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Antioxidants and Cognitive-Behavioral Therapy in Patients with Functional Dyspepsia

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Aim: development of an algorithm for the use of antioxidant cognitive-behavioral therapy in adult patients with functional dyspepsia.
Material and methods. The study included 112 adult patients with functional dyspepsia receiving the antioxidant drug Cytoflavin containing succinic acid, inosine, nicotinamide and riboflavin, and cognitive behavioral therapy according to the method of Beck and Jacobson in addition to the main therapy (prokinetics, proton pump inhibitors, psychotropic drugs).
Results. Of the total group, 74 patients had an optimal response to the inclusion of an antioxidant and psychotherapy in the treatment regimen (increased quality of life and reduced anxiety) and 38 patients had the insignificant response. It has been established that the main predictors of the successful use of an extended treatment regimen are the patient's disadaptation in relation to the disease, a recent stress factor, the duration of functional dyspepsia, the presence of an overlap syndrome (combination with other functional gastrointestinal disorders).
Conclusions. Based on the collection of a small amount of anamnestic information (the duration of functional dyspepsia, the presence of an acute stress factor in the anamnesis), the assessment of the presence of an overlap syndrome and disadaptation in relation to the patient to his illness, the value of the discriminant function is calculated. After comparing it with a threshold, the probability of a positive response to a combination of antioxidant and cognitive-behavioral therapy is estimated. The developed prediction algorithm is valid (sensitivity — 91 %, specificity — 73 %, accuracy — 84.8 %) and allows to optimize the definition of treatment tactics for a patient with functional dyspepsia.
Keywords: antioxidants, cognitive behavioral therapy, "gut — brain" axis, discriminant analysis, functional dyspepsia
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Применение антиоксидантов и когнитивно-бихевиоральной терапии у пациентов с функциональной диспепсией

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Цель исследования: разработка алгоритма применения антиоксидантной и когнитивно-бихевиоральной терапии у взрослых пациентов с функциональной диспепсией.
Материал и методы. В исследование включены 112 взрослых пациентов с функциональной диспепсией, получающих помимо основной терапии (прокинетики, ингибиторы протонной помпы, психотропные препараты) антиоксидантный препарат «Цитофлавин», содержащий янтарную кислоту, инозин, никотинамид и рибофлавин, и когнитивно-поведенческую терапию по методике Бека и Якобсона.
Результаты. Из общей группы у 74 пациентов наблюдался оптимальный ответ на включение антиоксиданта и психотерапии в схему лечения (повышение качества жизни и снижение уровня тревожности), у 38 пациентов ответ был незначительным. Установлено, что основными предикторами успешного применения расширенной схемы лечения являются наличие у пациента дезадаптации в отношении к болезни, недавно возникший стрессовый фактор, длительность функциональной диспепсии, наличие синдрома перекреста (сочетание с другими функциональными гастроинтестинальными расстройствами).
Выводы. На основании сбора небольшого объема анамнестической информации (продолжительность функциональной диспепсии, наличие стрессового фактора в анамнезе), оценки наличия синдрома перекреста и дезадаптации в отношении пациента к своей болезни рассчитывается значение дискриминантной функции. После сравнения его с порогом оценивается вероятность положительного ответа на комбинацию антиоксидантной и когнитивно-бихевиоральной терапии. Разработанный алгоритм прогноза является валидным (чувствительность — 91 %, специфичность — 73 %, точность — 84,8 %) и позволяет оптимизировать тактику лечения пациента с функциональной диспепсией.
Ключевые слова: антиоксиданты, когнитивно-бихевиоральная терапия, ось «мозг — желудочно-кишечный тракт», дискриминантный анализ, функциональная диспепсия
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Introduction

Improving the tactics of managing patients with dyspeptic complaints and functional dyspepsia (FD) is an urgent problem in Russia [1] and in the world [2, 3 including due to the high prevalence of this functional disease. According to I. Aziz et al. about 10 % of the adult population of the USA, Canada and Great Britain fall under the criteria of FD [4]. The socio-economic significance of the disease is recognized as one of the main causes of health system costs [2–4].

