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UDC 616.36-002.895.8:615.1
DOI – https://doi.org/10.14300/mnnc.2017.12094
ISSN – 2073-8137

OLANZAPINE IN TREATMENT OF A SCHIZOPHRENIC PATIENT WITH ORTHOTOPIC LIVER TRANSPLANT

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ПРИМЕНЕНИЕ ОЛАНЗАПИНА ПРИ ЛЕЧЕНИИ ШИЗОФРЕНИИ У ПАЦИЕНТА С ОРТОТОПИЧЕСКОЙ ТРАНСПЛАНТАЦИЕЙ ПЕЧЕНИ

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Presents a clinical case of a patient with paranoid schizophrenia and orthotopic transplant of the liver (02.12.2011). Constantly takes immunosupressivny therapy: tacrolimus, mycophenolate mofetil. Start of mental illness is, in all probability, to 2011, when first appeared the verbal deceptions of perception and ideas of its specific mission and significance. In July 2014 the patient's mental state significantly deteriorated: he developed hallucinatory-paranoid state, katotonia-oneiric inclusions, and he was hospitalized in a psychiatric hospital. The main difficulty encountered in the management of this patient, was the choice of antipsychotic drug. As the pathogenetic treatment of schizophrenia, we used atypical antipsychotic olanzapine. The choice of this drug was due to the high clinical efficacy of olanzapine in the treatment of disease and a low risk of unwanted side effects – hepatotoxicity, extrapyramidal symptoms. It makes olanzapine the most preferred for the treatment of schizophrenia in a patient with hepatitis C and liver transplant.

Keywords: paranoid schizophrenia, chronic hepatitis C, liver transplantation, comorbidity, antipsychotic drugs, olanzapine

Представлено клиническое наблюдение пациента с параноидной шизофренией и ортотопическим трансплантатом печени (02.12.2011), который постоянно принимает иммунносупрессивную терапию: такролимус, микофенолата мофетил. Начало психического заболевания относится, по всей вероятности, к 2011 году, когда впервые появились вербальные обманы восприятия и идеи своей особой миссии и значимости. В июле 2014 года психическое состояние пациента значительно ухудшилось: развилось галлюцинаторно-параноидное состояние с кататоно-онейроидными включениями, был госпитализирован в психиатрический стационар. Основным затруднением, возникшим при ведении данного пациента, стал выбор антипсихотического препарата. В качестве патогенетического средства лечения шизофрении был использован атипичный нейролептик оланзапин. Выбор обусловлен высокой клинической эффективностью оланзапина в терапии заболевания и низким риском нежелательных побочных явлений – гепатотоксичности, экстрапирамидной симптоматики. Это делает оланзапин предпочтительным для терапии шизофрении у больного с гепатитом С и печеночным трансплантатом.

Ключевые слова: параноидная шизофрения, хронический гепатит С, трансплантация печени, коморбидность, антипсихотические средства, оланзапин

The comorbidity of somatic and mental diseases is an area of active investigation. Improved understanding of the mechanisms and pathophysiology of interaction between somatic and mental illnesses would allow to choose targeted approaches to optimize efficiency and minimize side effects of treatment. Taking into account that most of the psychotropic drugs are metabolized in liver, the combination of chronic mental illness and liver failure deserves special attention. The choice of psychotropic drug for treatment of patients with liver disease should be considered in the view of its hepatotoxicity and metabolic interactions between pharmacological agents.

We present a case of paranoid schizophrenia in patient with chronic hepatitis C in the liver transplant. The basic methods were clinical psychopathological, biochemical and psychometrical. The pathopsychological examination was carried out at the 1st and 8th weeks of hospital stay. To evaluate the psychopathological dynamics the positive and negative syndromes scale (PANSS) was used (Kay S. R. et al., 1987).

Patient R., 37 years old, male, was admitted to the observational department of psychiatric hospital.

