

Rakhman Lyudmyla, Markova Marianna. The issue of compliance in patients with treatment resistance depressions = Проблема комплаєнсу у хворих з терапевтично резистентними депресіями. Journal of Education, Health and Sport. 2015;5(8):111-118. ISSN 2391-8306. DOI [10.5281/zenodo.27441](https://doi.org/10.5281/zenodo.27441)
<http://dx.doi.org/10.5281/zenodo.27441>
<http://ojs.ukw.edu.pl/index.php/johs/article/view/2015%3B5%288%29%3A111-118>
<https://pbn.nauka.gov.pl/works/605290>
Formerly Journal of Health Sciences. ISSN 1429-9623 / 2300-665X. Archives 2011–2014
<http://journal.rsw.edu.pl/index.php/JHS/issue/archive>

Deklaracja.

Specyfika i zawartość merytoryczna czasopisma nie ulega zmianie.
Zgodnie z informacją MNISW z dnia 2 czerwca 2014 r., że w roku 2014 nie będzie przeprowadzana ocena czasopism naukowych; czasopismo o zmienionym tytule otrzymuje tyle samo punktów co na wykazie czasopism naukowych z dnia 31 grudnia 2014 r.

The journal has had 5 points in Ministry of Science and Higher Education of Poland parametric evaluation. Part B item 1089. (31.12.2014).

© The Author (s) 2015;

This article is published with open access at License Open Journal Systems of Kazimierz Wielki University in Bydgoszcz, Poland and Radom University in Radom, Poland
Open Access. This article is distributed under the terms of the Creative Commons Attribution Noncommercial License which permits any noncommercial use, distribution, and reproduction in any medium, provided the original author(s) and source are credited. This is an open access article licensed under the terms of the Creative Commons Attribution Non Commercial License (<http://creativecommons.org/licenses/by-nc/3.0/>) which permits unrestricted, non commercial use, distribution and reproduction in any medium, provided the work is properly cited.
This is an open access article licensed under the terms of the Creative Commons Attribution Non Commercial License (<http://creativecommons.org/licenses/by-nc/3.0/>) which permits unrestricted, non commercial use, distribution and reproduction in any medium, provided the work is properly cited.
The authors declare that there is no conflict of interests regarding the publication of this paper.
Received: 05.06.2015. Revised 15.07.2015. Accepted: 25.07.2015.

UDK: 616.89-008.19:615.015.46:614.253.8

**THE ISSUE OF COMPLIANCE IN PATIENTS WITH TREATMENT RESISTANCE
DEPRESSIONS
ПРОБЛЕМА КОМПЛАЄНСУ У ХВОРИХ З ТЕРАПЕВТИЧНО РЕЗИСТЕНТНИМИ
ДЕПРЕСІЯМИ**

Lyudmyla Rakhman¹, Marianna Markova²

Л. Рахман, М. Маркова

¹Danylo Halytskyi Lviv National Medical University, Lviv, Ukraine

²Kharkiv Medical Academy of Post-graduate Education, Kharkiv, Ukraine

Summary

The study revealed that the main causes of partial or non-compliance in patients with treatment resistance depression (TRD) at the beginning of therapy are the side effects of medications, as well as a significant reduction in self-esteem of patients. In period of discharge from hospital major factor for the lack of compliance is a low level of knowledge about factors and mechanisms of TRD and lowered financial opportunity for ensuring required maintenance therapy. The cooperation between doctor and patient, so-called "therapeutic alliance" is one of the most important aspects of treatment effectiveness in TRD.

Keywords: compliance, treatment resistance depression, treatment, remission.