The debut of FD in some cases is associated with psychoemotional stress, it invariably proceeds with a change in a person's attitude to his/her condition and other negative deviations of mental state [2, 5]. The presence of a psychosomatic component in the pathogenesis (disturbances of interaction in the axis "brain — gastrointestinal tract" [6]) determines the effectiveness of psychotherapeutic techniques and psychoactive drugs in the treatment of FD, on which a consensus has been reached among gastroenterologists from different countries [2, 7, 8]. It is impossible not to mention the significant contribution of elevated levels of oxidative stress markers in the blood in patients with FD [9, 10]. The addition of antioxidants to standard FD therapy in our pilot study resulted in a significant improvement in the quality of life on the SF-36 questionnaire in terms of physical functioning scales, pain intensity, role functioning, physical component, as well as a decrease in the level of anxiety on the Hospital Anxiety and Depression Scale (HADS) [8]. According to the analysis of our own data, the effect on the psychological status of patients and antioxidant capacity in some diseases has proven to be a significant addition to existing conservative therapy regimens [12–15].

The history of the use of psychotherapy in the treatment of FD from the perspective of evidence-based medicine spans more than a decade, ranging from meta-analysis of several publications [16] and unproven efficacy to the synthesis of convincing evidence on the good effect of psychotherapy [7]. Among psychotherapeutic approaches, cognitive behavioral therapy, particularly the Beck and Jacobson technique, which effectiveness in the treatment of FD has been confirmed in a clinical trial [17], has been highlighted. Currently, psychotherapeutic techniques are successfully used as part of the complex therapy of chronic pain syndrome [18], skin diseases [19], multiple sclerosis [20] and oncology [21], rehabilitation after trauma and surgery [22].

Despite the sufficient elaboration of the application of psychotherapeutic techniques, currently no algorithms have been developed to predict their success and, accordingly, to determine the indications for prescription.

In our opinion, the joint application of psychotherapy aimed at removing and reducing neurotic manifestations, mobilization of the patient's will for the exact fulfillment of medical prescriptions, and antioxidant therapy, reducing oxidative stress in the CNS and stomach, affecting several links of FD pathogenesis at once, will increase the effectiveness

of the prescribed treatment. Evaluation of predictors of the effectiveness of this combination determined the purpose of the present study.

Aim of the research: to study the efficacy and develop an algorithm for the use of antioxidant cognitive behavioral therapy in adult patients with functional dyspepsia.

Material and methods

The study was conducted on the basis of the Medical Center of LLC "Expert Center "Academic"", St. Petersburg. The inclusion criterion was the diagnosis of "Functional dyspepsia". Diagnosis clarification and differential diagnosis were performed according to the Rome IV criteria (2016), and the recommendations of the Russian Gastroenterological Association [8].

The diagnosis of FD was established on the basis of the absence of signs of an organic lesion of the gastrointestinal tract on gastroduodenoscopy, abdominal ultrasound; the absence of the contamination of *H. pylori* or preliminary eradication with the control using acceptable diagnostic methods upon discontinuation of proton pomp inhibitors; the absence of anxiety symptoms, compliance with the criteria for functional dyspepsia.

The duration of the anamnesis of functional dyspepsia was assessed based on an oral questioning of patients about the duration of complaints, the alleged cause of the onset of their illness, indications of significant stressful domestic factors, as well as an analysis of the medical documentation provided by them.

Associated functional gastrointestinal disorders (FGIDs) were distinguished according to Rome IV criteria (predominantly irritable bowel syndrome and functional disorders of the gallbladder).

The sample included 112 people at the age of 25–56 years (54.5 % men, 45.5 % women) who received Cytoflavin in addition to the main therapy and also underwent sessions of cognitive-behavioral therapy. One tablet of Cytoflavin contains 0.3 g of succinic acid, 0.05 g of inosine, 0.025 g of nicotinamide and 0.005 g of riboflavin. Cytoflavin prescription scheme was as follows: two courses of 25 days, 2 tablets (300 + 50 + 25 mg) orally twice a day. The interval between the courses was 1 month. The main course of therapy included the appointment of all patients with omeprazole 20 mg twice a day for 3 weeks with a gradual dose reduction until withdrawal during the 4th week, as well as metoclopramide 10 mg 3 times a day for 10 days. The scheme was applied simultaneously during each of the two courses of Cytoflavin. Some patients participated in the study on the background of periodic course therapy with aminophenylbutyric acid 250 mg 3 times a day (for patients with neurosis — as prescribed by a neurologist) or amitriptyline 50 mg per day (for patients with sleep disorders — as prescribed by a neurologist).

The study design was approved at the meeting of the Scientific and Technical Council of the Expert Center Academic LLC, protocol No. 1/3 of 14.01.2022 (order of the General Director of ECA LLC No. 24 of 17.01.2022).

