamin as part of a comprehensive treatment at a dose of 1 tablet q.i.d. for 1 month.

The clinical dynamics of the manifestations during treatment was assessed on the 3rd, 7th, 10th day, and after 1 month. During the last visit, an examination and psychological testing were carried out.

Statistical processing of the obtained data was carried out with the calculation of parametric and nonparametric criteria using standardized tools of Microsoft Excel 2010 and the *R* programming language for statistical data processing [19]. In the article, the data obtained are presented in the form of relative values and their deviations ($M \pm m$), absolute values from which the relative values are calculated, in *n*/*N* format, where n is the number of cases and *N* is the size of the corresponding group. Since the quantitative characteristics had a predominantly nonparametric distribution, they are presented in the *Me* format [*QR*: 25 %; 75 %], where *Me* is the median, *QR* is the quartile range. The normality of distribution was determined by the Kolmogorov-Smirnov and Shapiro-Wilk criteria, and the Smirnov-Grabs test was also carried out to determine gross errors of normally distributed data. The power of the sample is represented as (π), with the generally accepted $\pi = 0.80$, which was determined using the T-test. When comparing the dependent variables, since their distribution was nonparametric, the Wilcoxon T-test was used, and when comparing the independent variables – the nonparametric Kruskal-Wallis test. The difference between the values was considered statistically significant when the test significance level was $p < 0.05$.

3. Results

The main complaint of the children who participated in the study was abdominal pain, which by definition is the main diagnostic criterion for functional dyspepsia. A comparison of complaints with the Rome III and IV criteria made it possible to establish the presence of epigastric pain syndrome in 42.5 ± 0.5 % (34/80) of children, postprandial distress syndrome – in 57.5 ± 1.2 % (46/80) of examined patients. The average age of the children participating in the study was 10 years. The power of the sample was $\pi = 0.712$, which is slightly less than the generally accepted value ($\pi = 0.80$).

Quality of life assessment carried out using the PedsQL questionnaire, demonstrated the presence of disorders of physical functioning in all examined children. The highest score was obtained for the sense of pain – in 97.5 ± 1.2 % (78/80) of the examined patients, feeling weak – in 86.3 ± 2.2 % (69/80). A low energy level was also determined in 81.3 ± 2.4 % (65/80) of children. Thus, the median of indicators for the «physical functioning» block equaled 5 points [*QR*: 4; 5], which indicates a high level of disorders. According to the questionnaire data, children had frequent disorders in the field of emotional functioning – 5 points [*QR*: 4; 5]: most often, children were worried about a sense of fear for their health – in 91.3 ± 1.6 % (73/80) of cases and loss of sleep (poor falling asleep, troubled sleep), which was reported by 77.5 ± 2.2 % (62/80) of patients. The examined children had problems with functioning at school as well: the median of the assessment equaled 5 [*QR*: 4; 5], which corresponds to the «I feel problems very often» statement. Children's problems were associated with their absence at school due to sickliness in 88.8 ± 2.7 % (71/80) of patients and due to the need to see a doctor in 66.3 ± 1.7 % (53/80) of the examined patients. The level of problems with the social functioning block equaled 2 points [*QR*: 2; 3], which corresponds to the «sometimes I feel problems» statement.

After 1 month, when testing under the PedsQL questionnaire, children of the four groups reported an improvement in the quality of life. So, children, who received Phenibut, had physical functioning disorders with an intensity of 1 point [*QR*: 1; 1.25], which corresponds to the «I never have problems» statement, versus 5 points [*QR*: 4; 5] before treatment ($p_1 = 0.005$), the intensity of the physical functioning disorders in children in the control group after 1 month equaled 2 points [*QR*: 1; 2] versus 5 points [*QR*: 4; 5] before treatment ($p_1 = 0.063$), the children who took organic magnesium compounds as part of the comprehensive treatment, reported an improvement in this block of questions after treatment as well – 2 points [*QR*: 1.5; 3] versus 5 points [*QR*: 4; 5] before treatment ($p = 0.056$). The group of patients who took calcium hopantenate after treatment assessed the physical functioning disorders according to the «I never feel a problem» statement compared to the same option before treatment ($p = 0.013$). When comparing groups with each other, statistically better results in a month after treatment were found in groups taking GABA derivatives: thus, the physical functioning disorders in children taking Phenibut was significantly less than in the control group ($p = 0.016$). Children from the calcium hopantenate group assessed physical functioning disorders after treatment as 1 point [*QR*: 1; 2], statistically different from the control group ($p = 0.03$) **(Fig. 1).**

