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ORIGINAL ARTICLE

THERAPY OF POST-COVID DEPRESSION: A PROACTIVE PSYCHOSOMATIC APPROACH

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ABSTRACT

Aim: Evaluation of the effectiveness of the early 8-week monotherapy with escitalopram as a form of proactive psychosomatic intervention for patients with post-COVID depression.

Materials and methods: 44 patients with post-COVID depression were involved in a proactive psychosomatic intervention in the form of an 8-week intake of escitalopram (Medogram, Medochemie Ltd) for 2–8 weeks in the case of a diagnosis of severe depression. Hamilton Depression Scale (HAM-D), Somatic Symptom Scale (SSS-8), Quality of Life Scale (CQLS) were used to assess symptoms and status dynamics.

Results: Patients with post-COVID depression after an 8-week course of escitalopram therapy showed a significant reduction in mental and somatic symptoms of depression and an improvement in quality of life. At the time of enrollment in the study, 12 (28.58%) individuals had mild depression, 15 (35.71%) had moderate depression, and 15 (35.71%) had severe depression. At the end of the 8th weeks of taking the drug in 24 (57.14%) there were no signs of depression on the HAM-D scale, in 18 people there were subclinical manifestations of depression. The effectiveness of escitalopram in reducing the symptoms of depression in this study was 66%.

Conclusions: With the introduction of pharmacotherapy with escitalopram there was a significant reduction in mental and somatic symptoms of depression and an improvement in quality of life. Escitalopram (Medochemie Ltd) may be an effective drug for psychopharmacotherapy of depressive symptoms in patients who have had COVID-19. Further studies are promising its effectiveness in the treatment of post-COVID depression.

KEY WORDS: proactive psychosomatic medicine, COVID-19, depression, escitalopram

INTRODUCTION

In recent years, the world has been developing and implementing a proactive approach to providing psychiatric care to patients of multidisciplinary hospitals, based on the theoretical foundations of psychosomatic medicine and its clinical embodiment – consultative-liaison psychiatry [1]. Proactive psychosomatic medicine (PPM) is a new way of providing psychological and psychiatric services in general medical departments, based on the principles of initiative, dedication, intensity and integration into general medical care [2].

The basis for the evolution of the system of psychological and psychiatric care was the need to effectively manage the psychological and social aspects of any disease, because it is these aspects that are partly an important reason for the lack of effectiveness of therapy and the patient's long stay in the hospital [3]. Recent baseline studies, meta-analyses and expert consensuses on proactive psychiatric counseling in 2011–2018 [2–5] noted that 20 to 40% of patients in multidisciplinary hospitals also suffer with mental illness, which can significantly complicate the course, effectiveness of therapy and prognosis of somatic pathology. Mental illness in patients of multidisciplinary hospitals partly interferes with timely discharge from the hospital, causes a greater number of additional consultations of related specialists and increases the overall cost of medical care. Based on these studies, it was recognized that psychiatric counseling is of great importance for the

Table 1. Consultative-liaison psychiatry: traditional and proative models (modif. Sledge W.H., Lee H.B., 2015) [4]

Characteristic	Traditional model	Proactive model
Type of assistance	Sole proprietorship: psychiatrist	Multidisciplinary: psychiatrist, primary care physician, nurse, social worker
Case definition	Consultation at the request of the attending physician	Screening based on anamnesis, medical records and report of nursing staff
Method of intervention	Recommendations for the attending physician (entry in the outpatient card / medical history)	Joint supervision with close supervision
Purpose of the intervention	Recommendations for treatment, risk reduction =and crisis management	Prevention of behavioral barriers to care, avoidance of crises, synergy of suppliers
Permanent location	Outside the multidisciplinary hospital	Multidisciplinary team in the staff of a multidisciplinary hospital

supervision of patients of a somatic profile, and the main features of the traditional and proactive models of consultative and communicative psychiatry were identified (Table 1.) [4].

Published in 2019 HOME studies [6] have made more specific recommendations on how hospital psychiatric services should be organized and what specific interventions are needed for patients:

1. Early proactive biopsychosocial evaluation of newly hospitalized patients using a biopsychosocial approach to identify all problems, including mental illness.
2. Creating a plan for comprehensive supervision and systematic management of problems that create potential obstacles to a quick discharge from the hospital.
3. Implementation of a comprehensive supervision plan with daily examinations of the patient on the progress of the psychosomatic state.
4. Integrated work with the staff of local departments (doctors, nurses, other consultants and social assistance specialists) and out-of-hospital services to ensure the implementation of the comprehensive supervision plan.

In 2019 The American Psychiatric Association's Board of Consultative and Communication Psychiatry initiated the development of a resource document on proactive counseling and communication psychiatry, which was approved for publication on December 12, 2020. This document notes the implementation of the model of proactive consultative-liaison psychiatry which contents four elements:

- systematic screening for actual mental health problems in patients with a somatic profile (patients admitted to certain medical institutions are systematically checked for signs of active mental health problems, especially those that may jeopardize the provision of care);
- early clinical intervention (proactive measures adapted to individual patients, with acombination of interventions for somatic and mental disorders);
- providing care on the basis of a team multidisciplinary approach (the mental
- health team is part of the structure of the multidisciplinary hospital and provides comprehensive mental health care directly in the general hospital);
- integration of care with primary teams and services (a proactive psychological and psychiatric team closely coordinates work with primary services in real time, often between clinicians of relevant experience: from doctor to doctor, from nurse to doctor /nurse, from social worker to social worker / rehabilitation specialist, and vice versa).

It is the proactive models of mental health care that have been tested by the COVID-19 pandemic. Some hospitals have decided to create separate departments specifically designed to treat patients with acute psychiatric needs and COVID-19 [7]. The rest have chosen to create units of psychological-psychiatric or consultative-liaison psychiatric care in the structure of multidisciplinary hospitals [8, 9]. The latest scientific medical literature highlights the potential of proactive psychological and psychiatric care, to help reduce costs and length of hospital stay, which are critical goals during this pandemic [10–13].

In addition to psychoeducation, increased motivation and adherence to treatment and emotional support, the authors note that clinically defined depression and other mental disorders seen in patients requiring infectious isolation in hospitals are also expected to be prevented and treated. [11].