Резюме

Дослідження показало, що основними причинами часткового або відсутнього комплаєнсу у хворих з терапевтично резистентними депресіями (ТРД) на початку терапії є

побічні ефекти лікарських препаратів, а також значне зниження самооцінки пацієнтів. У період виписки зі стаціонару основними факторами дефіциту комплаєнсу є низький рівень знань про фактори розвитку і механізми ТРД і знижена фінансова спроможність пацієнтів для забезпечення необхідної підтримуючої терапії. Співпраця між лікарем і пацієнтом, так званий "терапевтичний альянс", є одним з найбільш важливих аспектів ефективності лікування хворих, які страждають на ТРД.

Ключові слова: комплаєнс, терапевтично резистентні депресії, лікування, ремісія.

Резюме

ПРОБЛЕМА КОМПЛАЕНСА У БОЛЬНЫХ ТЕРАПЕВТИЧЕСКИ РЕЗИСТЕНТНЫМИ ДЕПРЕССИЯМИ. Исследование показало, что основными причинами частичного или отсутствующего комплаенса у больных терапевтически резистентными депрессиями (ТРД) в начале терапии являются побочные эффекты лекарственных препаратов, а также значительное снижение самооценки пациентов. В период выписки из стационара основными факторами дефицита комплаенса является низкий уровень знаний о факторах развития и механизмы ТРД и низкая финансовая способность пациентов для обеспечения необходимой поддерживающей терапии. Сотрудничество между врачом и пациентом, так называемый "терапевтический альянс", является одним из наиболее важных аспектов эффективности лечения больных, страдающих ТРД.

Ключевые слова: комплаєнс, терапевтично резистентні депресії, лікування, ремісія.

Analysis

According to research by many authors, despite the large number of modern antidepressants and significant progress in understanding the biological mechanisms of depression, the problem of treatment resistant states observed an average of 30-60% of patients with depressive disorders [1, 4, 11]. By current generally criteria, depression is resistant if during two consecutive courses (3-4 weeks) of monotherapy by pharmacologically different drugs in adequate dosage there is a lack or

insufficiency of clinical efficacy (reduction of symptoms by the Hamilton scale is less than 50%) [10, 14]. Modern scientific data evidence that 60-70% of patients with depressive disorders remain residual symptoms after treatment and not observed effect are in 5-10% of patients [24]. Growth of treatment resistant states in the course of depressive disorders is a significant social and economic problem, because the increase of treatment cost in depression is mainly due to the fact of treatment resistant depressions (TRD) [2, 3, 6, 13, 17]. The effectiveness in treatment of depressive disorders is means reduction of psychopathological symptoms and, most importantly, maintaining a person social active role in society, despite the quality of remission [5,12,18,20]. The success of the treatment of TRD depends on many factors. A key element is to achieve compliance [5,7,8,9,22,23].

Compliance (Patient compliance), or adherence to treatment - degree of correspondence between the behavior of the patient and recommendations received from the doctor [15,16]. In the systematic review cited data that in depressive disorders patients' compliance is in an average of 65%. Moreover, characterized by the fact that possibility for violation of compliance is increases with the duration of treatment, that is, the longer course of therapy contributes to breaking regime of drug intake, dosage changing or complete rejection from therapy motivating by low efficiency [6,8,16,19].

Assessment of compliance is difficult and approximate task. In studies using microelectronic monitoring showed that only 1/6 of the population of chronically ill patients is exactly followed the recommendations, although all patients are assure the doctor that they adhere to treatment [3,12,15]. In another study, in which 67.5% of patients claimed that they are taking all doses, it was found by counting pills that only 10.3% did not skip medications [19,23]. It was given evidence that among patients with a primary episode of depression and signs of resistance, who are not taking recommended treatment, the risk of exacerbation is grew in 8 times. During the year after hospitalization 43% of recurrences are the result of partial compliance. In cases of absolute non-compliance a recurrence observed in 70% of patients [20,21]. An important aspect of non-compliance is that patients and their family members usually are not ready for long-term treatment because they consider that long-term maintenance therapy in the background of improving mental condition is unreasonable. Patients interesting in treatment of TRD also depends on the pharmaceutical form, the amount of drugs for one medication intake, frequency rate reception, complexity of regimen, its duration and others. According to the scientific data fully perform all prescription 34% of patients, partially - 33%, does not fulfill the prescriptions 33% of patients [3,5,7]. Positive compliance in single medication taking for a day achieved in 79.6% of cases, twice - in 68%, with three times - in 37.7% of cases [1,12,15]. There are many ways to determine compliance: assessment of reappointment (although reappointments are only the first step in the