The technique of cognitive behavioral therapy by Beck and Jacobson was chosen as the psychotherapeutic influence [17]. Psychological support consisted of ten weekly sessions where the first eight ones were group sessions and the last two — individual sessions. During the sessions, patients received: a) information about functional dyspepsia; b) cognitive-behavioral therapy according to Beck's method, aimed at modifying the influence of certain cognitive problems on gastrointestinal symptoms; and c) progressive-muscular relaxation according to Jacobson, to provide the ability to relax in certain stressful situations. This technique was created to reduce anxiety by alternately tensing and relaxing muscles.

Before and after the treatment, patients were evaluated using the SF-36 quality of life questionnaire and the HADS anxiety and depression assessment questionnaire. The scope of the first examination also included the ATTD (attitude to the disease) questionnaire consisting of 12 scales describing different types of attitude to the disease, combined into 3 blocks according to the principles of "adaptability/maladaptability" and "interpsychic/intrapsychic orientation of maladaptation". The first block included patients whose mental and social adaptation was not significantly disturbed, while the second and third blocks included patients with mental maladaptation. The presence of maladaptation was established if any of the types of attitude to the disease, belonging to the block of intrapsychic or interpsychic maladaptation, received the maximum number of points among the others.

According to the dynamics of quality of life and clinical manifestations of anxiety, the effectiveness of adding the combination "Cytoflavin + Cognitive Behavioral Therapy" (hereinafter — "CTF + CBT") to the therapy of PD was evaluated. Thus, the shift of indicators of the scales "Physical functioning", "Pain intensity", "Role functioning due to emotional state", "Physical component of health" by 5 % from the initial one, by 2 points for the level of anxiety was taken as reference values. If the patient's dynamics on the background of complex treatment exceeded the established threshold values, the result was considered clinically significant, and if they were not reached, the result was considered insignificant. According to the results of this evaluation, 74 people were classified into the group with clinically significant improvement (optimal efficacy of the combination "CTF + CBT", group 1), and 38 people were classified into the group with insignificant improvement (insufficient efficacy of the combination "CTF + CBT", group 2).

The search for predictors of clinical improvement in patients with FD, who in addition to the main

therapy receive the combination of "CTF + CBT" was the basis for the development of the algorithm of prescribing this combination.

As the factors that were tested for the presence of connection with efficacy, we selected sex and age, anthropometric data, values of the scales of the attitude to the disease questionnaire (ATTD), the presence of bad habits (smoking, alcohol), acute stress factor in the anamnesis (up to 4 weeks), the presence of combination of FD with other functional disorders of the gastrointestinal tract (GIT) (overlap syndrome).

Statistical processing of the obtained data was performed on the basis of a personal computer in Excel 2013 tabular processor and IBM SPSS Statistics 22.0 application program package.

Taking into account different group sizes, the allocation of significant quantitative predictors was performed using the nonparametric Wilcoxon *U*-criterion. The description of the data and their variance was as follows: *Me* (Q25; Q75), where *Me* is the median, Q25 and Q75 are 25 % and 75 % quartiles, respectively. The selection of significant nominal predictors was performed using Fisher's exact criterion. Predictors that differed significantly between groups were selected for the classification rule construction step.

The decisive rule was constructed using discriminant analysis. The applicability of this method was tested using cross-validation (leave-one-out type) and M-Box criterion. The smaller sample size (38 cases) allows us to develop a classifier function on it. The stepwise selection criterion chosen is the Mahalanobis distance. According to the results, a canonical discriminant function was obtained, which determines on the basis of the available data under the condition of a priori known classification the patient's belonging to the prognostic group. The validity of the function was checked by calculating the eigenvalues of the function (Wilks' Λ) and the canonical correlation. The critical level of significance at which the null hypothesis of no differences between groups and subgroups was rejected was chosen as $p < 0.05$.

Results

According to the results of preliminary evaluation, discriminant analysis was found to be applicable to the obtained data: equivalence of covariance matrices was achieved (M-Box = 17.95; $p > 0.05$), loss of accuracy on cross-validation was less than 1 %.

The group of patients with optimal and insufficient efficacy of the combination of "CTF + CBT" with standard therapy differed significantly in the frequency of smoking, presence of maladaptation in attitude to the disease according to the results of the ATTD questionnaire, presence of stress factor in the last three months, presence of overlap-syndrome and FD duration in general (Table 1).

The specified variables were admitted to the step of classifying rule construction. The result of the step-by-step inclusion is presented in Table 2: the unstandardized coefficients of the equation of the classifying discriminant function, as well as the standardized coefficients for the comparative evaluation of the variables' contribution to the case classification are given.

