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Cand. of Med. Sc., Assoc. Prof. L. V. RAKHMAN[1],
Doc. of Med. Sc., Prof. M. V. MARKOVA[2]

CLINICAL AND THERAPEUTIC LEVELS OF PATHOMORPHOSIS OF TREATMENT-RESISTANT DEPRESSION

[1] *Danylo Halytsky Lviv National Medical University*
[2] *Kharkiv Medical Academy of Post-graduate Education*

The analysis of archival medical records of patients with treatment-resistant depression for the period of 20 years (from 1991 to 2000 and from 2001 to 2010) identified the presence of pathomorphological changes of resistant depression. Clinical and therapeutic indicators that allow establishing the patterns for pathomorphism of treatment resistant depression were distinguished.

Key words: treatment-resistant depression, pathomorphism, clinic, therapy.

The problem of treatment-resistant depression (TRD) is very urgent at present. With the increasing prevalence of depressive disorders in general, according to many authors, in 40–60 % of cases depressive symptoms show stability to treatment, which in turn leads to a significant reduction in quality of life, increasing the period of temporary disability and often causes sustained reductions of social functioning [1–6]. Thus, the question of TRD is of significant scientific and practical interest. At current stage the following classification of resistance is commonly used [1, 6–8]:

- Primary (true) therapeutic resistance. This resistance is associated with an unfavorable course of the disease and depends on various biological factors. Primary resistance is due to genetic causes, is an individual patient's sensitivity to treatment and occurs extremely rare in clinical practice.
- Secondary therapeutic resistance (relative resistance). This resistance is due to development of the so-called phenomenon of adaptation to psychopharmacotherapy that means this is acquired syndrome formed as a result of taking the drugs and following adapting receptors into medicinal acting. In case of secondary resistance therapeutic response develops slowly, only a few elements of psychopathology are reduced.
- Pseudoresistance. The above type of resistance as usually associated with inadequate antidepressant therapy and is present in 50–60 % of all cases of TRD (inaccuracy in medicine choice, insufficient dose, the dose calculated excluding other medical conditions).
- Intolerance (negative resistance). This is increased sensitivity to the side effects, the severity of which exceeds the basic psychotropic action of administered drugs and the consequent inability to use adequate doses of medications and failure to achieve the desired therapeutic effect. However, there is scientific evidence about interaction between different types of resistance [9–11]. Therefore, the origin of resistance to therapy of depressive disorders is a multifactor model. In terms of the above, correction of these conditions involves consideration of many factors; one of the most significant is pathomorphism of treatment resistant depression [1, 12–15]. Research of modification of the clinical and dynamic parameters of TRD, including determining the most stable characteristics can clarify main patterns of pathomorphism at different levels (psychological, psychopathological, etiological, pathogenetic, clinical, nosological, therapeutic), which in turn will solve urgent issues due to improvements in diagnosis, treatment and rehabilitation of patients suffering from depressive disorders with resistance to the treatment taken. [1, 16–21]

The aim of our study was to establish the patterns of pathomorphism for TRD at clinical, nosological and therapeutic levels. To achieve this goal we used retrospective analysis of medical records with focusing on clinical, psychopathological, nosological and therapeutic aspects. During this study 200 medical records of inpatients with depressive disorders with phenomena of resistance to therapy from different nosological groups within the period of 20 years (from 1991 to 2000 — 100 medical records (Group 1) and from 2001 to 2010 — 100 medical records (group 2) were processed. This study was performed at archive of the Municipal Institution «Lviv Regional Clinical Psychiatric Hospital». The special «Analytical study maps for pathomorphism of TRD» was designed, in which sociodemographic, clinical and nosological, psychopathological, clinical-phenomenological, clinical and dynamic characteristics of depression were entered together with the data about treatment within this period. The subject of the study was a clinical and therapeutic aspect of TRD pathomorphism. Clinical

