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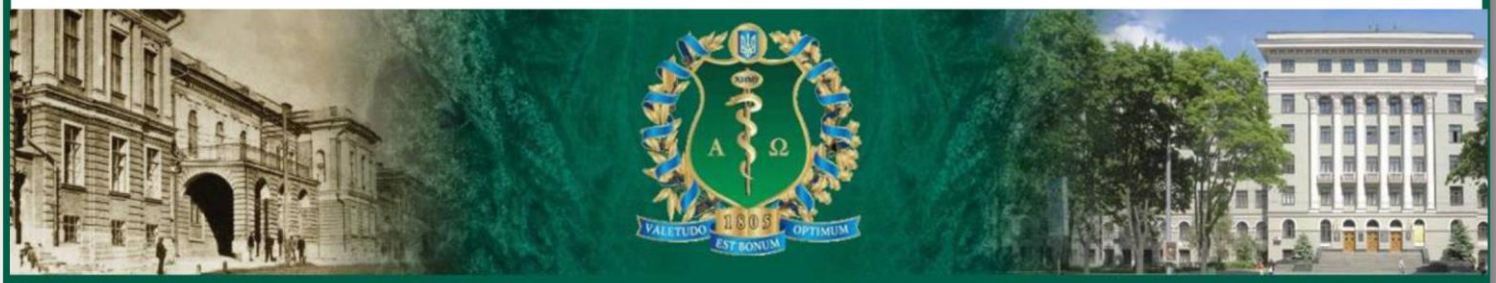

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PSYCHIATRICS

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EXPERIENCE OF EXTENDING ANTIPSYCHOTIC AID TO WOMEN WITH EPILEPSY COMPLICATED BY PSYCHOTIC DISORDERS

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Abstract: This research introduces classifications of epileptic psychoses, current views on etiopathogenic mechanisms of epileptic psychoses development, different aspects and types of their course, considers modern recommendation and describes presentation of epileptic psychoses as well as major approaches to their treatment. The article presents the results of Quetiapine administration in the treatment of epileptic psychoses.

KeyWords: Epileptic psychoses, clinical picture, therapy, Quetiapine.

INTRODUCTION

The issue of epileptic psychoses has recently received the deepest attention due to the fact that patients who suffer from this pathology quite often get full-time treatment in psychiatric clinics as well as receiving necessary aid in out-patient psychiatric institutions. According to the WHO data epileptic psychoses vary in different countries within 2.5% to 8% and mostly depend on the prevailing type of psychotic disorder [1]. Most common are epileptic psychoses of transitory (acute) type (64%) and paroxysmal type (24–28%) with chronic epileptic psychoses being observed much more rarely (8–12%).

Developing efficient strategies for correcting and preventing epileptic psychotic disorders remains an urgent issue in clinical practice since the current level of expertise in this pathology does not provide an unanimous understanding of the pathogenesis of these disorders.

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There is also no relevant evidence of efficient prescribing psychotropic drugs to the patients who suffer from this pathology. Implementing the means and methods of epileptic psychoses pharmacopeia is a topical direction in neuropharmacology and psychiatry. It is determined by the significance of epilepsy itself as well as a number of associated psychotic disorders (epileptic personality changes, epileptic dementia, epileptic psychoses), leading to social misadaption, increased full-time clinic periods and disablement of this category of patients.

The majority of epileptic patients have various psychotic disorders, and the probability of their development increases proportionally to the disease duration. Their origin is determined by a variety of factors, such as the patient's age at the beginning of the disease, the form of epilepsy, its type, the disease resistance to pharmacotherapy, the patient's compliance level, anti-epileptic drugs intake in regular and adequate dosage, additional health hazards, accompanying disorders and duration of the disorder.

Significance of epileptic psychoses is preconditioned by both difficulties of differential diagnosis (the difficulty of differential diagnosis of organic and epileptic psychoses is determined by the primary cause of epilepsy onset since epileptic psychoses may as well be regarded as organic ones once the morphological basis is proven) and the present social and economic consequences for the society

since such complications, when improperly treated or prevented, lead to disability as well as developing or intensifying the features of epileptic dementia.

Epileptic psychoses are disorders of mental presentation characterized by obfuscation which means explicit affective disorders, delusion, hallucination and catatonic disorders related to non-obfuscation, which significantly reduce the understanding of what the patient's surroundings, self-awareness and ability to establish adequate contacts with surroundings [1].

Epileptic psychoses are not unique psychopathic disorders of epilepsy; they are a manifestation of the epileptic disease or its complication. They are mostly observed in patients with symptomatic or conventionally-symptomatic (cryptogenic) epilepsy with unfavorable or medium-progredient epilepsy with long duration. Epileptic psychoses develop in pathogenic connection with active paroxysmal epileptic conditions and specific personality changes or epileptic dementia.