Using the data in Table 2, formula (1) is constructed.

$$d = 0.214 - 0.146 \times FD + 0.631 \times OS + 1.081 \times SF + 0.858 \times DD, \quad (1)$$

where d is the discriminant function; FD — duration of FD history, years; OS — overlap syndrome

Table 1. Parameters that differ in groups of patients with functional dyspepsia depending on the effectiveness of the "Cytoflavin + CBT" combination

Таблица 1. Показатели, отличающиеся в группах пациентов с функциональной диспепсией в зависимости от эффективности комбинации «ЦТФ + КБТ»

Parameter Показатель	Group 1 Группа 1 $n = 74$	Group 2 Группа 2 $n = 38$	Significance Значимость
Smoking, % Курение, %	29.3 %	59.5 %	$p = 0.004$
Misadaptation in relation to the disease, % Дезадаптация в отношении к болезни, %	58.7 %	32.4 %	$p = 0.015$
There was a stressful factor in the last three months, % Был стрессовый фактор за последние три месяца, %	68.0 %	24.3 %	$p < 0.001$
Overlap syndrome, % Сочетание ФД с другими функциональными заболеваниями ЖКТ, %	61.3 %	37.8 %	$p = 0.026$
Duration of functional dyspepsia, years* Длительность анамнеза ФД, лет*	8 (5; 11)	14 (11.5; 20)	$U = 532.0$; $Z = -5.0$; $p < 0.001$

Note: FD — functional dyspepsia; overlap syndrome — a combination of functional dyspepsia with other functional disorders of the gastrointestinal tract; * — data are presented in the form of median, 25 % and 75 % quartiles.

Примечание: ФД — функциональная диспепсия; * — данные представлены в виде медианы, 25%-го и 75%-го квартилей.

Table 2. Obtained coefficients of the discriminant function

Таблица 2. Полученные коэффициенты дискриминантной функции

Component Компонент	Non-standardized coefficient Нестандартизованный коэффициент	Standardized coefficient Стандартизованный коэффициент
Misadaptation in relation to the disease Дезадаптация в отношении к болезни	0.858	0.419
There was a stressful factor in the last three months Был стрессовый фактор за последние три месяца	1.081	0.496
Overlap syndrome Сочетание ФД с другими функциональными заболеваниями ЖКТ	0.631	0.310
Duration of functional dyspepsia Длительность анамнеза ФД	–0.146	–0.771
Constant Константа	0.214	–

Note: FD — functional dyspepsia; overlap syndrome — a combination of functional dyspepsia with other functional disorders of the gastrointestinal tract.

Примечание: ФД — функциональная диспепсия.

(1 — there is one, 0 — there is none); *SF* — a stressor in the last three months (1 — there was one, 0 — there was none); *DD* — maladaptation in relation to the desease (1 — there is one, 0 — there is none).

The group centroid values were 0.604 and –1.224 for the group of successful inclusion of the "CTF + CBT" combination in standard FD therapy and unsuccessful use, respectively. The discrimination constant (arithmetic mean of centroid values) was –0.310. If the value of the function d for any patient is exceeded, a conclusion is made about the predicted success of the combination "CTF + CBT", otherwise — the effectiveness of this combination is considered unproven.

Thus, the indicators of maladaptation in relation to the disease, the appearance of a clear stress factor in the last three months and the detection of other GI diseases in the patient have a positive relationship with the success of the combination "CTF + CBT", because their value of "1" (there is a sign) allows increasing the probability of assigning the case to the group of "successful". On the contrary, the relationship is negative for FD experience: as it increases, the probability of assigning the patient to the "unsuccessful" group increases. It should be noted that the greatest influence on the classification of a case (standardized coefficients of Table 2) is exerted by the number of years of FD history; to a lesser extent, the presence of crossing syndrome has an impact on the efficacy of adding the combination of "CTF + CBT" to the main therapy.

The function construction result was satisfactory ($\Lambda = 0.57$; $p < 0.001$; $r_{canon} = 0.66$), sensitivity was 91 %; specificity was 73 %, and the overall percentage of correctly classified cases was 84.8 % (Table 3). Thus, the quality of the function performance was recognized as valid.

Discussion

Based on the results of our study, we selected several predictors of the success of the inclusion of antioxidant treatment and psychotherapy in the course of standard therapy of FD.

Thus, we found that the success of the combination of "CTF + CBT" significantly depends on the time of having FD. A long history of the disease is often inherent in patients with chronic external influence (bad habits, occupational hazards, etc.), which explains both the decrease in the effectiveness of psycho- and antioxidant therapy in this category of individuals, and the "dropping out" of the model of the factor "smoking" as not contributing additional information to the classification.

