Chapter 3
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Study on Psychiatric Disorders and Their Medical-Social Consequences in Patients with Amyotrophic Lateral Sclerosis and Members of Their Families

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ABSTRACT

A total of 118 ALS patients and 97 family members were evaluated. Psychiatrists observed all of the patients and their relatives. Study objectives were to detect anxiety, depression, habitual intoxications, frontotemporal dysfunction, unjustified expenses and poor collaboration with physicians among ALS patients and their families. The Hamilton Depression Scale (for patients and their families) and the frontotemporal dementia scale were used in the evaluation (for patients).Psychiatric illnesses were discovered in 101 ALS patients (85%) and 51 family members (52.5%) (significantly more frequently in ALS patientsp<0.05). In ALS patients, the spectrum of situation-mediated illnesses was rather evenly represented, with no apparent predominance of situation-mediated depression.Rare occurrences of ALS combined with endogenous psychological problems have been reported.Frontotemporal cognitive deficits reaching the degree of dementia were seen in 4.2 percent of cases in 33 individuals (28 percent). Only situation-mediated psychiatric problems with a clear predominance of anxiety (28 percent, p<0.05) were seen among family members of ALS patients. Habitual intoxication affected 49 ALS patients (41.5%) and 80 members of their families (82.4%) (significantly more frequently in family members, p<0.05). Due to the high incidence of anxiety problems, people refuse to cooperate with professional physicians (73-76%), reject aggressive treatment approaches (74.5%), approach fraudsters, and bear the burden of unjustifiable spending (29.6 percent of cases). Consistent patronage of ALS patients' families by neurological and psychotherapeutic services, with involvement of psychiatrists and narcologists in individual cases, is recommended, as this can increase the number of life-saving procedures performed at ALS and improve the quality of life of patients and their families.

Keywords: Amyotrofic lateralsclerosis; psychiatry; anxiety; depression; frontotemroral dysfunction; habitual intoxications; sialorea.

1. INTRODUCTION

Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disease accompanied by gradual development of complete movement loss, dysarthria, dysphagia, respiratory failure, and, in a number of cases, frontotemporal cognitive impairments or dementia [1,2]. According to international writers' data, almost half of ALS patients have depression that requires ongoing monitoring by a psychiatrist and/or psychotherapist [3]. ALS becomes a heavy load for caregivers (family members, friends, nurses), which cannot remain concealed in their psychiatric state, and, to the greater extent, the psychiatric state depends on impairments of behavior of ALS patients, rather than the motor deficit [1,4,5,6]. ALS patients and their caregivers intensively searches sources in the internet about palliative care issues and need evidence-based stalks to avoid costly helpless treatments and to makedecisionsthat leadto improve life quality of patients, relatives and caregivers [7].

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Study objectives were to detect anxiety, depression, habitual intoxications, frontotemporal dysfunction, unjustified expenses and poor collaboration with physicians among ALS patients and their families.

2. MATERIALS AND METHODS

In 2007 - 2013, 118 ALS patients and 97 members of their families were examined. The psychiatric examination was performed at the Department of Psychiatry and Suicidology, Eramishantsev Hospital in Moscow (V.M.G.), and at home (A.S.L.) and included interviewing and assessment on the Hamilton Depression Scale (HDS) at personal meeting with the patient or by e-mail and the scale of frontotemporal dementia (FTDS) at personal meeting with the patient's relative or by phone [8,9]. The diagnosis ALS was set based on the Revised El-Escorial Criteria of 1998 taking in consideration the results of examination by the neurologist or revision of medical document with registration of results of neurological examination, needle and stimulation electromyography and magnetic resonance imaging of the central nervous system [10]. The follow up observation 1 time in 2-3 months (out-patient examination by neurologist and psychiatrist at home0 was offered to all patients. All patients and their relatives were examined by psychiatrists (V.M.G. or A.S.L.) The diagnosis of different psychiatric disorders was determined based on the ICD-10. Single episodes were taken in account. At that, the urge to be examined more than twice for confirmation of the diagnosis, multiple attempts to obtain the information about ways of ALS treatment from the internet, including ones at the night time and wish to spend more money on the disorder and the treatment were referred to manifestations of the spectrum of anxiety. Tobacco smoking more than 10 cigarettes a day, consumption of more than 200 ml of alcohol a week, drug dependence with constant intake (non-steroid anti-inflammatory, antihistamine drugs) for more than 1.5 months with withdrawal syndrome, the use of cholinolytics as remedies for sialorrhea treatment and psychotropic drugs (sedatives, tranquilizers, antidepressants) for more than 1.5 months with withdrawal syndrome as well as administration of narcotic medicines prohibited by Russian Federation law, were regarded as habitual intoxications (abuse) [11]. The study was approved by Ethics Committee of Eramishantsev Moscow City Hospital. All collected data was strictly confidential. Familial character of psychiatric disorders was not disclosed to any medical psychiatric institution. Patients were not put under registry of psychiatric disorders which may impose limitationon their employment. The statistical processing was carried out using Student's criteria and chi-square, Spearman correlation analysis. The statistical software package Statistica 7.0 was applied.