Indeed, infectious diseases, including respiratory viral diseases, quite often lead to longterm negative medical, biological and psychosocial consequences in sick persons [14]. Novel coronavirus disease of 2019 (COVID-19), a systemic infection that could potentially target various organs and functions, is the most complex pandemic in the twenty-first century [15]. The death rate from COVID-19 is approximately in the range of 3.4–5.5%, which is significantly higher than for seasonal influenza caused by the influenza virus (1%) [16]. Moreover, despite the fact that effective COVID-19 vaccines continue to be approved and distributed around the world, these injections are one step in a multi-step process to combat the challenges posed by the pandemic. Even with millions of people receiving COVID-19 vaccines, the virus will continue to spread, and viral mutations will continue to test the effectiveness of available vaccines. Many health experts argue that identifying a medication that can prevent people from developing severe COVID-19 illness is also important, especially when it is an inexpensive and widely available treatment [15].

COVID-19 has a significant impact on people's mental health and quality of life. It is associated with numerous psychological and societal effects, in particular with an increase in the number of reports of an increase in the number of mental disorders [17, 18]. Although recent evidence suggests that in about 18% of patients who have had SARS-CoV-2 infection, a psychiatric diagnosis is established between 14 and 90 days after infection, longterm data show that approximately 1 in 3 COVID-19 patients experiences neurological or psychiatric disorders 6 months after infection.

During the COVID-19 pandemic, the number of symptoms of depression reported by patients increased 3-fold compared to the previous period [19, 20]. Already during COVID-19, about 50% of patients report symptoms of depression [20]. A significant proportion of patients after coronavirus report persistent fatigue, shortness of breath and neuropsychological symptoms [21]. After overdressed depressive symptoms are also observed in most people – up to 39% [22]. Persistent mental problems with a critical level of depression are observed in COVID-19 survivors even 1 year after discharge from the hospital [23]. A number of researchers argue that due to depressive manifestations, persons who survived COVID-19 can be considered a risk group for suicide [24].

The mentally related effects of COVID-19 are likely to be present for a long time and reach their peak later than the pandemic itself [18, 25]. In addition to social phenomena, for example, associated with lockdown, the cause of disturbances may be that the coronavirus is able to stimulate the development of psychological consequences through direct infection of the central nervous system or indirectly through the immune response [26]. Various mental disorders, including those of the depressive spectrum, have been linked to neuroinflammatory processes [27].

Although mental health research currently focuses on social anxiety and quarantine measures, mental disorders caused by COVID-19 may become a problem to be addressed in the future [28]. Research is needed on how to reduce the negative burden of post-COVID mental problems, in particular depressive disorders [18]. Thus, a number of therapy issues should be addressed, including the question of effective psychopharmacological treatment of post-COVID depression.

A recent meta-analysis [29] of studies conducted in individuals with depressive disorder after antidepressant treatment, predominantly including selective serotonin severe reuptake inhibitors (SSRIs), confirms that in general, antidepressants may be associated with a decrease in plasma levels of 4 of the 16 inflammations, including IL-10, TNF-α and CCL-2, which are associated with the severity of COVID-19 [30], as well as IL-6, which is highly correlated with mortality from disease [31, 32]. These findings are consistent with a preliminary meta-analysis of 22 studies conducted by Hannestad et al. in 2011, where it has been shown that treatment with SSRIs can reduce levels of IL-1β, IL-6, and possibly TNF-α [33].

N. Hoertel et al. [34] reported the first major observational study of antidepressant use in COVID-19. They conducted a retrospective multicenter cohort study that examined the association between antidepressant use and the risk of intubation or death in 7345 adults hospitalized with COVID-19. 257 patients received SSRIs, 71 patients received SSRIs, 59 patients received tricyclic antidepressants, 94 – received tetracyclic antidepressants, 44 – antidepressants of α2-antagonists, 6885 patients did not receive antidepressant treatment. The authors concluded that the effects of escitalopram, fluoxetine, paroxetine, venlafaxine, or mirtazapine were largely associated with reduced risk of intubation or death (all $p<0.05$).

Escitalopram is a selective serotonin reuptake inhibitor used to treat depressive disorders and generalized anxiety disorder [35, 36]. The results of a number of studies indicate that escitalopram is a fairly effective antidepressant and causes a small number of side effects when taken [37]. No less interesting is the recent information about the antiviral effect of escitalopram (in particular on SARS-CoV-2 through inhibition of sphingomyelinase), which makes the study of the effectiveness of this drug in the treatment of depression in patients with COVID-19 who have recently had it and have post-COVID depressive manifestations especially interesting. However, at the start of this study, most of the information found in the scientific medical literature about studies conducted or planned mainly concerned the safe and/or potentially beneficial qualities of escitalopram, rather than its effectiveness in reducing depressive symptoms in patients who have had COVID-19 [33, 34, 38].

Table 2. Study design.

Screening assessment for eligibility n=67)
Not included due to non-inclusion criteria (n=25)
Signing of informed consent and involvement in the study (n=44)
T1: status rating by scales HAM-D, HADS-D, SSS-8, CQLS Before starting the medication
Early withdrawal from the study (n=2)
T2: HAM-D score 2 weeks after taking the drug
T3: HAM-D rating 4 weeks after taking the drug
T4: HAM-D status rating 6 weeks after taking the drug
T5: HAM-D status rating 8 weeks after taking the drug
Analysis and statistical processing of the data (n=44)

Table 3. Dynamics of results on scales on the first and last day of the study.

Scale	T1 (week 0)	T5 (Week 8)	t	p
HADS-D	15.00±3.09	7.09±2.36	–14.09	<0.001
HAM-D	21.26±3.59	7.04±2.45	–24.85	<0.001
SSS-8	6.90±3.46	4.52±2.72	5.37	<0.001
CQLS	58.23±14.61	69.54±10.61	4.58	<0.001

AIM

The aim of the work was to evaluate the effectiveness of proactive psychosomatic intervention in the form of 8-week monotherapy with escitalopram in patients with post-COVID depression.

MATERIALS AND METHODS

According to the proactive model of consultative-liaison and communication psychiatry, all patients admitted to the hospital with a diagnosis of coronavirus disease were screened for signs of active mental health problems, especially those that could jeopardize the provision of care.