procedure of taking drugs), counting tablets (which include elements of molestation that leads to unreliable method), use of multiple sources from case history that often leads to opposite results; determine the level of chemical substance in the blood serum, which also can not be considered significant as it shows only the most recent activity of the drug [7,8,9,15]. Despite the importance of determining the presence or absence of compliance in patients, a leading place of research occupy studies which aimed on identifying the causes of treatment regime infraction.

Methods

Our research work was conducted to identify the causes of partial compliance or non-compliance achieve in patients with TRD. The study of this issue was conducted using anonymous survey based on a specially designed questionnaire. This questionnaire consisted of 13 questions: to each question was given several variants of answers, and was assigned a special column with the ability to write own version. Also the point at which patients noted their comments and suggestions regarding of the treatment course, its effectiveness and tolerability was envisaged in the questionnaire. Survey of patients with TRD and evaluate of received data was conducted twice: the first week of hospitalization (first stage) and the stage of remission with preparation for discharge from hospital (second stage). Patients with TRD who was involved to the study on the basis of their written inform consent underwent inpatient treatment in a communal institution "Lviv Regional Clinical Psychiatric Hospital". Nosological diagnosis based on ICD-10 criteria and included data received on clinical, psychopathological, laboratory and instrumental methods. For all patients from study group was diagnosed recurrent depressive disorder (F 33.2) with clear criteria for TRD. Patient's treatment was included antidepressants - selective serotonin reuptake inhibitors (SSRI), serotonin/ noradrenalin reuptake inhibitors (SNRI), mood stabilizers, as in most cases used the method of augmentation with atypical antipsychotic to overcome resistance of depressive symptoms. It was involved 69 patients in this study, 14 patients was discontinuation from study after reviewing the questionnaire on the first or second phase of the survey. 55 patients, including 19 men and 36 women, completed all procedures during study. The average age of patients was 37 ± 8 years. Questioning was provided in the morning in the hall of employment therapy, with a maximum occupancy requirement for independence of the questionnaire, allowed in rare cases to explain the essence of the issue only.

Results

According to our anonymous survey it was obtained the following results. In the first week of hospitalization the desire to stop treatment expressed 22 patients, representing 40% of respondents. Among those who sometimes thought about discontinuation from therapy was found 18 patients (32%). At the time of early remission 38 patients (69%) were wished to completely discontinue use of medicines, partly the desire to adhere to treatment was present in 25

questionnaires (46%). Among the possible and the likely causes of treatment discontinuation in the first phase of the study, patients have noted: a health worsening- 13 respondents (24%), weakness of adequate self-esteem- 12 respondents (21%), lack of therapy efficacy -42 respondents (76%). Repeated questioning in period of preparation for discharge from hospital showed that 40 patients (73%) indicated health worsening, presence of side effects and economic reasons as first reason to stop maintenance therapy.

The survey was conducted analysis of the most uncomfortable moments in the treatment of patients with TRD. According to a provided questionnaire 41 respondents (75%) noted the presence of side effects, 24 people (44%) the constant drowsiness and slowness as most uncomfortable moments in treatment of TRD during first phase of study. The second phase survey showed that the vast majority of patients expressed an inability of full social activity provided (46 respondents (84%)) and that is was most uncomfortable fact in process of treatment. In addition to the presented results majority of patients expressed a desire to reduce the dose and frequency of medication use because, in their opinion, this dose is too high, it was 36 patients in the first stage and 45 in the second, which is respectively 66% and 82%. Also, according to the survey, 22 patients (40%) noted that they already had experience in the past to reduce the dose or stop treatment even being at home by theirs own discretion. In this case, it should be noted that at now days there is the practice to prescribing of low doses of medication at the period of maintenance therapy which will be saved therapeutic effect. That means further dose reduction due to partial compliance will increases the risk of relapse and is one of the leading factors to depressive resistance formation. In addition to reducing the dose a skipping medication is also important factor in compliance violating in patients with TRD. In performed study 42 respondents (76%) indicated that sometimes may forget to take the medicine at the first stage and 44 patients (80%) at the remission period answered yes about possibility skip or forget to take the medicine.