It is important to point out that there are a few classifications of epileptic psychoses. The classification by B. A. Kazakovtsev [1] distinguishes transitory, paroxysmal and chronic epileptic psychoses. Transitory psychoses have an acute beginning, last from a few hours to a few days, may be with obfuscation (dreamy state after a series of tonic-clonic seizures, hallucinatory and delusion states, psychomotor agitation, aggression, epileptic delirium, epileptic oneiroid) or without it (acute paranoid, dysphoric psychosis). Paroxysmal epileptic psychoses are more prolonged in time and last up to one month.

These include affective, affectively delusive, delusive, catatonic and catatonic-paranoid psychoses. Chronic epileptic psychoses last a few months or years, develop at the later stages of the disease (10–15 years), are characterized by distinct polymorphism and retained consciousness. Psychiatrists most often deal with paranoid, hallucinatory paranoid syndromes, verbal hallucinosis, Kandinsky-Clérambault syndrome, dementia with delusion-like utterances, schizophrenoidea states. In clinical practice, epileptic psychoses are customarily systematized according to the time of onset as to paroxysm seizures [12] as pre-ictal (appear before seizures and end when those develop); ictal (appear at the time of seizure or as a consequence to the status of non-paroxysmal epileptic seizures); post-ictal (appear immediately after the epileptic seizure or within 12–72 hours after its end, often after a series of complex partial seizures with or without secondary generalization) and inter-ictal (emerge in the inter-seizure period and are not connected with epileptic seizures). Inter-ictal psychoses are mostly acute or chronic.

There is also a separate type of epileptic psychoses, particularly alternating psychosis being regarded to as inter-ictal psychosis also referred to as Landolt syndrome. The development of this kind of psychosis is associated with "forceful normalization" of EEG curve. This kind of psychosis is characterized by the development of psychotic symptomatology secondary to paroxysm activity reduction and a decrease in seizure frequency. This psychosis may last from a few days to a few weeks. Nowadays medically induced psychosis is distinguished as a side effect to anti-epilepsy therapy. This kind of psychosis can be provoked by any kind of drugs which are used to decrease epileptic activity as a response to taking traditional anti-epilepsy drugs as well as a result of taking new generation drugs. Most authors believe this kind of psychosis does not belong to epileptic psychoses, though it should be taken into account when carrying out differential diagnosis with alternating psychosis [5].

Etiological agents triggering epileptic psychoses are the presence of cryptogenic temporal lobe epilepsy with complex partial seizures with or without generalization, with psychic symptoms and automatisms, improper medication treatment when the prescribed anti-epilepsy drug does not correspond to the seizure type, violating the mode of basic anti-epilepsy therapy, interrupting medication intake, increasing the number of seizures before developing a psychotic episode, the presence of a persistent psychotraumatic factor related to the emotions of fear and anxiety [6].

According to various studies, the development of psychoses is determined by epileptic disorders in neuron activity mostly in limbic structures related to emotion and motivation regulation, complex automatic forms of behavior, which is proven by EEG examinations. Specific changes and dynamics of bioelectrical brain activity while developing psychoses are characterized by an increase and expansion of the epileptic system, low-rate low-amplitude diffusion activity in combination with hyporeactivity to external stimuli for spontaneous psychoses formation or a decrease in intensity of epilepsy mechanism of brain functioning with desynchronization phenomena while developing psychotic states with alternative formation mechanism [7]. Epileptic process in the brain itself is the main factor for psychoses development in epilepsy, which is of fire of polyfire character and always involves mediobasal structures, temporal and frontal lobes on both sides, with mostly complete lateralization. Such disorders develop due to prenatal, perinatal or postnatal brain damage as well as an increase in secondary organic process in brain due to neuron collapse during epileptic bursts.

Taking into account the two components of epileptic process development, namely paroxysm and non-paroxysm mechanisms [9, 10], which are the main triggers of epilepsy psychoses and various types of epileptic psychoses at any stages of illness, the therapeutic tactics must be comprehensive and include anti-psychotic therapy, tranquilizers, antidepressants, anti-epileptic drugs, neuro-metabolic therapy, normalizing brain CSF circulation, psychotherapy correction and so on.

The therapy, when rendering help to those patients, with the exception of the ictal epileptic psychosis type, should start with anti-psychotic drugs, which are the basis in this case. All anti-psychotic drugs by the mechanism of action affect productive psychotic disorders thus providing full or partial reduction of these psychopathologic signs. The first generation antipsychotics (neuroleptics) are mostly antagonistic to dopamine receptors and may provoke and increase neuron epileptic activity. Moreover, most neuroleptics even in small doses may provoke side effects in the form of extrapyramidal disorders on account of changes in the state of the extrapyramidal system.