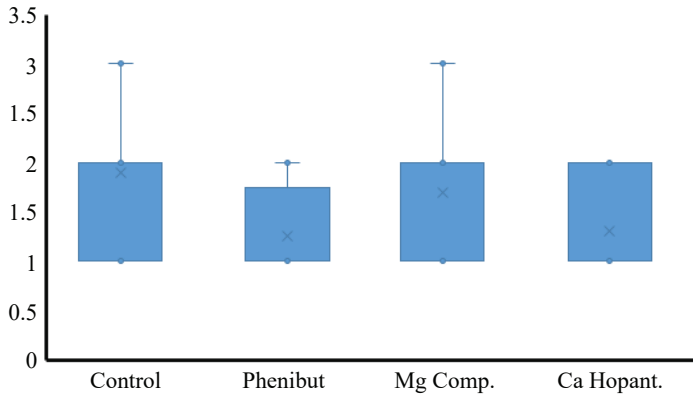

Fig. 1. Physical functioning

After 1 month, children from the Phenibut group did not report emotional functioning disorder – 1 point [*QR*: 1; 1] versus 5 points [*QR*: 4; 5] before treatment ($p=0.016$) and 3 points [*QR*: 2; 3] in children of the control group ($p<0.001$). No differences have been found one month after treatment between the group taking calcium hopantenate and the group taking Phenibut ($p=0.178$). Also, the Phenibut group showed the best results 1 point [*QR*: 1; 1] versus 2 points [*QR*: 1.5; 3] of the group taking the vitamin-mineral complex ($p=0.009$). The emotional functioning of children taking calcium hopantenate in a month equaled 1 point [*QR*: 1; 2], which corresponds to the «I never have problems» statement, versus 5 points [*QR*: 4; 5] before treatment ($p=0.032$) and 3 points [*QR*: 2; 3] of the control group ($p<0.001$). No differences have been found between the group taking calcium hopantenate and mineral-vitamin complex ($p=0.078$). Children who took mineral-vitamin complex, emotional functioning equaled 2 points [*QR*: 1.5; 3] versus 5 points [*QR*: 4; 5] before treatment ($p=0.059$) and 3 points [*QR*: 2; 3] of the control group ($p=0.04$) (**Fig. 2**).