Psychosocial rehabilitation is an important step in the formation of long-term remission in patient with TRD. According to the survey only 11 patients (20%) visit measures of psychosocial rehabilitation (various trainings, psychoeducational discussions, thematic sessions, book and music therapy, and physical exercises) in the first week of inpatient treatment, 35 respondents (64%) see no reason for visiting the rehabilitation. Further positive dynamics in the clinic of resistant depression remains this ratio in the same level- 16 people have expressed a desire in the future to be actively engaged in rehabilitation work, which is 21%, 41 patients (75%) do not consider requires the participation in psychosocial rehabilitation. Despite these negative aspects of antidepressant therapy 45 patients (82%) in the first stage and 42 patients (76%) in second feel the need for treatment. Consider their treatment effective 37 patients (67%) at the beginning of inpatient treatment and 51 patients (93%) at the stage of remission.

In the process of this research work we found that the problem of compliance in patients with TRD is actually in psychiatry. The main components of non-compliance at the beginning of therapy are the side effects of medications, as well as a significant reduction in self-esteem of patients. In period of discharge from hospital major factor for the lack of compliance is a low level of knowledge about factors and mechanisms of TRD and lowered financial opportunity for ensuring required maintenance therapy. The cooperation between doctor and patient, so-called "therapeutic alliance" is one of the most important aspects of treatment effectiveness in TRD. In this sense, the doctor must not only find the right therapeutic tactics, but also to provide intensive explanations about ethiological factors and pathogenesis mechanisms of TRD, need of lengthy treatment, importance of participation in psychosocial rehabilitation. In addition, it is necessary to change the patient attitude to the disease and treatment, correctly set accents priority. Of course, the mostly important points are the primary patient concern about his recovery, family support, the ability to be socially needed person.

The task of improving compliance in patients with TRD is remain a topical issue in modern psychiatry, And in future need for further study to identify the causes, consequences and ways of its optimization.

References

1. Al-Harbi KS. Treatment-resistant depression: therapeutic trends, challenges, and future directions/ KS. Al-Harbi // Patient Prefer Adherence. — 2012.— Vol.6.—P.369-388.
2. Bannan N. Multimodal therapy of treatment resistant depression: a study and analysis/ N. Bannan // Int J Psychiatry Med. —2005. — Vol.35(1) . — P.27–39.
3. Becker M. H. Strategies for enhancing patient compliance./ M. H. Becker, L. A. Maiman // J Community Health. -1980.- Vol.6.-P.113–135.
4. Berlim MT. What is the meaning of treatment resistant/refractory major depression (TRD)? A systematic review of current randomized trials. / MT. Berlim, G. Turecki //Eur. Neuropsychopharmacol. —2007. —Vol.17 (11) . —P. 696-707.
5. Bollini P. Improving compliance in depression: a systematic review of narrative reviews./ P. Bollini , S. Pampallona , B. Kupelnick , G. Tibaldi , C. J. Munizza// Clin Pharm Ther. – 2006.- Vol. 31(3).- P.253-260.
6. Corey-Lisle P. K. Response, partial response, and nonresponse in primary care treatment of depression/ P.K. Corey-Lisle, R. Nash, P. Stang, R.Swindle // Arch Intern Med.— 2004.— Vol.164(11) .— P.1197–1204.
7. Delgado P. L. Approaches to the enhancement of patient adherence to antidepressant medication treatment./P. L.Delgado // J Clin Psychiatry. -2000.-Vol.61.-P.6–9.

