ANNALES
UNIVERSITATIS MARIAE CURIE-SKŁODOWSKA
LUBLIN – POLONIA
VOL. LX, N 2, 146 SECTIO D 2005

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Current views on developement and treatment of rapid cycling bipolar disorder

Bipolar affective disorder in its natural course may present a tendency towards accelerating the frequency of episodes or rapid changes of polarity. Primary observations of this phenomenon has been made by Jan Pierre Falrest in 1854. In 1913 Kraepelin described the natural progressive course of bipolar disorder. He also demonstrated, in a group of 409 patients, that the period of time between the first and the second episodes was 4.3 years but before the fifth episode it was reduced and lasted only up to 1.5 years.

Rapid-cycling bipolar disorder, as defined by the DSM-IV is at least 4 discrete episodes of mania or depression in a single year demarcated by clear periods of remission or by switches to the episodes of opposite polarity (9). Some authors suggest distiguishing the course specifiers like ultra-rapid cycling or ultra-ultra rapid cycling, where the shifts of mood and activity can occur within days or even hours (6). Rapid cycling (RC) is estimated to be present in 14–50% of patients with bipolar disorder (3). It is emphasized that RC occurs more frequently in women than in men (4:1) (15) and more often in patients with bipolar disorder type II. In 1/3 of patients RC begins in 20–30 year of age; that is the typical age of onset for bipolar affective disorder. In the majority of patients it begins after 40 year of age, after the period of "normal" course of illness (7, 12). Some researches underline the co-occurence of RC course specifier with earlier onset of illness and the depressive pattern of the first episode (4).

A significant amount of data confirm the comorbidity of RC with other psychiatric conditions, like substance abuse, anxiety disorder or borderline personality disorder (8). RC course specifier is considered to cause rather "malignant" course of the illness, as it is usually connected with some diadvantageous features of the prognosis like frequent hospitalizations or the increase of suicide risk. Genetic studies of RC indicate frequent family history of affective disorder. It has been observed in approximately 50 % of the patients. Moreover, rapid switching of mood was observed in families with multiple cases of bipolar disorder. Affestive spectrum disorders appear to occur more frequently in families of the patients with RC (9). Molecular association studies suggest that the gene encoding catechol-O-methyltransferase (COMT) may be the candidate gene in rapid cycling bipolar disorder. It was found that ultra-ultra rapid cycling bipolar disorder is associated with the low activity COMT allele (5). .

There exists a significant amount of data suggesting that several antidepressants may change, at least in some patients, the "natural" course of illness and accelerate the onset of RC (1). There may exist other factors potentially inducing RC, like: the head injury, the features of organic brain dysfunction, hypothyroidism, the known history of circadian rhythms disturbances. However, antidepressants, and especially tricyclic, are known to play an important role in the developement of RC course specifier. The mechanism of this phenomenon is not completely understood. However, it is clear that tricyclic antidepressants may cause the effect of 'down regulation' of β-adrenergic receptors,

which may lead to the stimulation of NA and DA neurons. That may in turn cause vulnerability to the phase change. Selective serotonine reuptake inhibitors (SSRI) are considered to be safer and the risk of inducing RC during SSRI treatment is lower. However, there are several mechanisms of antidepressants action that are common for tryciclic and SSRIs (and these include regulatory proteins, secondary neurotransmitter systems or protein kinase systems (PLC)), though both groups of antidepressants may play a significant role in the phenomenon of accelerating episodes. The drugs of low cholinolytic potential (mianserin, noksyptylin) are known to cause the highest risk of inducing RC. Mood stabilizers are widely used in the treatment of bipolar disorder but their role and efficacy varies considerably. Lithium seems to have a reduced validity in the treatment of RC course pf bipolar disorder (2). Anticonvulsants used in the treatment and prophylaxis of bipolar disorder are more often used in the prevention and treatment of RC. It is probably linked with their influence on the neurotransmitter system in the brain. Most of these drugs cause reduction of the presynaptic DA activity, which may be linked with the anti-manic effect. Mood stabilizers (including lithium) stimulate serotoninergic transmission in the brain. There exists a hypothesis that the serotoninergic hypofunction constitute the basis of the manic state. Thus, the anti-manic activity of these drugs is joined with the advantageous influence on the RC course of bipolar disorder. Mood stabilizers act as agonists of GABA system and as the antagonists of AMPA and NMDA receptors system. This is probably connected with their antidepressive activity and may also cause an advantageous influence of these drugs on the RC course of bipolar disorder.

In the present standards of treatment of RC bipolar disorder the discontinuation of antidepressants and especially tricyclic is highly recommended. A very important step in the management of rapid cycling bipolar disorder is thorough assessment of any factors that may precipitate mood changes and especially these that may be controlled (thyroid hypofunction, environmental factors). In case mood stabilizer (carbamazepine, valporate) does not give the expected result, it is advised to give lithium additionally. The next choice would be the combination therapy with two anticonvulsants as mood stabilizers (VPA and carbamazepin) (14). In case of no result, it is recommended to use the II generation antipsychotics (promising effects of olanzapine and quetiapine 13). A significant amount of data confirms the benefitial influence of lamotrygine on rapid cycling bipolar disorder (7). It is emphasized that this drug, although reducing the symptoms of depression, does not induce manic symptoms.

Sometimes the progress of therapy leads to the effects disturbing the "natural" course of the disease. These changes may be disadvantageous, as in the case of RC bipolar disorder. The chaos theory as regards RC emphasizes tiny changes within primary conditions (such as stress or medication selection) that may cause several distant changes including the "chaos" of the course. Therefore, the optimalization of treatment strategies in bipolar disorder appears to be of great significance.

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SUMMARY

The natural course of bipolar affectve disorder may be characterized by the acceleration of the frequency of episodes or rapid changes of polarity. Rapid-cycling bipolar disorder is defined as at least 4 discrete episodes of mania, hipomania or depression within 12 months. We present the analysis of studies on clinical, demographical and molecular features of rapid cycling bipolar disorder, as well as studies concerning comorbidity of the condition. The studies concerning the influence of antidepressants on the course of bipolar affective disorder have been analysed. The current treatment strategies of rapid cycling bipolar disorder have been presented.

Współczesne poglądy na powstawanie i terapię zaburzenia dwubiegowego o typie szybkich cykli

W przebiegu choroby afektywnej dwubiegunowej dochodzić może do przyspieszania częstości epizodów lub szybkiej zmiany biegunowości. Przebieg choroby afektywnej dwubiegunowej o typie szybkich cykli obserwujemy w przypadku wystąpienia czterech epizodów zaburzeń nastroju w ciągu 12 miesięcy, o ile spełniają one kryteria dużej depresji, epizodu maniakalnego, mieszanego lub hipomanii. W pracy dokonano przeglądu doniesień dotyczących danych klinicznych, demograficznych, podłoża molekularnego oraz współwystępowania przebiegu o typie szybkich cykli z innymi jednostkami chorobowymi. Przeanalizowano badania dotyczące zagadnienia wpływu leków przeciwdepresyjnych na przebieg choroby afektywnej dwubiegunowej. Przytoczono nowoczesne standardy leczenia choroby afektywnej dwubiegunowej z przebiegiem o typie szybkich cykli.