The incidence and clinical significance of these disorders depend on the presence and the intensity of organic encephalopathy in patients with epilepsy. These disorders are undesirable and poorly tolerated by patients. Clinicians should avoid the drugs of major distinct proconvulsive action when prescribing neuroleptic drugs to patients with epileptic psychoses. It is a well-known fact that phenothiazine drugs are most capable of epileptic threshold reduction. The least proconvulsive action belongs to phenyl propyl ketones although their usage significantly increases the risk of extrapyramidal disorders and late dyskinesia. The second generation antipsychotics (atypical antipsychotics) are characterized by a significantly smaller proconvulsive effect, with medium therapeutic doses they rarely cause extrapyramidal disorders and late dyskinesia, most of them cause insignificant rise in blood serum prolactin level, they not only efficiently function for productive symptomatology but also detain the development of negative symptomatology or mitigate and level its manifestation.

Considering the above said we believe that patients with epileptic psychoses should be prescribed atypical antipsychotic drugs which can have a direct impact on most mechanisms of epileptic psychoses development and decrease further destructive effect. According to recommendations by a number of scientists, such as S. Koch-Stoecker [11], L. M. Yurieva, S.G. Nosov [8], A. E. Dubenko, V. I. Korostiy [5] and others, when choosing antipsychotic drugs it is advisable to prescribe those with minimum potential side effects, to take into account side reactions and toxic influence, to prescribe minimum effective doses, to strictly keep to their titration, not to exceed small or medium day doses and the period of antipsychotic drug intake should not exceed the period of psychosis but be minimally sufficient.

Considering the fact that any antipsychotic drugs by their action mechanism may provoke or enhance epileptic activity, practically any research in the field of estimating

the risks of epileptic seizures after taking antipsychotic drugs, has been carried out involving patients with psychic disorders without epilepsy, our own observation and analysis of the recent scientific publications enables us to consider quetiapine as one of the most acceptable drugs for treating epileptic psychoses patients. No difference as to patient seizures has been registered with the patients without epilepsy who received quetiamine or placebo treatment (0.4 and 0.5 respectively) [5].

The advantage of quetiapine lies in the wide clinical and pharmacological spectrum: antipsychotic, antimania, antiaggression, anxiolytic and sedative effects. Besides, quetiapine is capable of forming a rapid clinical effect accompanied by a high safety profile, it has lower spectrum of side effects compared to other antipsychotic drugs (hyperprolactinemia, metabolic and extrapyramidal complications, the anticholinergic effect; it has an insignificant potential as to body mass increase).

Quetiapine and its active metabolite norquetiapine act as antagonists to dopamine D2-receptors with moderate affinity [13, 14], norquetiapine increases the concentration of the pre-frontal dopamine and serotonin [13,15], blocks the presynaptic receptors 5-HT7 [14, 15], which explains its antipsychotic effect and the influence on the wide spectrum of affective and cognitive disorders. Improvement of cognitive functions in patients treated for schizophrenia and other psychoses can be explained by its low relationship and quick dissociation with dopamine D2-receptors [13, 14, 15], in this research patients were given a medium drug dose – 600 mg a day. According to Chang et al., 2012 Dell`Osso et al., 2012, it can improve life quality in any forms of affective disorders. Quetiapine is a pleiotropic drug which can affect a few targets and can be efficient for treating various psychotic disorders [14]. Quetiapine treatment stipulates symptomatic remission and improves the life quality [15]. In the research by Miljevk et al., 2013 quetiapine demonstrated the neuroprotective effect, within the oxidant system, the drug promoted a decrease in superoxide dismutase and prooxidant effects, antioxidant inhibition, induced hydrogen peroxide in vitro [13, 14, 15] and was capable of protecting cell cultures from oxidative stress related to cytotoxicity induced by the ß-amyloid [13, 15]. These data prove the important role of the drug in reducing the level of active intracellular oxygen and calcium forms, which enhances its antioxidant properties [13, 14, 15]. It can also prevent overproduction of intracellular enzymes of superoxide dismutase, catalase, glutathione peroxidase [14, 15]. Other neuroprotective effects of quetiapine include its capability of removing neurogenesis oppression in hippocampus caused by chronic stress [13, 14, 15].

2 PURPOSES, SUBJECTS and METHODS:

2.1 Purpose

The aim of the study was to study the quetiapine clinical effectiveness for treating patients with epileptic psychoses.