After screening and obtaining informed consent, 44 patients with post-COVID depression were involved in the study. 2 patients withdrew from the study prematurely; their data were not taken into account in the final processing of the results.

Inclusion criteria: The study included men and non-pregnant non-breastfeeding women between the ages

Table 4. Changes in average values on the first and last day of the study.

Scale	Changes in averages T1 and T5	95% CI
HADS-D	–7.90	–9.03; –6.77
HAM-D	–14.21	–15.36; –13.05
SSS-8	–2.38	–3.27; –1.48
CQLS	+11.31	6.32; 16.28

Table 5. HAM-D scores for 8 weeks.

HAM-D indicators at different time points, M±SD				
T1	T2	T3	T4	T5
21.26 ±3.59[3,4,5]	20.45 ±3.48[3,4,5]	16.33 ±2,50[1,2,4,5]	10.54 ±2.43[1,2,3,5]	7.04 ±2.45[1,2,3,4]

Notes:
[1] difference from T1 indicators is statistically significant, p<0.05;
[2] the difference from T2 indicators is statistically significant, p<0.05;
[3] the difference from the T3 indicators is statistically significant, p<0.05;
[4] the difference from the T4 indicators is statistically significant, p<0.05;
[5] the difference from the T5 indicators is statistically significant, p<0.05.

of 18 and 75 who had had COVID-19 less than 1 month ago and had ≥11 points on the Depression subscale of the Hospital Anxiety and Depression scale.

Exclusion criteria: Patients who participated in another study for 1 month prior to or during screening who had undergone surgery in the previous 6 months were not included in the study. Patients who abused psychoactive substances at the time of screening, had uncontrolled or unstable cardiovascular, pulmonary, gastrointestinal, urogenital, endocrine, neurological or psychiatric disorders were not enrolled in the study. Patients who used accounting drugs or opiate analgesics for >5 days during the month before screening were not included in the study.

ENDPOINTS

The primary endpoints were the depression severity level on the Depression subscale of the Hospital Anxiety and Depression Scale (HADS-D) and the Depression Severity Level on the Hamilton Depression Scale (HAM-D) for assessing depression. Secondary endpoints were somatic symptoms on the Somatic Symptom Scale (SSS-8) and Quality of Life Scale by A.S. Chaban (CQLS) were used.

PSYCHODIAGNOSTIC TOOLS

To assess the symptoms, the 17-factor Hamilton Depression Rating Scale, Hospital Anxiety and Depression Scale (Depression subscale), Somatic Symptoms Scale and Chaban A.S. Quality of Life Scale were used.

The 17-item Hamilton Depression Rating Scale (HAM-D) consists of 17 items (9 of which are rated from 0 to 4 points, and 8 from 0 to 2 points) filled out by a specialist during a structured clinical interview [39]. Interpretation of the final score was carried out according to the updated in 2019 NICE recommendations for the treatment and management of depression in adults: 0–7 – absence of depression, 8–13 – subclinical manifestations, 14–18 – moderate manifestations, 19–22 – moderate manifestations, 23+ – severe manifestations of depression [40].

The Hospital Scale of Anxiety and Depression (HADS-D) is a self-esteem scale often used to assess anxiety and depression. Developed by Zigmond & Snaith in 1983, it includes two subscales – anxiety and depression [41]. The depression subscale contains 7 statements, estimated from 0 (absence of a sign) to 3 (maximum severity of a sign). The maximum score for the depression subscale is from 0 to 21. The interpretation is as follows: 0–7 – normal, 8–10 – risk zone, 11 or more – clinically pronounced depression [42].

The Somatic Symptom Scale (SSS-8) is a brief self-questionnaire of the somatic manifestations of depression developed by Gierk B. et al. [43]. The scale consists of 8 questions, each of which is rated from 0 to 4 points, where 0 is "Not at all bothered", 4 is "Very disturbing". The assessment of somatic symptoms occurs by calculating the total score, which can vary from 0 to 32 points. The results are interpreted as follows: 0–3 points – the minimum degree of intensity of manifestations, 4–7 – low, 8-11 – average, 12–15 – high, 16–32 – a very high degree of intensity of manifestation of somatic symptoms [44].

Chaban A.S. Quality of Life Scale (CQLS) is a questionnaire designed to assess the quality of life, containing 10 questions on different aspects of the life of the subject. It is necessary to indicate the number of points that is most suitable, from 0 ("Not at all satisfied" to 10 ("Extremely satisfied"). Assessment of the quality of life occurs by calculating the total score, which can vary from 0 to 100. A score of up to 56 points corresponds to an extremely low level of quality of life, from 57 to 66 – low, 67–75 points correspond to an average level, 76–82 points – high, from 83 points – a very high level of quality of life [42].

PROTOCOL AND DESIGN

The study was conducted on the clinical basis of the Department of Medical Psychology, Psychosomatic Medicine and Psychotherapy of the Bogomolets National Medical University. After obtaining informed consent and conducting a screening procedure, if the inclusion criteria were met, the participants filled out the CQLS and SSS-8 questionnaires and a structured clinical interview was conducted with them to assess depression (HAM-D), which corresponds to the time point T1. The study design is presented in Table 2.

A structured clinical interview (HAM-D) was conducted with participants every 2 weeks after 2 weeks (T2), 4 weeks (T3), 6 weeks (T4), and 8 weeks (T5). After the 8th week, a second assessment was carried out on the CQLS, SSS-8 and HADS-D scales. Pharmacological intervention consisted of taking escitalopram (Medoprom, Medochemie Ltd) 5 mg per day for the first week and 10 mg per day for 2–8 weeks for the initial level of mild to moderate depression and taking escitalopram (Medoprom, Medoche-