8. Demyttenaere K. Compliance and acceptance in antidepressant treatment./ K. Demyttenaere // *Int J Psychol Clin Pract.* -2001.-Vol.5.-P.529–535.
9. Demyttenaere K. Risk factors and predictors of compliance in depression.// *Eur Neuropsychopharmacol.*- 2003.-Vol.13(suppl 3).-P69-75.
10. Fava M. Diagnosis and definition of Treatment - Resistant Depression. // *Biol Psychiat.*- 2003. –Vol. 53. –P. 649-659.
11. Fava C.A. The concept of recovery in major depression/ C.A. Fava, C. Ruini, C. Belaise // *Psychol Med.* — 2007. – V. 48. – P. 103–111
12. Holma I.A. Treatment attitudes and adherence of psychiatric patients with major depressive disorder: a five-year prospective study. / I.A. Holma, K.M. Holma, T.K. Melartin, E.T. Isometsa. // *J Affect Disord.*-2010.-Vol.127.-P.102-112
13. Keller MB. Issues in treatment-resistant depression. // *J Clin Psychiatry.*– 2005.–Vol. 66 (suppl. 8) .–P.5–12.
14. Maalouf F.T. Treatment-resistant depression in adolescents: review and updates on clinical management/ F.T. Maalouf, M. Atwi, D.A. Brent // *Depress Anxiety.* – 2011. –Vol. 28. – P.946-954
15. Maddox J.C. The compliance with antidepressants in clinical practice. /J.C.Maddox, M. Levi, C. Thompson// *J. Psychopharmacol.* -1994.-Vol.8.-P.48–53.
16. Masand P. S. Tolerability and adherence issues in antidepressant therapy./ P. S.Masand//*Clinical Therapeutics.*-Vol.25(8).-P.2289-2304
17. Mathew SJ. Treatment-resistant depression: recent developments and future directions/ S.J. Mathew // *Depress Anxiety.*– 2008.– Vol.25(12) .–P.989–992.
18. Nemeroff CB. Prevalence and management of treatment-resistant depression.// *J Clin Psychiatry.*– 2007.–Vol.68 (suppl. 8) .– P.17–25.
19. Pampallona S. Patient adherence in the treatment of depression./ S. Pampallona, P. Bollini, G. Tibaldi, B. Kupelnick, C. Munizza // *Br. J. Psychiatry.*- 2002.-Vol.180.-P.104–109.
20. Papakostas G.I. Treatment of SSRI-resistant depression: a meta-analysis comparing within- versus across-class switches. / G.I. Papakostas, M. Fava, M.E. Thase // *Biol Psychiatry.*- 2008.-Vol. 63.-P.699–704.
21. Souery D. Treatment-resistant depression/ D. Souery, GI. Papakostas, MH. Trivedi// *J Clin Psychiatry.*– 2006.–Vol. 67 (suppl. 6) .–P.16–22.
22. Vergouwen A.C. Patient adherence with antidepressant treatment./ A.C.Vergouwen, A. Bakker // *Br. J. Psychiatry.* -2002Vol.-181.-p.78–79.
23. Woldu H. Pharmacokinetically and clinician-determined adherence to an antidepressant regimen and clinical outcome in the TORDIA trial. / H Woldu, G Porta, T Goldstein,

D Sakolsky, J Perel, G Emslie, T Mayes, G Clarke, ND Ryan, B Birmaher, KD Wagner, JR Asarnow, MB Keller, D Brent.// J Am Acad Child Adolesc Psychiatry.-2011.-Vol.167.-P.782-791

24. Zajecka J.M. Clinical issues in long-term treatment with antidepressants. / J.M. Zajecka //J Clin Psychiatry.- 2000/-Vol.61.-P.20–25.