Table 1

Clinical characteristics of TRD pathomorphism, %

Indicators	Signs	Group 1	Group 2	Total
Nosological forms	Bipolar affective disorder, current depressive episode (F31)	34	29	31,5
	Depressive episode (F32)	21	20	20,5
	Recurrent depressive disorder (F33)	28	36	32
	Dysthymia (F34)	17	15	16
Hereditary	Yes	47	57	52
	No	18	12	15
	No information	35	31	33
Age of manifestation	< 20	8	13	10,5
	20–29	20	41	30,5
	30–39	41	26	33,5
	40–49	23	11	17
	50–59	4	8	6
	> 60	4	1	2,5
Duration of prehospital period	< 1 month	27	32	29,5
	1–3 months	40	49	44,5
	3–6 months	33	19	26
Severity of depressive signs	Mild	14	19	16,5
	Moderate	51	36	43,5
	Severe	35	45	40
Clinical characteristic of depressive syndrome	Anxiety (agitated)	31	38	34,5
	Melancholic	43	32	37,5
	Senesto-hypochondrical	10	20	15
	Aapathy-adynamic	5	7	6
	Astheno-nonenergetical	4	2	3
	Depressive with obsessions	7	1	4
Duration of depressive episode	< 3 months	18	12	15
	3–6 months	39	42	40,5
	6–12 months	26	35	30,5
	> 12 months	17	11	14
Comorbid pathology	Cardiovascular diseases	11	18	14,5
	Respiratory system diseases	14	19	16,5
	Digestive system diseases	27	25	26
	Metabolic-endocrine diseases	5	12	8,5
	Genitourinary system diseases	4	7	5,5
	Alcohol addiction	11	16	13,5
	No information	28	3	15,5
Suicide tendency	Yes	36	42	39
	No	64	58	61
Remission	Complete	3	1	2
	Partial	48	53	50,5
	Absent	49	46	47,5

and statistical evaluation of the data was carried out using the software package Statistica 6.0. In the study group comprised the patients with the following diagnosis (according to ICD-10 criteria): depressive episode of bipolar affective disorder in varying severity (F31.3–F31.5), depressive episode (F32), recurrent depressive disorder (F33), dysthymia (F34.1), and who demonstrated the signs of resistance to treatment (absence or partial response to therapy).

Retrospective analysis of medical records from 1991 to 2010 allowed establishing basic clinical parameters that characterize TRD pathomorphism (Table 1).

The findings obtained in the course of the study clearly indicated the subsistence of TRD pathomorphism at the clinical level. The most significant factors are due to increasing prevalence of TRD in a young age (20–29 years), the tendency to recurrence, increase the length of depressive episodes and severity of depressive symptoms, the prevalence of atypical forms of depressive disorders, combination of TRD with comorbid pathology, significant reduction in the quality of life (partial or complete remission or absence of remission).

Table 2

Therapeutic characteristic of TRD pathomorphism, %

Methods of treatment	Assessment criteria		Group 1	Group 2
Psychopharmacotherapy	Antidepressants	TCAs	100	88
		GCAs	12	21
		MAOIs	6	21
		SSRIs	52	100
		SNRIs	12	68
		HaCCAs	—	34
	Normothymics	Lithium	26	28
		Anticonvulsant drugs	73	92
	Tranquilizers		69	37
	Antipsychotics	Typical	17	14
		Atypical	15	36
	Psychostimulants		15	37
Bracing and symptomatic therapy			100	82
ECT			53	26
Plasmapheresis			4	2
Intravenous laser blood irradiation			—	1
Sleep deprivation			8	—
Psychotherapy			18	49
Physiotherapy			45	39
Alternative methods			24	21

One of the components of TRD pathomorphism is modifying therapeutic algorithm to overcome the resistance of depressive symptoms. It was shown that all types of resistance could interact with each other and had complex mechanisms of development. The analysis of medical records of patients in the study groups identified the following types of treatment resistance. Thus, in patients of group 1 primary resistance was observed in 2%, secondary in 28% of cases, inadequate antidepressant therapy (pseudoresistance) was found in 52 patients (52%), adverse events, which enabled the treatment were observed in 38 patients (38%). The characteristics of resistance types of depressive symptoms in patients from group 2 were as follows: primary resistance — 7 cases, secondary — 34 patients, pseudoresistance occurred in 48 patients, intolerance to the administered treatment was noted in 28 patients.