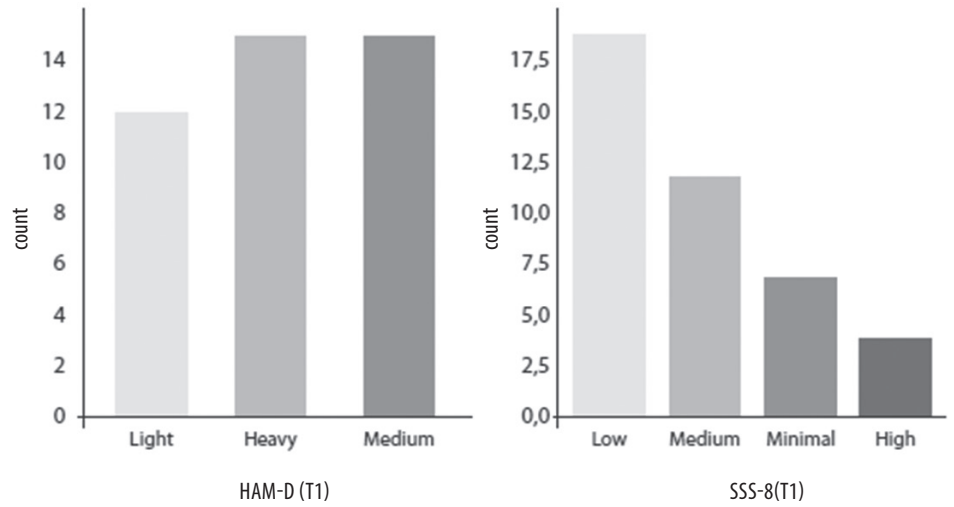

Fig. 1. Distribution of examined persons by severity of depression (by HAM-D) and the severity of somatic symptoms (SSS-8).

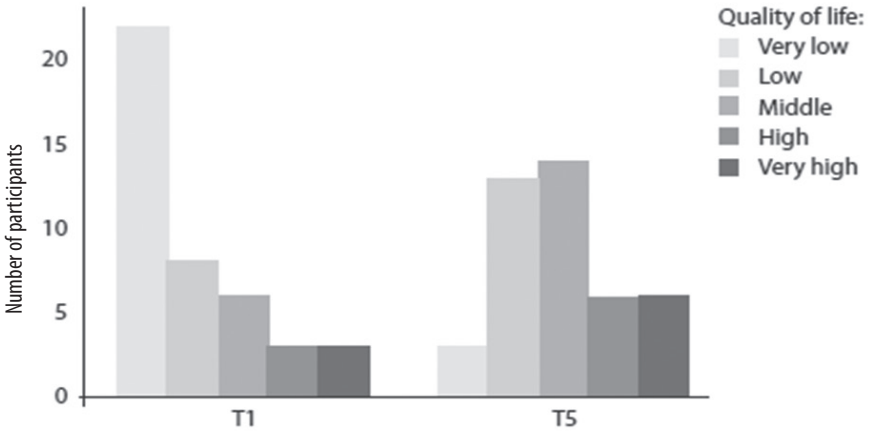

Fig. 2. Distribution of the studied persons by the level of quality of life at the time of T1 and T5.

mie Ltd) 10 mg per day for the first week and 20 mg per day for 2–8 weeks for severe initial levels of depression.

STATISTICAL ANALYSIS

To assess the normality of the distribution, the Shapiro – Wilk criterion was used. Quantitative data are presented by mean value and standard deviation [M±SD]. Qualitative data are presented through n and %. To compare treatment outcomes at time points T1 and T5 Student's'-t Test was used for related samples; to compare HAM-D results at points T1–T5 the Repeated Measures Analysis of Variance (rANOVA) (rANOVA) was applied. The Bonferroni Correction Method was used for the post-hoc evaluation. Correlation analysis was performed using the Pearson criterion. To statistically process the results, Microsoft Excel and Python were used with packages NumPy, Pandas, scipy, statsmodels. The data visualization was done using Python with the Seaborn package. The statistical significance was set to $p<0.05$.

RESULTS

According to the proactive model of consultative-liaison and communication psychiatry, 67 patients hospitalized with a diagnosis of coronavirus disease were screened for signs of active mental health problems, namely depressive manifestations. 44 people (65.7%) were confirmed to have clinically significant symptoms of depression (≥11 on the depression subscale of the hospital anxiety and depression scale).

42 (95.5%) patients with post-COVID depression completed the study; 2 (4.5%) patients left the study early, their data were not taken into account in the final processing of the results. Among the persons studied, there were 31 (73.80%) women and 11 (26.19%) men. The average age of the participants was 38.02±9.50 years. All quantitative indicators obeyed the normal law of distribution.

At the time of enrollment in the study, 12 (28.58%) individuals had mild depression, 15 (35.71%) had moderate depression, 15 (35.71%) had severe depression (Fig. 1).

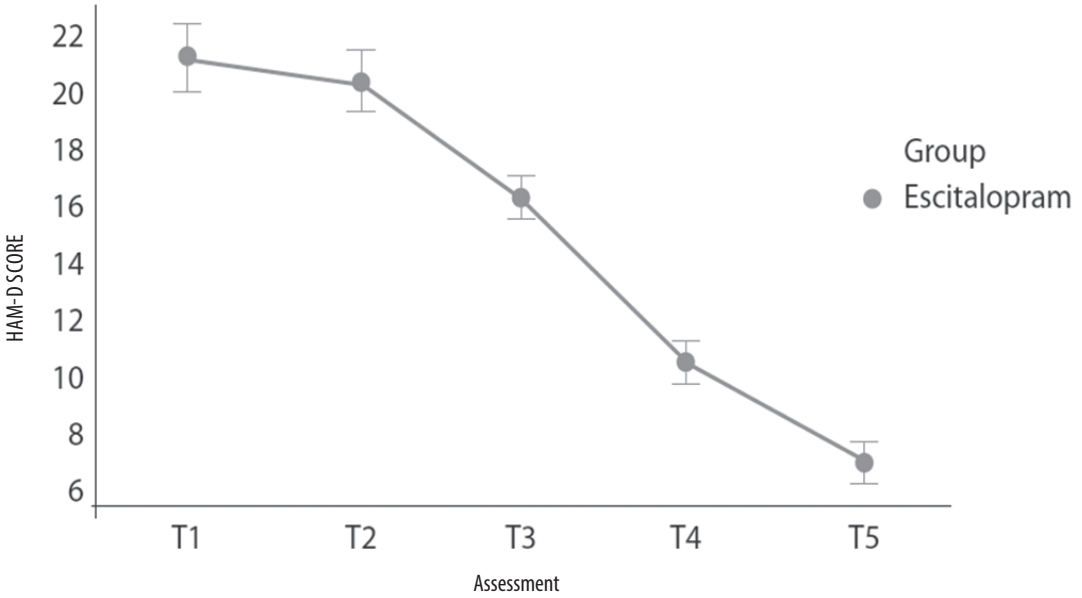

Fig. 3. Dynamics of HAM-D indicators during 8 weeks.

