Increased β-Endorphin Level in Blood Plasma as an Indicator of Positive Response to Depression Treatment

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Preliminary data indicate that increased blood plasma level of β-endorphin in patients with nonpsychotic unipolar depression after 2 weeks of treatment correlates with the positive response to therapy. This parameter can be regarded as an objective indicator of potential improvements. Further studies aimed at determining the value of blood β-endorphin levels in patients with mood disorders for the diagnostics and estimating the therapeutic success in this disease are required.

Key Words: *depression; stress; endogenous opioid system; β-endorphin*

High prevalence of affective disorders in the general population, particularly among those seeking treatment in the primary care network is a well-known fact [3,5]. At the same time, there are no objective criteria for identification these health problems and, hence, their instrumentally confirmed correction [4]. In this context, the development of objective measures of therapeutic prognosis and the search for indicators of treatment effectiveness with affective disorders are urgent problems. The endogenous opioid system is known to be directly involved in the formation of emotional states [6,10]. Prospects of using plasma β-endorphin levels as an indicator of activation of the stress adaptation mechanisms are now widely discussed [10,11], which has some experimental substantiations [6,7].

In light of this, we studied peripheral blood levels of β-endorphin in patients with unipolar depression of mild to moderate severity and assessed the possibility of using this parameter as a potential objective measure of chosen treatment effectiveness.

MATERIALS AND METHODS

A prospective study was performed in accordance with current ethical standards. The examined group consisted of 21 patients (7 males, 14 females) of working age from 22 to 56 years, mean age 38.2 years. Criteria for inclusion in the study were primary or secondary depressive episodes of mild to moderate severity under recurrent depressive disorder. Exclusion criteria were severe psychotic depression, suicidal thoughts or attempts, personality disorder, schizophrenia spectrum, alcohol and drug addiction, epilepsy and epileptiform syndromes, psychoorganic syndrome, dementia, physical and neurological diseases in decompensation stage, pregnancy in women.

Basic treatment included antidepressants sertraline and fluvoxamine, selective serotonin reuptake inhibitors. Four patients who were not prescribed antidepressants underwent biofeedback treatment and rehabilitative exercises. The survey was conducted before and 2 weeks after the therapy. Dynamic moni-

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toring included evaluation of the mental status and β-endorphin plasma levels in the peripheral blood. A clinical and psychometric survey determined the level of depression and response to treatment with 17-item Hamilton Depression Rating Scale (HDRS) [3,9]. ELISA was performed using Thermo Scientific Multiskan EX microplate photometer (Thermolabsystems). Plasma β-endorphin concentrations were measured by Peninsula reagents with a measurement range from 0 to 25 ng/ml. The optical density of standard peptide dilutions after ELISA reactions were used to produce a curve of optical density versus β-endorphin concentration. Concentrations of β-endorphin in dialysates were determined from the curve.

The data were compared [2] using parametric *T*-test for related samples. The differences were considered significant at $p<0.05$. Kolmogorov–Smirnov test was used to check distribution normality (the applicability of parametric *t*-test). To study the correlation relationships, Pearson's correlation coefficient and Spearman's rank correlation coefficient were calculated. Tables and graphs were created as well as calculations and statistical analysis performed in standard programs Microsoft Excel 2010 and SPSS 13.0.

RESULTS

Irrespective of the treatment, all patients showed significant ($p\approx10^{-9}$) decrease in HDRS score: from 17 to 10 over 2 weeks after the start of therapy. At that time, significantly increased ($p=0.03$) β-endorphin level was detected in the peripheral blood in the test sample compared with the baseline values during the second week of treatment. The absolute level of the peptide increased in 15 of 21 patients (in 3 of 4 patients not receiving antidepressants) with high sampling variability of this parameter, from 0.003 ng/ml to 1.144 ng/ml before treatment and from 0.017 ng/ml to 1.797 ng/ml after 14 days of treatment. The mean β-endorphin concentration changed from initial 0.21±0.13 to 0.42±0.21 ng/ml ($\alpha=0.05$).

There was no significant linear correlation between peripheral blood β-endorphin levels and psychometric scores in this sample, which agreed with published data [12]. The lack of linear relationships can be explained by individual variability of β-endorphin levels and some subjectivity of the traditional assessment tools, *i.e.* psychometrical scoring [4]. A more important aspect is the direction of changes in β-endorphin levels reflecting the response of the endogenous opioid system to the treatment, with individual values of the peptide level. Considering the above, we examined the association of qualitative features: the degree of change of β-endorphin levels and the state of patient using HDRS. Significant ($p=0.009$) relationship was found (Spearman's correlation coefficient $r\approx-0.6$). The degree of individual changes in the index was determined by dividing its value by the subsequent one. Hence, the more increased β-endorphin concentration, the stronger reduced HDRS score.

Elevated β-endorphin content (as a separate feature) corresponded to the better treatment results in this sample after two weeks (Fig. 1).

Thus, we can assume that elevated levels of β-endorphin in patients with depressive disorders after 2 weeks of treatment were the signs of readaptive remodeling and activation of the stress-limiting systems of the body, which reflects the systemic sanogenetic changes caused by the therapy. Increased plasma β-endorphin levels were found by the end of the acute period of traumatic disorders [1]. There are also indications for increased peptide level in patients with depression after the action of electric shock, a powerful stressor, which was explained by the "hypothalamic response" to the effect of the electric current [8].

Our results suggest that plasma β-endorphin levels are advisable to be used for assessing response to

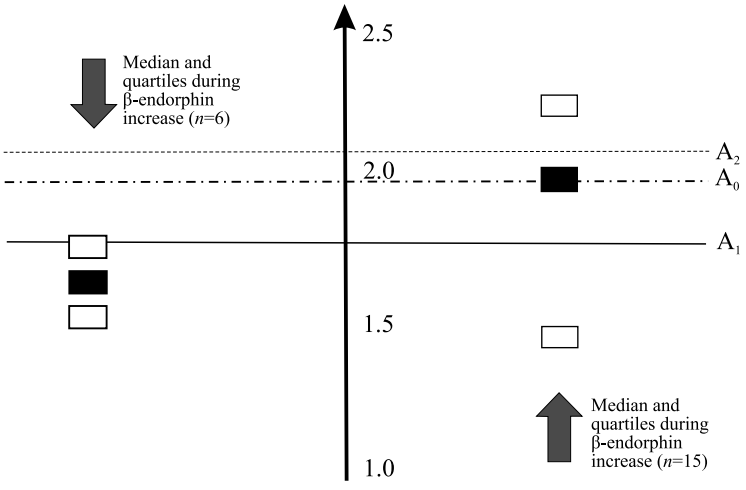

Fig. 1. The degree of reduction in depression with HDRS scores in patients showing multidirectional changes in β-endorphin levels in peripheral blood after 2 weeks of treatment. A_0, the average severity of depression with HDRS scores for the sample ($n=21$); A_1, the average severity of depression with HDRS scores in the patients with reduced β-endorphin levels ($n=6$); A_2, the average severity of depression with HDRS scores in the patients with elevated β-endorphin levels ($n=15$). Dark and light rectangles correspond to medians and quartiles, respectively.

therapy of nonpsychotic unipolar depression. Reagents for determination of β-endorphin concentration and appropriate equipment for ordinary clinical laboratories are relatively available, which can contribute to widespread adoption of the new quantitative method to medical practice.

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