Patients with a recent onset of a stressor may respond better to the proposed combination due to the lack of persistent attitudes and incomplete adaptation to it. This may be due, on the one hand, to the incomplete reorganization of relationships in the "brain — gut" axis with the formation of persistent functional impairment, on the other hand, to the so far insignificant consequences of oxidative stress [23, 24].

The presence of patient's maladaptation in relation to their disease is also associated with the success of antioxidant treatment and psychotherapy. Perhaps, it is connected with actualization (up to accentuation) by patients of their disease in contrast to individuals who diminish its importance. In the presence of patient fixation on their condition, points of application arise for both psychotherapy due to the availability of a substrate to work with, and for prescribing antioxidants due to higher levels of psychological distress [16].

The combination of FD in a patient with other functional gastrointestinal disorders or with organic

Table 3. Case classification results

Таблица 3. Результаты классификации случаев

Group Группа		Predicted group membership Предсказанная принадлежность к группе	
		“successful” «успешная»	“unsuccessful” «неуспешная»
Actual group membership Фактическая принадлежность к группе *n* (%)	“successful” «успешная»	68 (90.7 %)	7 (9.3 %)
	“unsuccessful” «неуспешная»	10 (27.0 %)	27 (73.0 %)

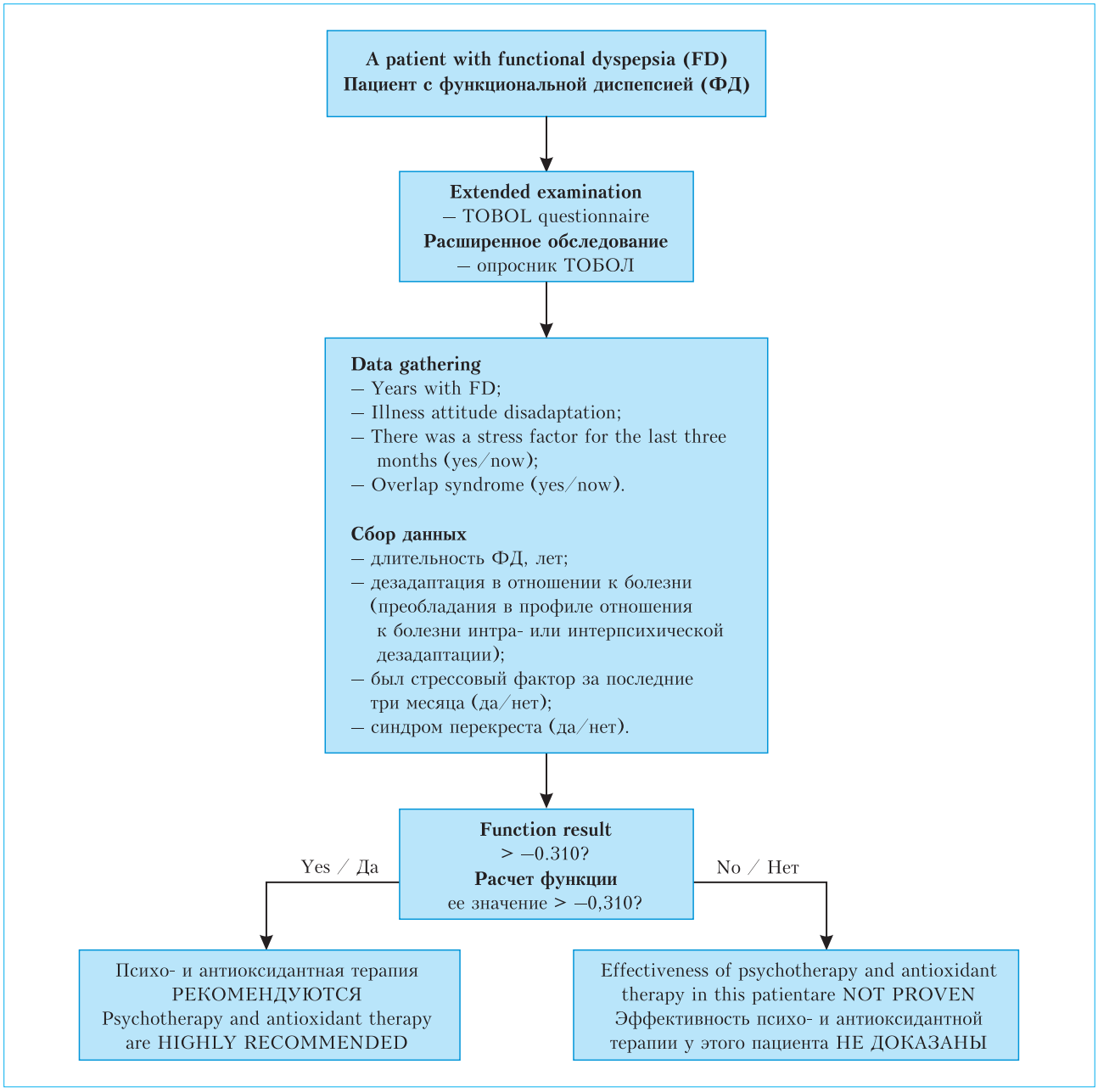

Figure. Decision support algorithm for prescribing psycho- and antioxidant therapy in adult patients with functional dyspepsia