3. RESULTS

Psychiatric disorders were revealed in 101 ALS patients (85%) and 51 members of their families (52.5%). ALS patients suffered from psychiatric disorders significantly more often than members of their families ($p<0.05$). The spectrum of revealed psychiatric disorders is represented in Table 1, and medical-social consequences of these disorders – in Table 2.

From Table 1 it can be seen that the majority of ALS patients had situation-mediated disorders (n=63, 53.3%), while 5 patients (4.2%) had endogenous diseases or syndromes (1 case of acute psychosis was registered). At that, in 33 patients (28%) frontotemporal cognitive impairment was observed (mean log rank 1.47 [1.92; 1.26]), reaching the level of dementia in 4.2% of cases (mean log rank -0.4 [1.07; -3.09]). The mean score on the HDS in ALS patients with situation-mediated depression was 17±4, with situation-mediated anxiety disorder - 15±5, and with situation-mediated anxiety-depressive disorder - 21±6 ($p>0.05$ between the groups). The spectrum of situation-mediated disorders in ALS patients was represented relatively evenly with insignificant predominance of situation-mediated depression. In the process of specification of family psychiatric history it was revealed that in ALS patients with endogenous psychiatric disorders family cases of psychiatric disorders were observed, while in patients with situation-mediated disorders indirect documentary unconfirmed data on psychiatric impairments in relatives were received in 15% of cases.

Table 1. The spectrum of psychiatric disorders in ALS patients and their brelatives

Psychiatric disorders	ALS patients(n=118)	Family members БАС(n=97)
Situation-mediated depression	26 (22%)	8 (8.2%)
Sitaution –mediated anxiety disorder	19 (16.1%)	29 (29.8%)
Situation-mediated anxiety and depressiondisorder	18 (15.2%)	8 (8.2%)
ALS phobia	-	1(1%)
Otherphobias	-	1 (1%)
Paranoya	1 (0.8%)	4 (4.1%)
Schizophrenia	1(0.8%)	-
Bipolar disorders	1 (0.8%)	-
Schoizoaffective disorder	2 (1.6%)	-
Frontotemporal cognitive changes/ dementia	33 / 5(28% and 4.2%)	-
Mentally healhy	17 (14.4%)	46 (47.4%)

Table 2. Medical and social consequences of psychiatric disorders in ALS patients families

Medical and social consequences of psychiatric disorders	Number of families (n=118)	
Denial of examination by doctor	9 (7.6%)	
Denial of follow-up visit	73 (61.8%)	
Denial of aggressive treatment (gastrostomy, non- invasive ventilation, artificial ventilation, eraly tracheostomy)	88 (74.5%)	
Habitual intoxicationa	**ALS patients (n=118)**	**Family members (n=97)**
- tobaccosmoking	20 (16.9%)	28 (28.8%)
-alcohol abuse	5 (4.2%)	17 (17.5%)
- medication abuse	22 (18.6%)	19 (19.5%)
- drug abuse	4 (3.4%)	1(1%)
Cholinolytic use (for sialorrea or aspsychotropic)	19 (16.1%)	15 (15.4%)
Methods not envisaged by the International Standard of ALS management	76 (64.4%)	
- appeal to scammers what lead to marked material expences	35 (29.6%)	
Treatment abroad	18 (15,2%)	

Among members of families of ALS patients, only situation-mediated psychiatric disorders were detected with obvious predominance of anxiety ($p<0.05$). The mean score on the HDS in family members of ALS patients with situation-mediated depression was 12±4, with situation-mediated anxiety disorder - 22±5 ($p<0.05$ in comparison with the previous parameter), and with situation-mediated anxiety-depressive disorder - 16±6. Single cases of ALS phobia and other types of phobia were noted, as well as cases of paranoiac syndrome in two families of ALS patients, which manifested with delusion ideas of causing material damage for medical personnel. It was not possible to collect family anamneses of psychiatric disorders in these families, however, the information about presence of cerebrovascular disease or post-traumatic encephalopathy and experience of work in extreme situations and/or on the leading position in members of these families was documented.