The characteristics of the treatment methods in the investigated category of the patients that illustrate therapeutic level of TRD pathomorphism are presented in Table 2.

These data suggest that psychopharmacotherapy is the preferred method of TRD treatment. Antidepressants play a leading role. Due to significant progress in synthesis and introduction of new antidepressants the structure of the prescribed drugs in the recent 10 years has changed in favor of SSRIs, a new generation of antidepressants (third or fourth wave) with more selective mechanisms of action and better tolerability profiles has appeared. Because of the proven data about normothymic activity of anticonvulsant drugs, the proportion of their use in TRD treatment increased, but the use of lithium mainly for supportive therapy remains. In the majority of cases, the process of overcoming resistance of depressive disorders requires administration of combination therapy with antidepressants and often requires introduction of other drugs (antipsychotics, tranquilizers) in the treatment protocol, the use of polypharmacy with special antiresistance measures. Reducing the proportion of tranquilizers caused development of addiction to the next drug. But this group is still quite common in medical prescriptions for patients with TRD. As this study shows, during the recent 10 years antipsychotics were used in more than a third of TRD cases, especially with drugs possessing an atypical effect. At present, increase in the frequency of use of neurometabolics is observed, it is caused by significant advances in the study of the role of neurometabolic disorders in the brain that correlate with phenomena of resistance to therapy in depressive disorders. It remains relevant to use of restorative therapy, but its value in some cases is significantly exaggerated; the presence of frequent comorbid pathology entails to use symptomatic treatment. During the recent decade among non-pharmacological methods

psychotherapy has been applied almost in half the cases, and availability and variety of psychotherapeutic techniques have expanded due to the appearance of medical psychologists in the medical staff, as well as to the improvement of the psychotherapy center in the hospital, opening of a rehabilitation center. The analysis of the medical records illustrates the significant decrease in the use of ECT in treatment of patients with TRD. Physical therapy (mainly manual therapy, exercise therapy, massage, water therapy) is also used in the treatment. Such methods as plasmopheresis and intravenous laser blood irradiation are not widely used in the clinic due to lack of appropriate technical equipment, single procedure was performed on other medical facilities in the region.

In conclusion, the analysis of medical records of the patients with TRD showed pathomorphism existence at the clinical and therapeutic levels. The indicators of clinical pathomorphism change in nosological structure, clinic, dynamics and psychopathological phenomenology of treatment-resistant depressive disorders. Prior to the therapeutic pathomorphism, it includes the new generation of psychotropic drugs, increasing segment of psychotherapy in complex models of overcoming treatment-resistant depressive symptoms.

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КЛІНІЧНІ І ТЕРАПЕВТИЧНІ АСПЕКТИ ПАТОМОРФОЗУ ТЕРАПЕВТИЧНО РЕЗИСТЕНТНИХ ДЕПРЕСІЙ

Л. В. РАХМАН, М. В. МАРКОВА

В результаті проведеного аналізу архівної медичної документації пацієнтів із терапевтично резистентними депресіями за період 20 років (з 1991 по 2000 та з 2001 по 2010 роки) ідентифіковано наявність патоморфологічних змін резистентних депресій, вивчено клінічні та терапевтичні показники, які дають змогу встановити закономірності патоморфозу терапевтично резистентних депресій.

Ключові слова: терапевтично резистентні депресії, патоморфоз, клініка, терапія.

КЛИНИЧЕСКИЕ И ТЕРАПЕВТИЧЕСКИЕ АСПЕКТЫ ПАТОМОРФОЗА ТЕРАПЕВТИЧЕСКИ РЕЗИСТЕНТНЫХ ДЕПРЕССИЙ

Л. В. РАХМАН, М. В. МАРКОВА

В результате проведенного анализа архивной медицинской документации пациентов с терапевтически резистентными депрессиями за период 20 лет (с 1991 по 2000 и с 2001 по 2010 годы) идентифицировано наличие патоморфологических изменений резистентных депрессий, изучены клинические и терапевтические показатели, позволяющие установить закономерности патоморфоза терапевтически резистентных депрессий.

Ключевые слова: терапевтически резистентные депрессии, патоморфоз, клиника, терапия.

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