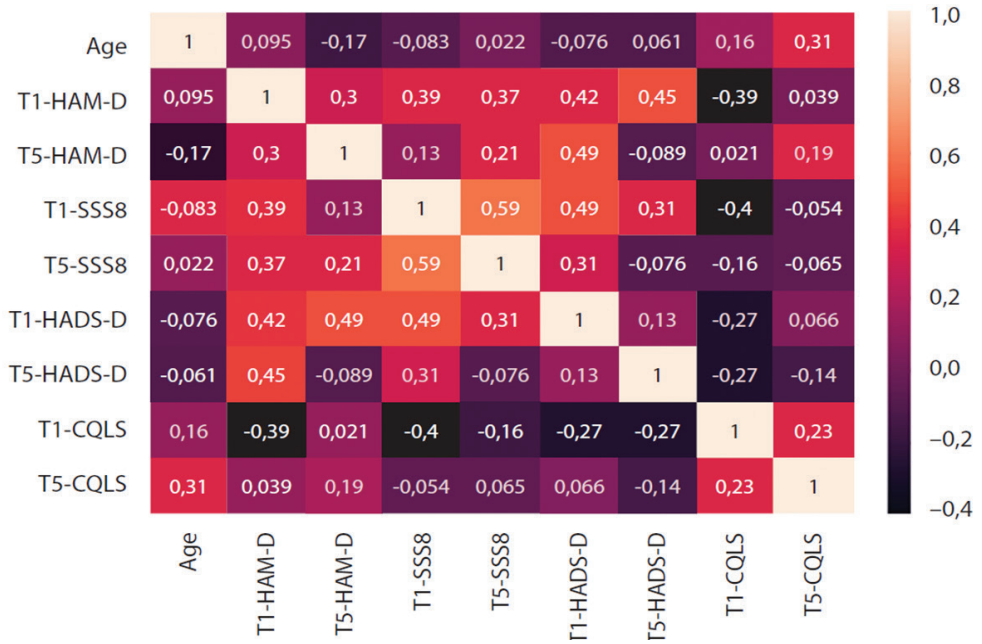

Fig. 4. Correlation matrix of scale and age characteristics.

The average value on the HAM-D scale was 21.26±3.59, on the HADS-D scale – 15.00±3.09.

The minimum level of manifestations of somatic symptoms had 7 (16.66%) subjects, low – 19 (45.23%), medium – 12 (28.58%), high – 4 (9.52%). The average score on the SSS-8 scale was 6.90±3.46.

22 (52.38%) participants at the time of enrollment in the study rated their level of quality of life as very low, 8 (19.04%) as low, 6 (14.28%) as average, 3 (7.14%) as high and 3 (7.14%) as very high. The average value on the CQLS scale at the time of attraction (T1) was 58.23±14.61.

After 8 weeks (T5), there was a statistically significant decrease in HADS-D, HAM-D and SSS-8 and a statistically significant increase in CQLS (Table 3.).

At the end of the 8th week of taking the drug, 18 (42.86%) subjects remained subclinical manifestations of depression on the HAM-D scale, the rest of the study contingent had no signs of depression at all. The number of subjects with a minimum level of somatic symptoms increased – at the end of the 8th week, 17 subjects (40.47%) had such a result. Thus, a low level of somatic symptoms was in 21 (50%) subjects, average – in 3 (7.14%) subject, high – only in 1 person (2.38%). Changes in average indicators on the first and last day of the study are presented in Table 4.

We noted an improvement in the quality of life – within 8 weeks, a significant shift to the left decreased, towards a low quality of life. Thus, at the time point T5, only 3 (7.14%) subjects had a very low level of quality of life, a low – 13 (30.95%) subjects, an average – 14 (33.3%) subjects, a high – 6 (14.28%) subjects, a very high – 6 (14.28%) subjects (Fig. 2).

The dynamics of the overall score on the Hamilton Depression Scale over 8 weeks was statistically significant ($F=225.32$, $p<0.000$). Post-hoc tests showed a statistically significant difference between the averages of the Hamilton Scale at individual time points (Table 5), with the exception of T1 and T2.

The graph of the dynamics of depressive symptoms (Fig. 3) allows us to visually assess that a significant decrease could be observed after 4 weeks (T3) of taking escitalopram.

Correlation analysis revealed that at the beginning of the study the total score on the HAM-D scale (T1) had a moderate directly proportional correlation with the total scores on the HADS-D scale ($r=0.419$, $p<0.01$) and the SSS-8 scale ($r=0.393$, $p<0.01$), and there was also a moderate inversely proportional relationship with the CQLS quality of life shower ($r=–0.385$, $p<0.012$).

The overall HADS-D score at the beginning of the study had a moderate, directly proportional relationship with the result of the HADS-D scale at the end of the study (point T5, $r=0.419$, $p<0.01$), with the shower of the HAM-D scale at point T5 ($r=0.488$, $p<0.001$), with indicators of the SSS-8 scale at point T1 ($r=0.489$, $p<0.001$) and point T5 ($r=0.307$, $p<0.05$).

The CQLS score at the start of the study had a moderate inversely proportional relationship also to the SSS-8 score at the same time point ($r=–0.403$, $p<0.008$). The patients' age had a moderate, directly proportional relationship with the CQLS score at 8 weeks ($r=0.311$, $p<0.05$). The thermal correlation matrix is shown in Fig. 4.

DISCUSSION

Post-COVID depressive manifestations are a serious challenge for the mental health system, so the introduction of a proactive model of consultative-liaison and communication psychiatry to provide patients with depressive disorders with specialized care within the department of a multidisciplinary hospital was timely and appropriate [44].

At the time of involvement in this study, most patients had moderate manifestations of depression. These results are consistent with data obtained by Raman et al. in 2021: 2–3 months after the onset of the disease, patients with COVID-19 were more likely to report symptoms of moderate and severe depression compared to the control group [45]. High rates of depression make it relevant to develop a number of actions aimed at rehabilitating and re-adaptation of the persons who have had COVID-19 [46].