From Table 2, it can be seen that the majority of families at different stage of the disease of the ALS patient refused follow-up visits (personal or virtual communication) (61.8%) and addressed to methods of ALS treatment not envisaged by the International Standard (64.4%). The denialof primary examination by the doctor from our group was seen in patients with probably severe psychiatric disorders and syndrome of social isolation only in 7.6% of cases.

Methods envisaged by the International Standard of ALS treatment were Riluzole, non-invasive (NIV) and artificial lung ventilation (ALV), drugs for sialorrhea, psychotropic drugs, adaptive home devices

[12]. It should be noted that the single treatment method currently not included in the International Standard of ALS treatment, but offered to patients by the co-author (G.N.L.), was early tracheostomy (ET), which was justified for the treatment of impairment of expectoration in patients with bulbar debut of ALS not able to adapt to the NIV The NIV, ET and ALV were referred by the authors to the methods of aggressive palliative therapy.

Methods not included in the International Standard of ALS treatment comprised any experimental pharmaceutical treatment methods, high doses of neuroprotective drugs in the form of infusions on the physiological solution with the risk of development of central pontine myelinolysis in patients with long-term hyponatremia and impaireds wallowing, injections in collapsed veins with the risk of thrombophlebitis; intramuscular injections in atrophied muscles with the risk of post-injection complications and non-absorption of (expensive) drugs; treatment with stem cells, as well as hyperbaric oxigenation, immunotherapy, haemotherapy and physiotherapeutic methods in case if these methods were presented by people offered them as means directed to slowing of progression of the disease. In case if experimental treatment methods were offered on the commercial basis and presented as means able to cure the ALS patient or improve their condition, the authors regarded these activity as fraudulent.

The denial of any aggressive ALS treatment methods indicated at the moment of examination was registered in 74.5% of families of ALS patients. It should be noted that the ALV (that is artificial prolongation of life at ALS) is not indicated to elderly ALS patients, as well as in case of frontotemporal cognitive impairments, psychiatric disorders, expressed toxic abuses, since it is not possible to determine clearly a patient's determination for this action and document a will specifying conditions for disconnection of these patients from the device in the future [13].

It is necessary to mention that the denial of the use of aggressive ALS treatment and, sometimes, repeated visits of doctors and administration of drugs, was always seen in families of ALS patients with endogenous psychiatric disorders, frontotemporal cognitive impairments or dementia and psychiatric disorders, however, members of these families were either adapted (in case of presence of premorbid psychiatric peculiarities in ALS patients) or de-adapted (at development of psychiatric peculiarities in patients within the frame of this disease) to this difficult situation.

Addressing to scammers that resulted in significant material expenses was seen approximately in one third of families of ALS patients (29.6%). This being the case, only 15.2% of the addressed people were treated abroad. From them, about one third of families were treated in organizations regarded by us as fraudulent.

At analysis of habitual intoxications in families of ALS patients, it was found out that 49 patients (41.5%) and 80 members of their families (82.4%) suffered from them. In family members of ALS patients, habitual intoxications were observed significantly more often ($p<0.05$) (Table. 2). Among ALS patients, tobacco smoking and drug abuse were distributed almost evenly (16.9% and 18.6%), while alcoholic and narcotic dependence were represented by single cases (4.2% and 3.4%) ($p<0.05$). Among members of families of ALS patients, toxic abuse (with the exclusion of one case of narcomania) were represented approximately equally (17.5% and 19.5%) with slight predominance of tobacco smoking (28.8%) ($p>0.05$). Drug dependence both in ALS patients and members of their families, in general, was observed in connection with administration of hypnotic and non-steroid anti-inflammatory drugs (painkillers).