Mental status: the patient is conscious. During the conversation seemed confused, looked back, periodically looked in one direction, and listened to something. From time to time he tried to get out of bed saying: «Now I will come closer to you». He was emotionally unstable, shouted and laughed. He said: «It is difficult to collect thoughts; I was in two realities, I heard God's voice reported telepathically». He declared that he had invented a formula for the ideal bank credit with fair interest charge. He called himself the «chosen one». He was indifferent and cold when talking about his wife and said that it was impossible to continue their relationship.

He had no family history of psychiatric illness. His father worked as a chief engineer and was described as being strong-willed and confident in character. His mother (61 years old) is healthy and Rh-negative, a teacher of German language; described herself as resolute, persistent and confident. Up to 1 year of age R. was described as «loud and restless», but after his first birthday he became «silent and obedient». In early childhood he suffered from upper respiratory infections. At the age of two years R. has undergone a direct blood transfusion for treatment of severe pneumonia. According to his mother he had got hepatitis C virus as a result of the above blood transfusion. At the age of 10 years, he suffered a severe meningitis, was treated in hospital, thereafter no cerebrosthenic phenomena were observed. Graduated from school at the age of 17 with High Honors («gold medal»). Since childhood, had difficulties in communicating with peers. He did not make close friends since he considered himself «head and shoulders above all others» and didn't share any common interests with his schoolmates.

R. entered Institute of Automation and Computer Sciences and after graduation worked as a software engineer and was successful in his career. He is married. His wife described him as a »homebody» as well as a «person who preferred to stay by himself». His marriage was childless but family relationships continued to be warm and friendly. The patient denied alcohol and drug abuse. In 2006, at the age of 29 he tested positive for hepatitis C antibodies and, according to his physician, the diagnosis of «liver cirrhosis, class C (Child-Pugh) with portal hypertension and hepatocellular insufficiency» was identified. Shortly thereafter R. moved to Moscow where he was placed on a waiting list for liver transplantation, received disability group 2, continued to work as a programmer.

Successful orthotopic liver transplantation in February of 2011 was followed by post-transplant immunosuppressive therapy with tacrolimus, mofetilmicophenolate (Sellsept), which was tolerated satisfactorily. Signs of transplant rejection, hepatic encephalopathy were not observed.

At the age of 34 and prior to the transplant surgery R. started to hear the «hints» in other people's conversations that he «was elected to rescue the world and all the people in it», but remain cold and. Since then he became more religious, «more attentive and humane», while he was cold and indifferent with his mother. Still, he grew self-contained, spent all my free time playing computer games. Once, while waiting in line at the Cathedral of Christ the Savior for the worship of relics, suddenly noticed a halo around his body and so realized that he was «chosen to save the world and people.» After the transplant surgery, while in the intensive care unit, he also «heard that the doctors called him elected».

One year prior to the psychiatric admission R. started experience obsessive thoughts that banks «deceive people by charging extremely high interest rates for the loans». He invented an «optimum, fair formula» based on calculation of bank interest on credits. In July 2014, insomnia began; R. felt as if he was «in two realities, «hear the voice of God», called himself « the chosen one» and got a «mental revelation» from which he learned that there are «many parallel options for the development of the future».

Pathopsychological examination: the patient was oriented to time, place and his own personality, easily engageable and also understood the purpose of the examination and willingly participated in testing. In conversation the patient was mostly monotonic with flat emotions, inclined to philosophical reasoning, could not maintain focus and was easily distracted, switching to random subjects. His estimates and judgments were illogical and unusual. He made various strange

proposals, while at the same time remaining suspicious and constantly highlighting mistakes of other people and «the whole system». Results of MMPI indicated high level of psychological tension, focus on self-significant controversial ideas and experiences. The patient demonstrated introversive personality orientation and absence of the critical evaluation of his own mental state.