The effectiveness of escitalopram in reducing symptoms of depression in this study was 66%. A systematic review and meta-analysis by Cipriani et al. (2018) shows that escitalopram is significantly more effective than most other antidepressants and easier to tolerate in patients [37]. Another meta-analysis is 2020 also showed that escitalopram is associated with a rapid reduction in the severity of symptoms of depression after critical somatic conditions (using the example of a stroke) [47].

A study by Pastoor D., Gobburu J. (2013) indicates that with 8 weeks of use of escitalopram, there is a decrease in symptoms of depression compared to the initial level by at least 50%, fluctuating in various studies from 44 to 55% [48]. In a recent study by Si T., Wang et al. (2018), a 68% reduction in symptoms of depression was reported (from 29.7 to 9.4 on the Hamilton scale) for 8 weeks at a dosage of 10 mg per day [30]. Thus, it can be assumed that the effectiveness of escitalopram in reducing depressive symptoms after suffering COVID-19 is not lower than the effectiveness of the drug in other populations.

Starting escitalopram as early as possible with depressive symptoms due to COVID-19 has the potential to reduce the mental effects of coronavirus illness and stop the further development of post-COVID depression. Given that taking escitalopram along with antiviral drugs is considered safe [49], it is promising to take already during COVID-19 therapy, that is, within the proactive model of psychosomatic medicine. Further studies on this topic could clarify which format of therapy is most effective.

An interesting finding was a stronger association of quality of life with somatic symptoms than with a depressive state as such. In our opinion, this can be explained by a significant somatization of depressive symptoms in patients with post-COVID depression, that is, manifestations of somatized (masked, larval) depression. Such depression is characterized by the same biochemical changes in the brain as depression with typical symptoms, but a variety of, partly non-specific, somatic symptoms come to the fore.

Therefore, in patients with post-COVID depression, affective symptoms, exacerbated by a state of loneliness and isolation, can be hidden or poorly differentiated may be hidden. for numerous complaints of a somatic nature. However, the reduction of somatized depressive manifestations under the influence of escitalopram affected the improvement of the quality of life. Improving the quality of life and simultaneously reducing the degree of manifestation of somatic symptoms after 8 weeks of taking escitalopram may be serve as an argument in favor of this hypothesis. In a study of the effectiveness of escitalopram in the treatment of somatoform disorders, Muller et al. found that the drug significantly reduces symptoms and improves the functioning of such patients [50]. Somatization of symptoms of anxiety and depression in the era of COVID-19 has become common [51,52] and is a promising topic for further research. Given the inversely proportional relationship of somatization with resilience and resilience with depressive manifestations [51, 53], it is no less interesting to study the effectiveness of psychopharmacotherapy in improving the resilience of patients with post-COVID depression. Especially since, according to the World Happiness Report 2021 on the effects of the COVID-19 pandemic [54], as well as last year's Xinli Chi et al. study [55,56], nearly 2/3 of the people showed post-traumatic growth after suffering PTSD, anxiety, or depressive disorder.

CONCLUSIONS

The introduction of a proactive model of consultative-liaison psychiatry within the COVID department of a multi-

disciplinary hospital for patients with depressive disorders was timely and appropriate, as it ensured early screening for depression and early initiation of escitalopram for the onset of depressive symptoms due to COVID-19.

Based on current knowledge of SARS-CoV-2, drugs combining anti-inflammatory and antiviral effects and a favorable adverse effect profile should be the most promising therapeutic strategies to combat this viral infection. In this context, SSRIs are not only inexpensive and widely available drugs with a safe tolerability profile (even in elderly patients), but also fit significantly into this effects profile.

Patients with post-COVID depression who underwent an 8-week course of escitalopram therapy (Medopram, Medochemie Ltd) had a significant reduction in the mental and somatic symptoms of depression and an improvement in quality of life. Thus, escitalopram may be a promising drug for psychopharmacotherapy of depressive symptoms in patients who have had COVID-19. Further study of its effectiveness in randomized controlled trials is needed to obtain a promising drug for psychopharmacotherapy of depressive symptoms in patients who have had COVID-19.

Further research is also needed on the effectiveness of the implementation of the proactive model of consultative-liaison and communication psychiatry in multidisciplinary hospitals for patients with comorbid psychosomatic pathology.