2.2 Subjects & Methods

The program of research on the clinical effect of quetiapine has been carried out with 19 female patients aged 26 to 59 with various types of epileptic psychoses except those of the ictal type. Of them, 12 patients were diagnosed with post-ictal epipeptic psychosis, 6 patients with inter-ictal epileptic psychosis and 1 patient with alternating psychosis. By ICD-10, all the patients who took part in the research fall into the F 06 category and they took quetiapine in the combination with an anti-epilepsy drug. At the beginning of the research and during the whole period of treatment the patients were subject to clinical psychopathology, laboratory, neurovisual, ECG examination, the glycaemic and lipidic blood serum profiles being under control.

Within the term of research patients were given quetiapine in different therapeutic doses. Titration started at 25 mg a day on the first day of treatment with a gradual dose increase, which did not exceed the existing recommendations and in some cases even did not go as high as 50 mg a day during titration. The maximum daily dose was 600 mg, the minimum efficient one was 200 mg a day in

two takes. Depending on the type of epileptic psychosis the correction of quetiapine doses and intake duration was performed. Basing on current recommendations, the drug was prescribed in minimum efficient doses and for the minimum sufficient period.

Conflict of interests

There is no conflict of interests.

3 RESULTS AND DISCUSSION

In the process of research, the initial therapeutic effect for most of the patients was observed during the first week of drug titration (52.6% of patients) and was manifested by sleep improvement, reducing the intensity and duration of psychotic affect; the patients had more gentle and moderate attacks and were more responsive to the surroundings. At the end of the second and the beginning of the fourth week of quetiapine treatment positive alterations of the mental state were observed with proven reduction of the major psychotic symptomatology, leveling of affect, normalizing the mood, stabilizing somatic-vegetative status. There was clinical psychopathological evidence of mental state stabilization on the sixth week of therapy in 73.6% of the patients under investigation.

After the reduction of psychotic state for preventing the withdrawal syndrome the drug dose was gradually reduced with continuous control of the patient's mental state until the ultimate stop of quetiapine intake. It is necessary to point out that clinical psychopathological, laboratory and neurovisual examination repeatedly performed during the whole period of study showed a positive effect of the drug intake on cognitive functions of the patients (36.8% of the patients), praxis improvement (26.3%), neurodymanics improvement (42.1%), voluntary regulation and thinking (68.4%). ECG examination showed no signs of cardiotoxic effects of the drug on any of the patients. According to glycemic and lipid profiles, the deviation from standardized parameters was not statistically significant ($p<0.05$). None of the patients was found to have clinical manifestations of extrapyramidal disorders.

The research showed that the majority of the patients (84.2%) gave a positive response to treatment and displayed good therapy endurance. No clinically important side effects as to higher mental functions have been registered. The most common side effects were sedation (42.1% of the patients), drowsiness (47.3%), orthostatic hypotension (26.4%), dyspepsia (15.7%) and headache (21.1%). These side effects were mostly observed at the beginning of treatment depending on the drug dose, reduced with the process of dose correction and slowing the titration speed. Only one patient (5.2%) with epileptic psychosis stopped taking the drug due to a distinct summation of side effects and absence of substantial positive changes in the mental state within 4 weeks of therapy and 600 mg quetiapine intake.

4 CONCLUSIONS

1. While performing differential diagnosis and prescribing antipsychotic drugs to patients with epileptic psychoses, it is necessary to take into account not only the structure and clinical manifestations of a psychotic episode and the epilepsy form but also the presence and manifestation level of epileptic personality changes, affective disorders, cognitive disorders or dementia, organic epileptic encephalopathy.

2. It is necessary to remember about the complex interaction between antipsychotic and anti-epilepsy drugs, the possible potential side effects, side reactions and toxic influences. When providing therapeutic treatment to such patients, it is necessary to be consistent and avoid quick changes in drug dosage and change of drugs. A patient with epileptic psychosis must keep getting the earlier prescribed anti-epilepsy drugs and, if necessary, their dosage may be increased.

3. The brain epileptic activity may affect the structure, duration and time course of psychotic states.

4. The efficiency of quetiapine in patients with various types of epileptic psychoses was confirmed by various clinical and pharmacological antipsychotic, anti-mania,

anti-aggression, anti-depression, anxiolytic and sedative effects.

5. The drug was well-tolerated by patients because of the high safety level and a lower side effects spectrum compared to other antipsychotic drugs (hyperprolactinemia, metabolic and extrapyramidal complications, anticholinergic effect, it has an insignificant potential as to body mass increase). Also, quetiapine can promote a quick clinical effect, which improves the doctor-patient compliance. At the beginning of treatment and during patient's exit from psychosis it is necessary to perform clinical psychopathological, laboratory, neurovisual examination, to control glycemic and lipid profiles.

6. Quetiapine doses must be minimally sufficient, drug intake should stop after the patient's exit from psychosis with gradual canceling the drug on condition of continuous control of the patient's mental state.

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