The analysis of intake of cholinolytic drugs and abuse connected with their administration revealed that ALS patients used them, mainly, for sialorrhea treatment often ignoring their intake as psychotropic drugs (16,1%), while members of their families, in general, used them in the form of antidepressants (15.4%) ($p>0.05$).

The comparative analysis of distribution of frontotemporal cognitive disorders and the use of cholinolytic drugs for ALS treatment demonstrated that drug abuse from the latter developed in 15 from 33 patients (15.3%) with frontotemporal cognitive impairments. In general, it was characteristic for patients with bulbar onset ALS required several cholinolytic drugs for correction of sialorrhea, as

well as emotional disorders. Data reliably confirming strong correlation between the frontotemporal cognitive, bulbar disorders and requirement of two cholinolytics were obtained ($r=0.7$; $p > 0.001$). In one patient, withdrawal of cholinolytics penetrating the central nervous system with change to botulinum toxin for sialorrhea led to improvement of assessment by frontotemporal dementia score and ability to critical analysis based on the Hamilton scale in 2 months.

4. DISCUSSION

Previously, neither in the international nor domestic literature, the spectrum of psychiatric disorders in families of patients with one of the most severe disorders (ALS) was considered as a whole. Besides, the analysis of medical and social consequences of these disorders was not performed. Such factors as some types of toxic abuse (intake of alcohol and smoking) were previously regarded in the international literature only as risk factors of ALS development [14,15]. However, taking in consideration insufficient knowledge of genetics of this disease and the risk of its development in the family, in this work the authors made an attempt, in particular, to assess the risk of medical and social complications in families with the persisting huge medical-social problem, in cases with ill and not yet ill people. Investigations of cooperation of ALS patients are scarce and devoted only to some treatment methods, at that, studies of harm for families of ALS patients connected with fraudulent activity of cheating organizations have been never performed [1]. Currently, the only organization dealing with the informational struggle in this area is the site www.alsuntangled.com. The actuality of investigation of psychiatric condition of ALS patients and their relatives is connected with the circumstance that the lifespan of ALS patients directly depends on their psychiatric state [16].

It has been shown that severe depression in ALS patients can be diagnosed in 9% of cases, moderate and mild in 37% of cases [3]. The value of severe depression in this work approximately corresponds to the percentage of ALS patients refused primary examination by the physician in our study (7.6%). If the latter is added to the total percentage of situation-mediated depression in our work (moderate and mild based on the mean score on the HDS 17±4) the sum equals to 33.6% meaning that it is slightly lower than in the study of J.G.Rabkin [3]. At insignificant predominance of situation-mediated depression in the spectrum of situation-mediated disorders in ALS patients, the severity degree of all of these disorders on the HDS is approximately the same, being closer to moderate.

In the current study, in the spectrum of psychiatric disorders among members of families of ALS patients, anxiety disorders dominate significantly both on the number (29.8%) and severity degree (22±5). The second place is taken by situation-mediated anxiety-depressive disorders, with the role of situation-mediated depression being insignificant. The high share of anxiety cases appears to lead to impairment of healthy lifestyle, habitual intoxications (82.4% among all family members), the refusal from cooperation with professional physicians (73-76% of cases) and addressing to cheaters (29.6% of cases). Dissociation observed in the conscious of ALS patients can be the reason, based on the data of foreign studies: 94% of patients do not want to speed up approaching of the lethal outcome, but, at that, they refuse gastrostomy and NIV significantly more frequently, in comparison with their relatives, which causes feelings of “suffering” and “loneliness” in members of their families (according to the Hospital Scale of Anxiety and Depression) that are higher than in patients themselves [17]. It is quite obvious that both ALS patients and members of their families often need active psychological nursing and sometimes consultation of the psychiatrist or narcologist [18].

If a patient with ALS takes the drug Riluzole metabolized by cytochrome CYP2A1 and causing drug-induced hepatitis in 3-12% of cases, it is necessary that the patient have reduced the number of cigarettes a day, as smoking intensifies the work of this cytochrome, and abstained from strong alcoholic beverages for achievement of the maximal activity of the drug and minimization of adverse effects (1.2).

The analysis of correlation of frontotemporal cognitive, cognitive, bulbar disorders and administration of cholinolytics, which have not been earlier performed in the international and domestic literature, deserves special attention. The fact of partial regress of frontotemporal cognitive and psychiatric disorders at withdrawal of cholinolytics at ALS, which requires further investigation, has been performed for the first time.