REFERENCES

1. Oldham M., Desan P., Lee H. Proactive Consultation-Liaison Psychiatry: American Psychiatric Association Resource Document. J Acad Consult Liaison Psychiatry. 2021; 62(2):169–185. https://doi.org/10.1016/j.jaclp.2021.01.005.
2. Desan P., Zimbrean P., Lee H., Sledge W. Integrated Care In Psychiatry. [s. l]: Springer. 2014; 157–181.
3. Leentjens A., Rundell J., Wolcott D., Guthrie E., Kathol R., Diefenbacher A. Reprint of: Psychosomatic medicine and consultation-liaison psychiatry: Scope of practice, processes, and competencies for psychiatrists working in the field of CL psychiatry or psychosomatics. A consensus statement of the European Association of Consultation-Liaison Psychiatry and Psychosomatics (EACLPP) and the Academy of Psychosomatic Medicine (APM). J Psychosom Res. 2011; 70(5):486–491. https://doi.org/10.1016/j.jpsychores.2011.02.008.
4. Proactive Psychiatric Consultation For Hospitalized Patients, A Plan for the Future. Health Affairs Forefront. https://doi.org/10.1377/forefront.20150528.048026/full/ (accessed 11 January 2022).
5. Munjal S. Proactive consultation: A new model of care in consultation-liaison psychiatry. Curr Psychiatr. 2022; 17 (10): e3–e5.
6. Walker J., Burke K., Toynbee M. The HOME Study: study protocol for a randomised controlled trial comparing the addition of Proactive Psychological Medicine to usual care, with usual care alone, on the time spent in hospital by older acute hospital inpatients. Trials. 2019; 20 (1). https://doi.org/10.1186/s13063-019-3502-5.
7. Augenstein T. M., Pigeon W. R., DiGiovanni S. K., Brazill K. P., Olivares T. E., Farley-Toombs C., Lee H. B., Wittink M. N. Creating a Novel Inpatient Psychiatric Unit with Integrated Medical Support for Patients with COVID-19. NEJM Catalyst. 2020; 8. https://doi.org/10.1056/CAT.20.0249
8. Sharpe M., Toynbee M., Walker J. Proactive Integrated Consultation-Liaison Psychiatry: A new service model for the psychiatric care of general hospital inpatients. Gen Hosp Psychiatry. 2020; 66: 9–15. https://doi.org/10.1016/j.genhosppsych.2020.06.005.
9. Shalev D., Nakagawa S., Stroeh O. The Creation of a Psychiatry-Palliative Care Liaison Team: Using Psychiatrists to Extend Palliative Care Delivery and Access During the COVID-19 Crisis. J Pain Symptom Manage. 2020;60(3):e12–e16. https://doi.org/10.1016/j.jpainsymman.2020.06.009.
10. Oldham M.A., Chahal K., Lee H.B. A systematic review of proactive psychiatric consultation on hospital length of stay. Gen Hosp Psychiatry. 2019; 60: 120–126. https://doi.org/10.1016/j.genhosppsych.2019.08.001
11. Purssell E., Gould D., Chudleigh J. Impact of isolation on hospitalized patients who are infectious: systematic review with meta-analysis. BMJ Open. 2020; 10: e030371. https://doi.org/10.1136/ bmjopen-2019-030371
12. Montalvo C., Kao L. A Call to Arms, Not to Disarm: The Importance of Psychiatric Care in the Acute Medical Setting During the COVID-19 Pandemic. Psychosomatics. 2020; 61(5): 581–582. https://doi.org/10.1016/j.psym.2020.03.008.
13. Jhanwar S., Krishnan V., Rohilla J. Consultation-Liaison Psychiatry During COVID-19 Lockdown: A Retrospective Chart Review. Cureus. 2020. doi: 10.7759/cureus.11048.
14. Bohmwald K., Gálvez N., Ríos M., Kalergis A. Neurologic Alterations Due to Respiratory Virus Infections. Front Cell Neurosci. 2018; 12. https://doi.org/10.3389/fncel.2018.00386.
15. Pashaei Y. Drug repurposing of selective serotonin reuptake inhibitors: Could these drugs help fight COVID-19 and save lives? Journal of Clinical Neuroscience. 2021; 88: 163–172. https://doi.org/10.1016/j.jocn.2021.03.010.
16. Wu Z., McGoogan J.M. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. JAMA. 2020; 323: 1239–1242. https://doi.org/10.1001/jama.2020.2648.
17. Troyer E., Kohn J., Hong S. Are we facing a crashing wave of neuropsychiatric sequelae of COVID-19? Neuropsychiatric symptoms and potential immunologic mechanisms. Brain Behav Immun. 2020; 87: 34–39. doi: 10.1016/j.bbi.2020.04.027.
18. Khaustova E., Chaban O. Pharmacotherapy of mental disorders associated with COVID-19. Psychiatry, Psychotherapy and Clinical Psychology. 2021;12(1): 85–105. (in Russian) doi: 10.34883/PI.2021.12.1.008
19. Ettman C., Abdalla S., Cohen G., Sampson L., Vivier P., Galea S. Prevalence of Depression Symptoms in US Adults Before and During the COVID-19 Pandemic. JAMA Netw Open. 2020; 3(9): e2019686. https://doi.org/10.1001/jamanetworkopen.2020.19686.
20. Park H., Jung J., Park H. Psychological Consequences of Survivors of COVID-19 Pneumonia 1 Month after Discharge. J Korean Med Sci. 2020; 35(47). doi: 10.3346/jkms.2020.35.e409.
21. Garg P., Arora U., Kumar A., Wig N. The "post-COVID" syndrome: How deep is the damage? J Med Virol. 2020; 93(2): 673–674. https://doi.org/10.1002/jmv.26465.
22. Lam M. Mental Morbidities and Chronic Fatigue in Severe Acute Respiratory Syndrome Survivors. Arch Intern Med. 2009;169(22):2142. https://doi.org/10.1001/archinternmed.2009.384.
23. Kathirvel N. Post COVID-19 pandemic mental health challenges. Asian J Psychiatr. 2020; 53: 102430. https://doi.org/10.1016/j.ajp.2020.102430.
24. Sher L. Are COVID-19 survivors at increased risk for suicide? Acta Neuropsychiatr. 2020; 32(5): 270–270. https://doi.org/10.1017/neu.2020.21.
25. Norton A., Olliaro P., Sigfrid L. Long COVID: tackling a multifaceted condition requires a multidisciplinary approach. The Lancet Infectious Diseases. 2021; 21(5): 601–602. https://doi.org/ 10.1016/s1473-3099(21)00043-8.
26. Wu Y., Xu X., Chen Z. Nervous system involvement after infection with COVID-19 and other coronaviruses. Brain Behav Immun. 2020; 87: 18–22. https://doi.org/10.1016/j.bbi.2020.03.031.
27. Steardo L., Steardo L., Verkhratsky A. Psychiatric face of COVID-19. Transl. Psychiatry. 2020; 10 (1). https://doi.org/10.1038/s41398-020-00949-5.
28. Lyons D., Frampton M., Naqvi S., Donohoe D., Adams G., Glynn K. Fallout from the COVID-19 pandemic – should we prepare for a tsunami of post viral depression? Ir J Psychol Med. 2020; 37(4): 295–300. https://doi.org/10.1017/ipm.2020.40.

