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Cognitive deficits in patients with multiple myeloma undergoing chemotherapy and the level of selected biochemical parameters and psychosocial factors

Abstract

The aim of the research was to explain the reasons for such a wide diversity of negative effects of cancer and oncological treatment in the form of cognitive changes. An assumption was formulated that the cognitive state of cancer patients is an effect of the disease and the treatment, which both affect the level of biological factors, namely pro-inflammatory and anti-inflammatory cytokines and neurotrophin BDNF, and that the level of the selected parameters of laboratory tests, in an interaction with the level of psychosocial variables (depression, anxiety, fatigue, quality of life), affects the cognitive functioning of patients with multiple myeloma (MM). An attempt was made to check the hypothesis about the crucial importance of biological factors, such as cytokines TNF-α, IL-6, IL-10, and neurotrophin BDNF, whose level may affect the occurrence or lack of occurrence of cognitive changes in patients.

The studies were conducted at the Independent Public University Hospital No 1 in Lublin at the Clinic of Hemato-oncology and Bone Marrow Transplantation. Apart from conducting neuropsychological tests, the analysis included the level of selected cytokines TNF-α (tumour necrosis factor), IL-6 (interleukin 6), IL-10 (interleukin 10), and neurotrophin BDNF (brain-derived neurotrophic factor). Each time, the patients from the clinical group (N = 30) underwent the scientific procedure involving blood serum sampling at a hospital laboratory over the course of the same day. The level of selected biological factors was assessed with ELISA test. The research involved measuring cognitive, biological, and psychosocial variables twice: before the beginning of chemotherapeutic treatment (T_0) and after 4 months from the beginning of the anti-cancer therapy (T_1). Each patient from the clinical group was coupled with an individual from a control group (N = 30) made up of orthopaedic patients.

The study involved neuropsychological diagnosis based on the following test tools and experimental and clinical trials: *Montreal Cognitive Assessment; Battery of Tests for Assessing Cognitive Functions PU1* used experimentally (subtests: *Deferred Naming Test, Attention Divisibility Test, Park Map Test, Verbal Fluency I and II*); experimental and clinical trials based on *the Choynowski's Memory Scale* (subtests: *Auditory memory; Numbers directly, Numbers*

backwards, Long-term memory); *Stroop Colour-Word Interference Test* used experimentally*; Attention and Perceptiveness Test; Depression Measurement Questionnaire; State-Trait Anxiety Inventory – anxiety as a state* (X-1); *Brief Fatigue Inventory,* and *the Rotterdam Symptom Checklist.*

Based on the author's own research conducted on patients with a diagnosed multiple myeloma, it can be concluded that the cognitive and affective functioning of this group of patients was very diverse.

The differences between the diagnosed patients and the control group were observed within short-term auditory memory, working memory, and attention divisibility. When it comes to general cognitive functioning, short-term visual memory, long-term verbal memory, attention and perceptiveness, verbal fluency, planning, and execution control, both studied groups functioned similarly. At the diagnosis stage, disorders of cognitive changes almost in all measured functions, apart from long-term memory, were observed. 87% of patients experienced cognitive deficits during the first measurement. After 4 cycles of chemotherapy, 90% of patients presented cognitive deficits in such cognitive domains as: general cognitive functioning, working memory, short-term visual memory, visual attention, attention divisibility, verbal fluency, planning, and executive control.

The interaction between the state of health and age revealed significant differences among the studied individuals. Younger patients with MM exhibited worse short-term auditory memory compared to individuals of the same age without cancer. A similar situation was observed in case of long-term verbal memory – patients with MM in middle adulthood showed a worse state of long-term verbal memory compared to individuals without cancer. Also, in terms of phonemic and semantic verbal fluency, the level of some indicators was lower in younger patients with MM compared to older patients with MM. A better execution of tasks by younger individuals with cancer was noticeable only within short-term visual memory.

Patients presented an improved general cognitive functioning, better short-term auditory memory in repeating material based on words, more effective long-term verbal memory, and better attention divisibility during the treatment than before it.

A diversified level of biological factors determined the changing cognitive functioning within selected domains. Patients who experienced an increase in the level of IL-6 exhibited worse attention and perceptiveness compared to people with a decrease in the level of IL-6. Patients who experienced a decrease in the level of IL-6 were characterised by an improved

effectiveness of phonemic fluency compared to individuals with an increase in the level of IL-6. The studied patients who experienced a decrease in the level of IL-6 after 4 cycles of chemotherapy functioned more effectively in terms of short-term auditory memory, long-term verbal memory, attention divisibility, planning, and phonemic fluency compared to the diagnosis stage. Patients who experienced an increase in the level of IL-10 in blood serum had an improved attention divisibility compared to the group with a decrease in the level of IL-10, whereas patients with a decrease in the level of IL-10 had a worse executive control compared to patients with an increase in the level of IL-10. Additionally, it was observed that the group of patients who experienced an increase in the level of IL-10 during chemotherapy had an improved attention divisibility and short-term auditory memory compared to the measurement before chemotherapy.

Cytokine TNF-α and neurotrophin BDNF allowed for predicting short-term visual memory. Other biological variables, IL-6 and IL-10, allowed for predicting the functioning of long-term verbal memory. Similarly, IL-6 and IL-10 as well as IL-6 and BDNF allowed for predicting phonemic fluency, while the assessment of semantic fluency was possible based on IL-6 and BDNF as well as IL-10 and BDNF.

The author's own research did not reveal the intermediary impact of psychosocial variables (depression, anxiety, fatigue, quality of life) on the cognitive functioning of patients with MM.

The results of analysis allowed for understanding the processes of occurrence and changeability of the symptoms of cognitive deficits in the group of patients with plasma cell myeloma – a hematologic cancer.

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