Comparison of Different Doses of Escitalopram in the Prophylaxis of Dementia in Patients with Depression and Moderate Cognitive Dysfunction in Chronic Cerebral Ischemia

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Objective – to compare different doses of escitalopram (Cipralex) in the prophylaxis of dementia in patients with depression and moderate cognitive dysfunction on the background of chronic cerebral ischemia.

Materials and methods. Two groups of patients, aged 65–78 years, with chronic cerebral ischemia and mild-moderate depression and moderate cognitive dysfunction were studied and treated with different doses of escitalopram: 30 patients received escitalopram at a dose of 5 mg/day throughout the treatment period; 42 patients received escitalopram at a dose of 5 mg/day for the first week and then 10 mg/day. Treatment duration was six months and the observation period was eight months. Results and conclusions. Escitalopram was shown to be effective not only in the treatment of depression-associated cognitive dysfunction in patients with chronic cerebral ischemia but also in decreasing the risk of dementia in the long term. The effectiveness of the prophylaxis of dementia was found to depend on the escitalopram dose used.
showing that symptoms such as apathy may be linked with lesions in the basal ganglia [25–28]. There is also evidence that patients with depression have high blood glucocorticoid levels [29–33], rearrangements of neurotrophic factors [34–36], and atrophy of certain brain structures – the hippocampus, the olfactory and frontal areas of the cortex, and the amygdala [37–43]. This atrophy is connected with the development of cognitive decline, especially in elderly patients [44, 45].

The literature also contains active discussion of the relationship between depression and cognitive impairments. An important role is assigned to the hypothalamo-hypophyseal-adrenal system, which is activated in response to stressors, becoming the trigger component of the molecular events mediating the link between depression and cognitive impairments: glucocorticoids bind to receptors in the hippocampus and, acting by negative feedback, suppress the release of neurotrophic factors involved in learning and memory processes [44]. If inhibition of excessive hypothalamo-hypophyseal-adrenal system activity does not occur, this leads to injury to the hippocampus and cortical neurons. A two-year study reported by Diniz et al. [45] identified a link between depression in the elderly, accompanied by cognitive impairments, and the level of brain-derived neurotrophic factor (BDNF). Patients with depression but no cognitive impairments had relatively stable BDNF levels throughout the observation period, while patients with depression combined with cognitive impairments had significantly reduced levels. Decreases in BDNF Levels can lead to impairment to neuron growth and development in the hippocampus. It is important to recognize 20th-century data showing the possibility that neurogenesis can occur in adult mammals. By the 1990s, there were sufficient data constituting evidence that the human hippocampus is able to synthesize new neurons throughout life, with a small decrease only in old age [47]. This explains the high risk of persistent cognitive impairment with subsequent development of dementia in elderly patients [45]. We can also add recent data on the link between genetic polymorphism in the serotonin transporter and microstructural details of the white matter in the frontal and striate areas of the brain [48]. Thus, there appear to be regional differences in the neurogenic effects of antidepressants and their ability to activate neurogenesis, mainly in the anterior pole of the hippocampus [49]. Overall, current knowledge points to the need for the earliest possible initiation of antidepressant treatment in elderly patients with symptoms of depression with the objective of avoiding irreversible subsequent cognitive decline [44, 45].

Selection of an antidepressant for treating depression in any individual patient must be based on previous experience in the treatment of this condition with these drugs, taking due cognizance of concomitant pathology [50]. In the absence of any particular contraindications, the first-line drugs for treating depressive and anxiety disorders are selective serotonin reuptake inhibitors (SSRI) [51, 52]. Particular attention in recent years has been paid to studies of the effects of various antidepressants on cognitive functions. Escitalopram and duloxetine have been shown to be able to improve episodic and working memory, the rate of mental processes, and motor functions [53]; fluoxetine and paroxetine have been shown to improve attention, verbal learning, and memory [54], and sertraline to improve psychomotor activity associated with impaired attention and executive functions [55]. Katona et al. reported [56] that vortioxetine at a dose of 5 mg/day had more marked positive effects on cognitive status than duloxetine at a dose of 60 mg/day. Antidepressants which are agonists of sigma-1 receptors have advantages in relation to cognitive functions. Sigma-1 receptors are transmembrane proteins which regulate various ion channels, including calcium channels, NMDA receptors, the release of various neurotransmitters, neurogenesis, and synaptogenesis [57]. Sigma-1 receptor pathology is linked with the development of a number of important diseases involving the development of conformational changes to cell membranes, for example Alzheimer’s disease. The currently known SSRI with sigma-1 ligand properties potentiating neuroprotective effects particularly include escitalopram [58].

Some studies on the prophylaxis of poststroke depression using different antidepressants have demonstrated efficacy [59–61]. However, the potential of antidepressants in the prophylaxis of depression with moderate cognitive dysfunction on the background of chronic cerebral ischemia has received insufficient study. Data on the efficacy of low doses of antidepressants in the treatment of depression in the elderly have been reported [62–65]. At the same time, the question of the efficacy of low-dose antidepressants in relation to the prophylaxis of dementia in patients with cognitive dysfunction developing on the background of chronic cerebral ischemia remains unclear.

The aim of the present work was to compare different doses of escitalopram (Cipralex) in the prophylaxis of dementia in patients with depression and moderate cognitive dysfunction on the background of chronic cerebral ischemia.

Materials and Methods
A total of 72 patients aged 65–78 years with chronic cerebral ischemia and mild-moderate depression on the background of moderate cognitive dysfunction were studied.

Inclusion criteria were: presence of chronic cerebral ischemia corresponding to dyscascular encephalopathy grade 1–2 on the Yakhno et al. [2003] classification; presence of mild-moderate depressive syndrome (DSM-V criteria) (no more than 27 points on the Hamilton 21 scale) in patients with moderate cognitive disorder (NIA-AA criteria, MMSE scores ≥ 24); absence of severe somatic diseases; ability of patient to take medications orally and interact with the investigator.

Exclusion criteria were: presence of chronic cerebral ischemia corresponding to grade 3 dyscirculary encephalopathy on the Yakhno et al. [2003] classification; presence of severe depression (more than 27 points on the Hamilton