Рисунок. Алгоритм поддержки принятия решения о назначении психо- и антиоксидантной терапии у взрослых пациентов с функциональной диспепсией

pathology is invariably associated with increased afferent impulse in the CNS and increased levels of oxidative stress [5, 25], as well as with the aggravation of mental maladaptation and deepening of changes in the "brain — gut" axis [6]. Apparently, the presence of these points of application is associated with the success of the "CTF + CBT" combination.

The limitations of this study are the small sample size, the analysis on the patient population of St. Petersburg, and the use of only one combination of antioxidant and psychotherapy. A comparative evaluation of the efficacy of similar combinations of psycho-antioxidant therapy was not performed.

The main purpose of implementing the algorithm in practice is to rationalize therapeutic tactics in relation to a patient with functional dyspepsia.

Conclusion

The application of discriminant analysis allowed us to develop an algorithm for predicting the success of including the combination of "CTF + CBT" in the standard therapy of patients with FD (Fig.), which can be proposed for use in clinical gastroenterology. The basis of the algorithm is the calculation of the discriminant function value taking into account: the duration of FD, the presence of maladaptation in attitude to the disease according to the results of the ATTD (attitude to the disease) test, the presence of crossing syndrome, the presence of stress factor for the last three months. The value of this coefficient greater than –0.310 suggests a high probability of a positive response to the combination of "CTF + CBT".