Electroencephalogram: moderate general changes of bioelectric activity of the brain in the form of «flattening» of background curve with domination of beta activity on all convexital surfaces were noted. This suggests irritation of diencephalon structures. Reduced reactivity of cortical neurons was revealed. No evidence of epileptic activity. Ultrasonic encephaloscopy: no M-ECHO.

No pathological changes were found on electrocardiogram an chest X-ray.

Liver enzymes remained normal (ALT 14-20 U/l, AST 16–21 U/l), direct and indirect bilirubin levels were also in the range of norm. Prothrombin index was 86.5 %. HIV and hepatitis B antibodies were absent. Anti HCV were detected. No signs of portal hypertension were found by ultrasound. Conclusion of the ophthalmologist: early stage retinal angiopathy; moderate myopia. Conclusion of the neurologist: no evidence of neurological abnormalities. Conclusion of the internist: liver cirrhosis secondary to hepatitis C (genotype 1), portal hypertension and hepatocellular insufficiency. Status post orthotopic liver transplantation (December 2012). The patient continues to receive SellSept.

Atypical antipsychotic Ziprex (olanzapine) was applied 10 mg twice a day intramuscularly, PK-Merz 100 mg 3 times a day per os, elzepam (bromodihydrochlorophe nylbenzodiazepine) 1 mg per os at night. Subsequently, the patient was transferred to receive Ziprex (olanzapine) 20 mg per os (divided in two doses) in combination with cyclodol (trihexyphenidyl) 2 mg twice a day in the morning and evening as a corrector. After 2 months: Zalasta (olanzapine) 10 mg-0-10 mg in combination with cyclodol 2 mg-0-2 mg.

Upon admission R. was alert, but demonstrated unsociable behavior and dislike for staying in the supervised ward. Delirious ideas remained real for him, but sharp mood swings were not observed. He kept on referring to experiences that lead to his admission as real facts. At the same time he said: «I used to suffer from schizophrenia, but now my brain is functioning just as it should; feel in only one reality and my muscles are getting stronger». After discharge he was going to work at a bank, and could not wait to explain to his future colleagues their «mistakes» so that they could «start treating their clients with all the honesty the customers deserved». He denied delusions of perception.

The patient's behavior and attitude towards his family was similar to his behavior with other people that he encountered on the ward. At first he was indifferent to both his mother and his wife during their visits, but by in 6 weeks he became receptive and responsive and was glad to see them. Assessment of negative symptoms of schizophrenia by PANSS scale was 26 points.

Diagnosis: schizophrenia paranoid, incidental type, hallucinatory-paranoid syndrome with oneiroid and catatonic inclusions. F20.016

Conclusions. The interest of the clinical case is in the development and progression of schizophrenia in a patient with viral liver cirrhosis and background of hepatic encephalopathy that underwent orthotopic liver transplantation with the development of C-viral infection of the liver transplant. The main difficulty in treating this patient was to choose optimal antipsychotic drug in view of the potential inhibiting effect of psychotropic medications on the P450 (CYP) activity. Most of the psychotropic medications as well as immunosuppressants (which R. received permanently to prevent rejection of the liver transplant) are metabolized in the liver by the CYP system [4]. Impair of CYP activity potentially can change the pharmacokinetics of co-administered drugs, decrease the effectiveness of treatment and result in the development of life-threatening drug interactions [5]. The atypical neuroleptic olanzapine (Ziprex, Zalasta) was chosen for pathogenetic treatment of schizophrenia. This choice was based on olanzapine high clinical efficacy in patients with schizophrenia as well as on its relatively low side effects – hepatotoxicity and neurological extrapyramidal symptoms [1]. Based on pharmacological trials data, Olanzapine does not inhibit markers of catalytic activity of cytochrome P450 – CYP3A, CYP2C9, CYP2D6, CYP2C19 to the same degree as other antipsychotics [2, 3].

The lower P450 suppressive effect of Olanzapine made it a preferable choice for treatment of schizophrenia in patients with chronic hepatitis C and liver transplant.

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