5. CONCLUSIONS

The following general recommendations on the lifestyle for ALS patients and members of their families are obligatory: they should maintain the proper regimen of sleeping and wakefulness, avoid any types of toxic abuses, and address for help to specialists in the area of psychiatry, psychotherapy and narcology in difficult situations.

Taking in consideration high prevalence of psychiatric disorders among ALS patients and members of their families in the Russia, it is recommended to perform joint consultations for patients and members of their families by the neurologist and psychiatrist (psychotherapist), because other consultation conditions can be connected with high professional harmfulness for both the physician\neurologist and specialist in the area of ALS. Multidisciplinary monitoring of ALS patients should include, by all means, regular examination by the psychiatrist and/or psychotherapist, and, along with the disease progression, mostly at home, consultations of members of their families. Cholinolytic drugs should be used with caution in ALS patients taking in consideration the presence of frontotemporal cognitive disorders in some of them. In cases, when patients with ALS have frontotemporal cognitive and moderate or expressed psychiatric impairments, as well as endogenous psychiatric diseases, the psychiatric consultation is required. It should be actively recommended by other physicians having contacts with the ALS patient.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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He is graduated from Russian State Medical University in 1998. He obtained MD and PhD degrees from a reputed organization . He has 23 year experience in electromyography, neuromuscular diseases, neurodegenerative disorders and motor neuron disease. In 2010-2011, He wrote and published the complex monograph "Amyotrophic lateral sclerosis". Since 2006, He is a Director of Russian Charity ALS Foundation named by Nina Levitskaya. In 2016, He became the Laureate of Emissary Spade (Luxembourg). Since 2013, He served as a head of Gleb Levitsky clinic with private ALS center in Moscow. He is the author of more than 70 scientific publications. He Describes ALS phobia in 2012 first in world literature.



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He was born in 1976 . He is a psychiatrict and psychotherapeutist. In 1998, he graduated from State Academy of Maymonid and submitted thesis on intoxications caused by psychoactive drug abuse. He Improved qualification in narcology and psychiatry in the Institute of Narcology, worked in private clinics. In 1999, He started cooperation with Dr Gleb Levitsky and started to consult patients with amyotrophic lateral sclerosis. The attention was paid to problem of neurotic and depressive disorders in ALS patients. Together with Gleb Levitsky and Dr Vadim Gilod he elaborated criteria of diagnosis and pharmacotherapy in neurotic and depressive disorders in ALS patients. In2008 , he improved qualification in psychiatry in the Department of psychiatry headed by professor P A Baranov and he was assigned psychotherapeutic specialization. He consults ALS patients with Dr Gleb Levitsky, performs psychotherapy, and writes articles about peculiarities of psychotherapy in ALS patients and their family members. Since 2012, togetherwith Vadim Gilod and Gleb Levitsky described the phenomenon of ALS phobia and consults patients with this disorder.



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He was born in 1959. He is associated with Russian State Medical University, Russia. He is specialized in psychotherapy, qualification improvement in narcology, psychiatry, and psychotherapy. He has Certificates in psychiatry, psychotherapy, organization of healthcare. He served in different field: Since 1980, in Psychiatric hospital № 6 forchildren and adolescentls in Mosocw, from 1982 -1989 in Tula district Narcology ambulatory, from 1989 – 1990 as a psychotherapeutist in Psychiatric ambulatory in Moscow; from 1990 — 1997 as a psychiatrict in the Department of Psychiatry and Suicidology of Moscow City Hospital , and Since 1997 as a Director of in Department of Psychiatry and Suicidology of Moscow City Hospital He has over 20 articles in periodicals and methodical recommendations. He served as a Corporate executive of «Moscow city professional society of psychotherapeutists, psychologists and social workers, and Member of Russian psychiatric society. He has Participation in work with emergency situation sufferers, and creation of center of prevention of narcomany among youth in Baumann University. He received Certificate of Honor of Russian Federation Moscow Government, Certificate of Honor of Ministry of Health of Russian Federation, Certificate of Honor of Department of Healthcare of Moscow, Certificate of Honor of Prefecture of North Western District of Moscow, Certificates of Honor of Eramishantsev Moscow City Hospital and Tula Narcological Ambulatory. He has been rewarded by medal of the order of Merit of the Motherland the 2nd degree.

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