References / Литература

1. *Ивашкин В.Т., Маев И.В., Лапина Т.Л., Федоров Е.Д., Шептулин А.А., Трухманов А.С. и др.* Клинические рекомендации Российской гастроэнтерологической ассоциации и ассоциации «Эндоскопическое общество РЭНДО» по диагностике и лечению гастрита, дуоденита. *Российский журнал гастроэнтерологии, гепатологии, колопроктологии.* 2021;31(4):70–99. [*Ivashkin V.T., Maev I.V., Lapina T.L., Fedorov E.D., Sheptulin A.A., Trukhmanov A.S., et al.* Clinical recommendations of Russian gastroenterological association and RENDO Endoscopic Society on diagnosis and treatment of gastritis and duodenitis. *Russian Journal of Gastroenterology, Hepatology, Coloproctology.* 2021;31(4):70–99 (In Russ.)]. DOI: 10.22416/1382-4376-2021-31-4-70-99
2. *Wauters L., Dickman R., Drug V., Mulak A., Serra J., Enck P., et al.* United European Gastroenterology (UEG) and European Society for Neurogastroenterology and Motility (ESNM) consensus on functional dyspepsia. *United European Gastroenterol J.* 2021;9(3):307–31. DOI: 10.1002/ueg2.12061
3. *Miwa H., Nagahara A., Asakawa A., Arai M., Oshima T., Kasugai K., et al.* Evidence-based clinical practice guidelines for functional dyspepsia 2021. *J Gastroenterol.* 2022;57(2):47–61. DOI: 10.1007/s00535-021-01843-7
4. *Aziz I., Palsson O.S., Törnblom H., Sperber A.D., Whitehead W.E., Simrén M.* Epidemiology, clinical characteristics, and associations for symptom-based Rome IV functional dyspepsia in adults in the USA, Canada, and the UK: A cross-sectional population-based study. *Lancet Gastroenterol Hepatol.* 2018;3(4):252–62. DOI: 10.1016/S2468-1253(18)30003-7
5. *Koloski N.A., Talley N.J., Boyce P.M.* Predictors of health care seeking for irritable bowel syndrome and nonulcer dyspepsia: A critical review of the literature on symptom and psychosocial factors. *Am J Gastroenterol.* 2001;96(5):1340–9. DOI: 10.1111/j.1572-0241.2001.03789.x
6. *Drossman D.A., Hasler W.L.* Rome IV — functional GI disorders: Disorders of gut-brain interaction. *Gastroenterology.* 2016;150(6):1257–61. DOI: 10.1053/j.gastro.2016.03.035
7. *Rodrigues D.M., Motomura D.I., Tripp D.A., Beyak M.J.* Are psychological interventions effective in treating functional dyspepsia? A systematic review and meta-analysis. *J Gastroenterol Hepatol.* 2021;36(8):2047–57. DOI: 10.1111/jgh.15566
8. *Ивашкин В.Т., Маев И.В., Шептулин А.А., Лапина Т.Л., Трухманов А.С., Картавенко И.М. и др.* Клинические рекомендации Российской гастроэнтерологической ассоциации по диагностике и лечению функциональной диспепсии. *Российский журнал гастроэнтерологии, гепатологии, колопроктологии.* 2017;27(1):50–61. [*Ivashkin V.T., Mayev I.V., Sheptulin A.A., Lapina T.L., Trukhmanov A.S., Kartavenko I.M., et al.* Diagnosis and treatment of the functional dyspepsia: Clinical guidelines of the Russian Gastroenterological Association. *Russian Journal of Gastroenterology, Hepatology, Coloproctology.* 2017;27(1):50–61 (In Russ.)]. DOI: 10.22416/1382-4376-2017-27-1-50-61
9. *Ebik B., Aslan N., Ekin N., Bacaksiz F., Arpa M., Neselioglu S., et al.* Oxidative stress and the importance of *H. pylori* eradication in patients with functional dyspepsia. *Saudi J Gastroenterol.* 2022;28(6):434–40. DOI: 10.4103/sjg.sjg_114_22
10. *Suzuki H., Nishizawa T., Tsugawa H., Mogami S., Hibi T.* Roles of oxidative stress in stomach disorders. *J Clin Biochem Nutr.* 2012;50(1):35–9. DOI: 10.3164/jcbn.11-115SR
11. *Сапожникова Т.В., Парфенов С.А., Елькин А.А., Ризаханов Д.М., Ризаханова О.А.* Влияние цитофлавина на качество жизни пациентов с функциональной диспепсией. *Экспериментальная и клиническая гастроэнтерология.* 2022;8:133–40. [*Sapozhnikova T.V., Parfenov S.A., Elkin A.A., Rizakhanov D.M., Rizakhanova O.A.* Effect of cytoflavin on the quality of life of patients with functional dyspepsia. *Experimental and Clinical Gastroenterology.* 2022;8:133–40 (In Russ.)]. DOI: 10.31146/1682-8658-ecg-204-8-133-140
12. *Захаров К.И., Белов В.Г., Парфенов Ю.А., Парфенов С.А., Ершов Е.В., Сапожников К.В. и др.* Обоснование применения препарата «Цитофлавин» и когнитивно-поведенческой терапии в комплексном лечении пациентов старшей группы с деформирующим коксартрозом. *Успехи геронтологии.* 2019;32(3):439–44. [*Zakharov K.I., Belov V.G., Parfenov Yu.A., Parfenov S.A., Ershov E.V., Sapozhnikov K.V., et al.* Substantiation of the drug "Cytoflavin" application and cognitive-behavioral therapy in complex treatment of deforming coxarthrosis in elderly patients. *Advances in Gerontology.* 2019;32(3):439–44 (In Russ.)].
13. *Парфенов С.А.* Терапия хронических форм верхушечного периодонтита в пожилом возрасте. *Успехи геронтологии.* 2013;26(3):553–7. [*Parfenov S.A.* Therapy of chronic forms of apical periodontitis in old age. *Advances in Gerontology.* 2013;26(3):553–7 (In Russ.)].
14. *Парфенов Ю.А., Ильинский Н.С., Парфенов С.А.* Влияние препарата Цитофлавин на психофизиологический статус больных алкоголизмом. *Поликлиника.* 2016;4–3:39–42. [*Parfenov Yu.A., Ilyinsky N.S., Parfenov S.A.* The effect of the drug Cytoflavin on the psychophysiological status of patients with alcoholism. *Poliklinika.* 2016;4–3:39–42 (In Russ.)].