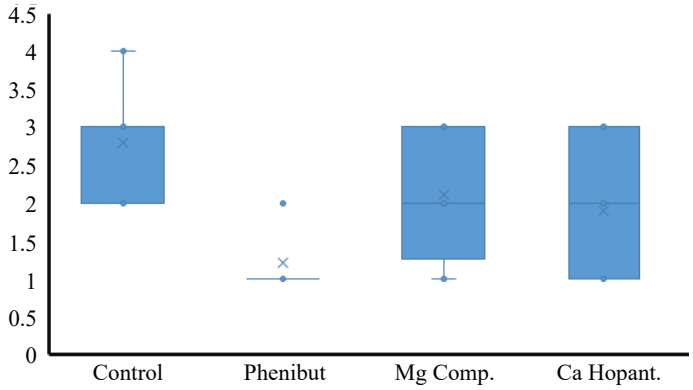

Fig. 2. Emotional functioning

The functioning at school in patients taking Phenibut 1 month after treatment equaled 1.5 points [*QR*: 1; 2], which corresponds to the «I never have problems» statement, versus 5 points [*QR*: 4; 5] before treatment ($p=0.003$), which corresponds to the «I feel problems very often» statement and versus 2.5 points [*QR*: 2; 3] of the control group ($p=0.005$) 2 points [*QR*: 2; 3] of the group taking the vitamin-mineral complex ($p=0.032$). No differences in this block of questions have been found at the group taking calcium hopantenate ($p=0.936$). Results on the functioning at school scale in patients taking calcium hopantenate, 1 month after treatment, equaled 1 point [*QR*: 1; 2] versus 5 points [*QR*: 4; 5] before treatment ($p=0.044$), also this indicator was statistically lower when compared with the control group ($p=0.004$) and the group taking the mineral-vitamin complex ($p=0.032$). No differences in functioning at school improvement one month after treatment have been found at the group taking the vitamin-mineral complex. There was also no statistical difference in the control group after treatment (**Fig. 3**).

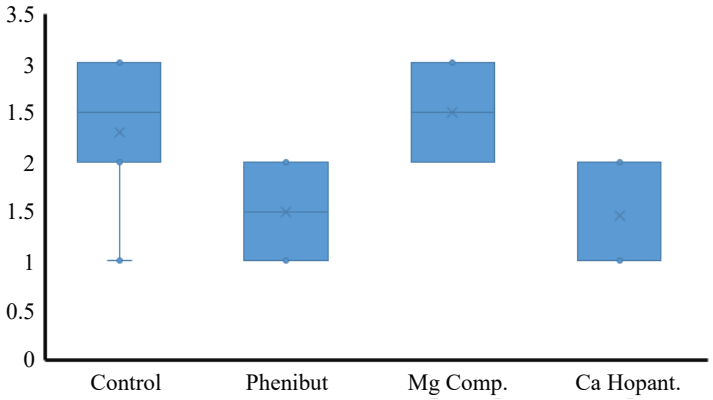

Fig. 3. Functioning at school

4. Discussions

The results of this study showed that patients with PD have significant impairments in quality of life in all areas of functioning, noted Varni et al., But we did not conduct psychological testing to detect depression and anxiety, which requires further study in combination with quality of life children [5, 8]. Tyurenkov and co-authors experimentally investigated and proved that GABA derivatives have a prophylactic effect in chronic psychoemotional stress [16, 17] and have a positive effect on the quality of life of patients [11, 16], which was noted in our study. GABA derivatives combine the properties of a neuroprotector and an anxiolytic [15, 17], so they can be used in the treatment of PD in children. As noted by MV Khaitovich in one study, GABA derivative therapy proved its effectiveness in schoolchildren with autonomic dysfunction: improved well-being, increased efficiency, anxiety and significantly improved, which is confirmed by the results of our study, but requires further deep study [12, 17].

Study limitations. The study was not conducted in case of identified concomitant pathology of another organs and in case of patients refuse to participate in the study.

Prospects for further research. Future studies on this issue should be randomized placebo-controlled, as well as in comparison with cognitive-behavioral therapy and in larger groups of patients with the calculation of cost-effectiveness.

5. Conclusion

1. Children with functional dyspepsia have a constant component of the clinical picture, along with gastroduodenal complaints, there is a violation of quality of life, namely physical and emotional dysfunction, as well as dysfunction at school, which occurs as a result of stress.

2. Inclusion in the complex therapy of functional dyspepsia of GABA drugs can significantly improve the quality of life of patients, their physical and emotional functioning and improve school performance.

3. The use of GABA drugs did not cause side effects and was well tolerated by the examined children, which indicates a high level of safety of this therapeutic approach.

4. The only possible disadvantage of this study is the somewhat insufficient statistical power, which indicates the need for further in-depth study of the use of GABA derivatives in the treatment of PD.

Conflicts of interest

The authors declare that they have no conflicts of interest.

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Received date 01.07.2020
Accepted date 20.10.2020
Published date 30.11.2020