RESEARCH LETTER

Analysis of growth hormone levels in the blood of patients with drug-resistant depression

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Introduction Human growth hormone (HGH), also called somatotropin, is a peptide that is excreted by somatotropic cells in the anterior pituitary gland. This hormone has multiple functions, with the most important being stimulation of cell growth, reproduction, and regeneration in humans.[1] The role of HGH in adults has not been fully understood for many years. Several studies involving patients with HGH deficiency have suggested the importance of HGH for both mental and emotional well-being, as well as cognitive function.[2] The beneficial effects of HGH replacement on the quality of life of adult patients with growth hormone deficiency were also confirmed by McGauley.[3]

HGH deficiency in adults, called somatopause, can be associated with brain injury, cancers, and radiotherapy of the pituitary gland. HGH secretion can also diminish with age, which is connected with a decrease in lean body mass, an increase in body fat, and an increase in low-density lipoprotein cholesterol levels.[4] A reduction in muscle mass, energy, and quality of life was observed in adults with HGH deficiency.[5] In another study, HGH deficiency was related to decreased energy, increased tiredness, pain, irritability, and depression.[6] Despite publications reporting mood disturbances in patients with age-related somatopause, the association between drug-resistant depression and HGH deficiency remains unknown. Therefore, the aim of the present study was to analyze serum HGH levels in patients with drug-resistant depression and to assess the effect of age-related somatopause on the symptoms of depression in adult patients.

Methods A total of 50 patients (19 men, 31 women) were enrolled. The study group included 24 patients (10 men, 14 women; mean [SD] age, 43 [12.36] years) with unipolar depression, who developed the first symptoms of the disease after the age of 20. Patients were diagnosed with drug-resistant depression according to the *International Classification of Diseases, Tenth Revision*. They received at least 2 treatments with different classes of antidepressants at an optimal dosage, and treatment ineffectiveness lasted for at least 4 weeks. The control group consisted of 26 patients (9 men, 17 women; mean [SD] age, 46.88 [17.73] years). Controls did not have any psychiatric disorders, such as depression. Individuals with any disease of the central nervous system or the pituitary gland were excluded.

In both groups, the serum HGH level was measured between 8 AM and 10 AM, using an immunoenzymatic method. Samples were obtained in the fasting state, and participants were only allowed to drink water. Physical examination was performed and medical histories were taken from all participants. Psychiatric examinations were also performed to exclude patients with any symptoms of depression from the control group. The study was approved by the local ethics committee.

Statistical analysis The Shapiro–Wilk and Mann–Whitney tests were used to compare the HGH results between groups. The correlation between body mass index (BMI) and HGH levels was analyzed using the Pearson R test. The χ^2 test was used to analyze the correlation between the HGH level and the occurrence of diabetes and arterial hypertension.

Results First, the Shapiro–Wilk test was used to test the analyzed variable (HGH level) for

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Received: October 10, 2017.
Revision accepted: March 17, 2018.
Published online: April 27, 2018.
Conflict of interest: none declared.
Pol Arch Intern Med. 2018; 128 (4): 263-265
doi:10.20452/pamw.4256

normal distribution. As the distribution was not close to normal (P = 0.0), the nonparametric Mann–Whitney test was used for comparison between groups. The control group had higher mean (SD) HGH levels compared with the study group: 1.02 (1.28) ng/dl and 0.66 (1.28) ng/dl, respectively (P = 0.01).

A significant correlation between BMI and HGH levels was observed in both groups (P = 0.01). Patients with a higher HGH level had a lower BMI.

Arterial hypertension tended to be more frequent in the control group than in the study group (P = 0.24). The occurrence of diabetes was similar in both groups.

Discussion Drug-resistant depression is a considerable challenge in modern medicine. Despite new treatment methods, 60% of patients with unipolar disease are still unable to achieve remission after treatment with 2 antidepressants at the adequate dosage. The role of HGH in the pathogenesis of depression in adults still seems to be underestimated and not fully understood. Several studies have suggested that HGH is crucial for mental and emotional well-being as well as cognitive function of patients, but its association with drug-resistant depression remains unclear.[6,7] Atypical depression connected with growth hormone deficiency was described by Mahajan et al.[8] In their study, 61% of patients with HGH deficiency had symptoms of depression, but their mood, energy level, and sleep disturbances improved after 2 months of HGH treatment. In a study by Matussek and Laakmaan,[9] patients with endogenous depression had a significantly reduced growth hormone response after desipramine administration, as compared with patients with neurotic depression and controls. In a 9-year follow-up, Gilchrist et al[10] observed a significant decline in mental and physical health in untreated HGH-deficient adults. In contrast, patients who received HGH showed improved quality of life, including mood, energy level, and vitality.

In our study, patients with drug-resistant depression, who developed the illness after the age of 20, had a significantly lower blood HGH levels compared with healthy controls. In all patients, depression was accompanied by lower energy levels, fatigue, and lack of motivation. HGH deficiency can be associated with symptoms of depression, especially in patients with disease onset after the age of 20, when the natural excretion of HGH starts to decrease. The hormone's mechanism of action on the brain has not been elucidated, but Johansson et al[11] revealed that the levels of insulin-like growth factor 1 and insulin-like growth factor-binding protein 3, as well as immunoreactive β-endorphin, were increased in the cerebrospinal fluid of patients after treatment with HGH when compared with pretreatment values. In the case of homovanillic acid and vasoactive intestinal peptide, reduced HGH levels were observed in the cerebrospinal fluid.[11] Another study revealed that changes in the levels of homovanillic acid and free thyroxine after HGH administration are similar to those reported after successful treatment of depressive disorders with antidepressant drugs.[12] Although studies have reported the beneficial effects of HGH substitution in patients with HGH deficiency on the quality of life, there have been no studies evaluating the effectiveness and safety of HGH in drug-resistant depression.

HGH deficiency can also cause other symptoms, such as increased adipose tissue mass accompanied by reduced lean tissue mass and reduced extracellular water, visceral obesity, reduced bone mineral density, reduced exercise capacity, increased risk of coronary heart disease, increased insulin resistance, and kidney function disorders.[2,7] In our study, patients with HGH deficiency had a higher BMI than controls. The occurrence of hypertension and diabetes was similar in both groups.

HGH is secreted by the pituitary gland in a pulsatile manner, so its blood level can change during the day. In the present study, blood samples were taken between 8 AM and 10 AM to reduce the probability of incorrect results due to the natural fluctuation of the HGH level. Further research with HGH stimulation by arginine, L-dopa, or clonidine is needed to evaluate the dynamics and periodicity of HGH secretion in patients with drug-resistant depression. Future studies should also include a larger group of patients with unipolar disease and evaluate the effectiveness and safety of HGH treatment.

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