15. *Белов В.Г., Парфенов Ю.А., Василевская М.А., Парфенов С.А., Коваленко А.Л., Заплутанов В.А.* Оценка влияния БОС-терапии и Цитофлавина на динамику клинико-психофизиологического статуса у пожилых пациентов с остеохондрозом. *Успехи геронтологии*. 2017;4(30):601–8. [*Belov V.G., Parfenov Yu.A., Vasilevskaya M.A., Parfenov S.A., Kovalenko A.L., Zaplutanov V.A.* Evaluation of the effect of BOS therapy and Cytoflavin on the dynamics of clinical and psychophysiological status in elderly patients with osteochondrosis. *Advances in Gerontology*. 2017;4(30):601–8 (In Russ.)].
16. *Soo S., Forman D., Delaney B.C., Moayyedi P.* A systemic review of psychological therapies for nonulcer duspepsia. *Am J Gastroenterol*. 2004;99(9):1817–22. DOI: 10.1111/j.1572-0241.2004.30086.x
17. *Orive M., Barrio I., Orive V.M., Matellanes B., Padierna J.A., Cabriada J., et al.* A randomized controlled trial of a 10 week group psychotherapeutic treatment added to standard medical treatment in patients with functional dyspepsia. *J Psychosom Res*. 2015;78(6):563–8. DOI: 10.1016/j.jpsychores.2015.03.003
18. *Турик Е.В.* Психокоррекционная работа с пациентами, страдающими хронической болью в спине. *Северо-Кавказский психологический вестник*. 2019;17(1):5–12. [*Turik E.V.* Psychocorrective work with patients suffering from chronic back pain. *Severo-Kavkazskii psikhologicheskii vestnik — North-Caucasian Psychological Bulletin*. 2019;17(1):5–12 (In Russ.)].
19. *Добаева Н.В., Кибрик Н.Д.* Психотерапевтическая коррекция сексуальных дисфункций у лиц с хроническими дерматозами. *Психиатрия, психотерапия и клиническая психология.* 2020;11(1):206–12. [*Dobaeva N.V., Kibrik N.D.* Psychotherapeutic correction of sexual dysfunctions in persons with chronic dermatoses. *Psychiatry, psychotherapy and clinical Psychology.* 2020;11(1):206–12 (In Russ.)]. DOI: 10.34883/PI.2020.11.1.020
20. *Каяшева О.И.* Экзистенциальные аспекты переживания страха смерти больными с рассеянным склерозом. *Современная наука: актуальные проблемы теории и практики. Серия: Познание.* 2022;6:47–52. [*Kayasheva O.I.* Existential aspects of experiencing the fear of death in patients with multiple sclerosis. *Modern science: actual problems of theory and practice. Series: Cognition.* 2022;6:47–52 (In Russ.)]. DOI: 10.37882/2500-3682.2022.06.12
21. *Блинова К.А., Пчелинцева Е.В., Лапочкина Н.П.* Клинический случай сочетанной коррекции детского психотравмирующего опыта и дистресса при развитии онкологического заболевания. *Исследования и практика в медицине*. 2020;7(1):75–82. [*Blinova K.A., Pchelintseva E.V., Lapochkina N.P.* A clinical case of combined correction of children's traumatic experience and distress in the development of cancer. *Research and Practical Medicine Journal*. 2020;7(1):75–82 (In Russ.)]. DOI: 10.17709/2409-2231-2020-7-1-8
22. *Гусакова Е.В., Пасечник И.Н.* Междисциплинарный подход к лечению хирургического больного: роль врача-реабилитолога. *Кремлевская медицина. Клинический вестник*. 2019;1:99–104. [*Gusakova E.V., Pasechnik I.N.* A multidisciplinary approach to the treatment of the surgical patient: The role of the physician rehabilitation. *Kremlin Medicine Journal*. 2019;1:99–104 (In Russ.)]. DOI: 10.26269/qk3v-8n89
23. *Foster J.A., Rinaman L., Cryan J.F.* Stress and the gut-brain axis: Regulation by the microbiome. *Neurobiol Stress*. 2017;19(7):124–36. DOI: 10.1016/j.ynstr.2017.03.001
24. *Maes M., Kubera M., Leunis J.C., Berk M., Geffard M., Bosmans E.* In depression, bacterial translocation may drive inflammatory responses, oxidative and nitrosative stress (O&NS), and autoimmune responses directed against O&NS-damaged neoepitopes. *Acta Psychiatr Scand*. 2013;127(5):344–54. DOI: 10.1111/j.1600-0447.2012.01908.x
25. *Wang Y., Chen Y., Zhang X., Lu Y., Chen H.* New insights in intestinal oxidative stress damage and the health intervention effects of nutrients: A review. *Journal of Functional Foods*. 2020;75:104248. DOI: 10.1016/j.jff.2020.104248

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