29. Köhler C., Freitas T., Stubbs B. Peripheral Alterations in Cytokine and Chemokine Levels After Antidepressant Drug Treatment for Major Depressive Disorder: Systematic Review and Meta-Analysis. Mol Neurobiol. 2017. https://doi.org/10.1007/s12035-017-0632-1.
30. Si T., Wang G., Yang F. Efficacy and safety of escitalopram in treatment of severe depression in Chinese population. Metab Brain Dis. 2017; 32(3): 891–901. https://doi.org/10.1007/s11011-017-9992-5.
31. Hojyo S., Uchida M., Tanaka K., Hasebe R., Tanaka Y., Murakami M. How COVID-19 induces cytokine storm with high mortality. Inflamm Regen. 2020; 40: 1–7. https://doi.org/10.1186/s41232-020-00146-3
32. Ye Q., Wang B., Mao J. The pathogenesis and treatment of the Cytokine Storm'in COVID-19. J Infect. 2020; 80: 607–13. https://doi.org/10.1016/j.jinf.2020.03.037
33. Hannestad J., DellaGioia N., Bloch M. The effect of antidepressant medication treatment on serum levels of inflammatory cytokines: a metaanalysis. Neuropsychopharmacology. 2011; 36: 2452–2459. https://doi.org/10.1038/npp.2011.132.
34. Hoertel N., Rico M. S., Vernet R., Beeker N., Jannot A. -S., Neuraz A. Association between SSRI antidepressant use and reduced risk of intubation or death in hospitalized patients with coronavirus disease 2019: a multicenter retrospective observational study. MedRxiv 2020. https://doi.org/10.1101/2020.07.09.20143339.
35. Landy K., Rosani A., Estevez R. Escitalopram. StatPearls Publishing; September 14, 2021.
36. Chaban O., Khaustova E., Kirilyuk S. Implementation of the new classification of psychotropic drugs in Ukraine: Problems and prospects. Psychiatry, Psychotherapy and Clinical Psychology. 2017; 8(2): 221–228. (in Russian) URL http://www.scopus.com/inward/record.url?eid=2-s2.0-85041911905&partnerID=MN8TOARS
37. Cipriani A., Furukawa T., Salanti G. Comparative efficacy and acceptability of 21 antidepressant drugs for the acute treatment of adults with major depressive disorder: a systematic review and network meta-analysis. The Lancet. 2018; 391(10128): 1357–1366. https://doi.org/10.1016/s0140-6736(17)32802-7.
38. Assanovich M. Escitalopram in the pharmacotherapy of psychiatric disorders in patients with COVID-19. Medicynskie novosti. 2021; 1:59–62. (in Russian).
39. Hamilton M. A rating scale for depression. J Neurol Neurosurg Psychiatry. 1960; 23(1): 56–62. https://doi.org/10.1136/jnnp.23.1.56.
40. National Collaborating Centre for Mental Health (UK) Depression: The Treatment and Management of Depression in Adults (Updated Edition). Leicester (UK): British Psychological Society; 2010.
41. Zigmond A.S., Snaith R.P. The hospital anxiety and depression scale. Acta Psychiatr Scand. 1983;67(6):361–370. https://doi.org/10.1111/j.1600-0447.1983. tb09716.x.
42. Khaustova O., Asanova A., Trachuk L., Assonov D. Practical Psychosomatics: Diagnostic Scales. Kyiv: Medknyga; 2019. (in Ukrainian).
43. Gierk B., Kohlmann S., Kroenke K. The somatic symptom scale-8 (SSS-8): a brief measure of somatic symptom burden. JAMA Intern Med. 2014; 174(3): 399–407. https://doi.org/10.1001/jamainternmed.2013.12179.
44. Gray M., Monti K., Katz C., Klipstein K., Lim S. A «Mental Health PPE» model of proactive mental health support for frontline health care workers during the COVID-19 pandemic. Psychiatry Res. 2021; 299: 113878. https://doi.org/10.1016/j.psychres.2021.113878.
45. Raman B., Cassar M. P., Tunnicliffe E. M. Medium-term effects of SARS-CoV-2 infection on multiple vital organs, exercise capacity, cognition, quality of life and mental health, post-hospital discharge. EClinicalMedicine. 2021; 31: 100683. https://doi.org/10.1016/j.eclinm.2020.100683.
46. Ameyaw E.K., Hagan J.E., Ahinkorah B.O., Seidu A.A., Schack T. Mainstream reintegration of COVID-19 survivors and its implications for mental health care in Africa. Pan Afr Med J. 2020; 36: 366. https://doi.org/10.11604/pamj.2020.36.366.25115.
47. Li X., Zhang C. Comparative efficacy of nine antidepressants in treating Chinese patients with post-stroke depression: A network meta-analysis. J Affect Disord. 2020; 266: 540–548. https://doi.org/10.1016/j.jad.2020.02.005.
48. Pastoor D., Gobburu J. Clinical pharmacology review of escitalopram for the treatment of depression. Expert Opin Drug Metab Toxicol. 2014; 10(1): 121–128. https://doi.org/10.1517/17425255.2014.863873.
49. Zhang K., Zhou X., Liu H., Hashimoto K. Treatment concerns for psychiatric symptoms in patients with COVID-19 with or without psychiatric disorders. Br J Psychiatry. 2020; 217(1): 351. https://doi.org/10.1192/bjp.2020.84.
50. Muller J. E., Wentzel I., Koen L., Niehaus D. J., Seedat S., Stein D. J. Escitalopram in the treatment of multisomatoform disorder: a double-blind, placebo-controlled trial. Int Clin Psychopharmacol. 2008; 23(1): 43–48. https://doi.org/0.1097/YIC.0b013e32825ea301.
51. Ran L., Wang W., Ai M., Kong Y., Chen J., Kuang L. Psychological resilience, depression, anxiety, and somatization symptoms in response to COVID-19: A study of the general population in China at the peak of its epidemic. Soc Sci Med. 2020; 262: 113261. https://doi.org/10.1016/j.socscimed.2020.113261.
52. Vus V., Puzyrina A. COVID-19 impact: new tendencies and trends in mental health research. Wiad Lek. 2021;74(11p1):2836-2839. doi:https://doi.org/10.36740/WLek202111127.
53. Chaban O., Khaustova O., Mishyiev V., Grinevich E., Assonov D. Resilience influence to healthcare professionals' emotional state during COVID-19 quarantine. Psychiatry, Psychotherapy and Clinical Psychology. 2021; 12(1): 150–157 DOI: 10.34883/PI.2021.12.1.013
54. Banks J., Fancourt D., Xu X. Mental Health And The COVID-19 Pandemic. World Happiness Report 2021. 2021: 107–130.
55. Chi X., Becker B., Yu Q. Prevalence and Psychosocial Correlates of Mental Health Outcomes Among Chinese College Students During the Coronavirus Disease (COVID-19). Pandemic. Front Psychiatry. 2020;11:803. https://doi.org/10.3389/fpsyt.2020.00803.
56. Illingworth P. Covid-19 the Trigger for SDG Solutions in Mental Health. Mental Health: Global Challenges Journal. 2021;4(1):4-8. doi: https://doi.org/10.32437/mhgcj.v4i1.103.

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CONFLICT OF INTEREST

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