POSTOPERATIVE COGNITIVE DYSFUNCTION IN MIDDLE-AGED FEMALE: INCIDENCE AND PREVENTION

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The current state of the demographic situation in many developed countries, and the life style increases the demands and expectations of the quality of anesthesia and surgery. Over the past decade, has became problem of the influence of anesthesia and surgery on cognitive function in patients early and remote postoperative period, including 10% of court desires in the field of medicine associated with this problem [1].

Postoperative cognitive dysfunction (POCD) - a cognitive disorder that develops in early and stored in the late postoperative period, clinically manifested by memory impairment, concentration difficulties and irregularities other higher functions of the cortex brain (thinking, language, etc.) [3]. To diagnose POCD standard recommended tests of cognitive function on a Folsteyn scale of mental status assessment (Mini-Mental State Examination, abbr. MMSE), where the development of decreasing POCD previous results to 10% or more [2].

However, great importance is the risk of POCD in middle age which significantly affects their performance and overall quality of life.

Hysterectomy is the second often surgery in women. Every year 600,000 hysterectomies performed and one in three women over 60 years of age underwent such an operation in the U.S. Among the publications available in the databases Medline, Pubmed, Cochrane publications on the incidence of POCD in female cancer patients there are no national publication. The purpose of our study was to determine the relevance of POCD for middle-aged women after hysterectomies, frequency of occurrence and potential risk factors POCD and to investigate the effectiveness of prevention POCD administration of neuroprotective drugs, including gliatylin.

Animal studies showed that gliatylin warns induced cholinergic deficit, prevents the development of dementia, facilitates learning and memory by increasing the synthesis and release of acetylcholine in the brain structures [7].

Another mechanism of gliatylin action is anabolic effect which manifests itself in the stimulation of membrane fusion by the formation of precursors phospholipids membranes with products of its metabolic decay [7, 8]. So gliatylin activates cholinergic neurotransmission, arised plasticity brain tissue, has membrane stabilizing and antioxidant action. Were conducted numerous studies that demonstrated the efficacy gliatylin against motor disorders, level of consciousness, cognitive impairment in patients in the acute period of stroke [9-15]. Demonstrated a beneficial effect on mental activity gliatylin patients, memory, recovery conversational functions [9-12].

Use of the drug was associated with a significant improvement of cognitive function in patients with Alzheimer's disease [9]. According to the review thirteen

clinical studies, which included 4054 patients with ischemic stroke gliatylin has a positive effect on cognitive function in examined patients.

Methods and Materials: at the Department of Anesthesiology and Intensive Care National Cancer Institute was conducted a prospective controlled study. The aim of the study was to determine the incidence of POCD in patients after surgery scheduled for oncogynecology surgery, as well as the efficacy and safety gliatylin to prevent development of POCD.

The study included patients who were preparing for the planned hysterectomies for cancer of the cervix or uterine cancer. The criteria for inclusion in the study were: consent of the patient, age 60 years or less, planned surgery under general anesthesia lasting 2 hours or more, anesthesia risk according to ASA II-III, absence of defects in a patient hearing, vision.

Exclusion criteria were: patient refusal, age over 61, the original score on a scale MMSE scores less than 23, severe concomitant diseases of the cardiovascular, respiratory, diabetes, diseases of the nervous system (dementia, encephalopathy, history of CVA, etc.), mental disease, antidepressants or sedatives, alcohol.

Patients were divided into 2 groups: Group 1 – Study group - patients gliatylin administered at a dose of 2g intravenously 20 minutes before the end of surgery and 1g intravenously in a 24 hours after the end of surgery, Group 2 - the control group - without gliatillin. After obtaining informed consent, the day before the operation was carried out tests of cognitive function with a MMSE. Repeated assessment of cognitive function was performed in a 3 and 7 days after surgery. Also noted speed awakening patients after general inhalation anesthesia and time to extubation.

Wakeup patients defined as the time from the stop inhalation sevofluran (with the transition to inhalation of oxygen) to the first productive contact with the patient (performance of basic commands, eg. open eyes). Extubation time was determined from stop inhalation of sevofluran to extubation patient with adequate breath. POCD criterion was to reduce test result evaluation Folsteyn mental status after surgery by 10% or more.

Monitored perioperative blood glucose as a marker of stress, duration of anesthesia. Blood glucose was measured in 6 and 24 hours after surgery.

In the analysis of the data determined development POCD in the postoperative period, odds ratio of POCD (ODDS RATIO, then OR) in the control and the study groups, length of time to awaken and extubation, statistical significance was assessed using Fisher's exact test (Statistica 8,0; WinPepi).

Results: The study included 40 patients (Group 1 and 2 - 20 patients, respectively) with a mean age of 44,2 [CI 95%: 41.2, 47.3]. Groups did not differ statistically by age and met the criteria for inclusion in the study. The groups were homogeneous ($p = 0.08$).

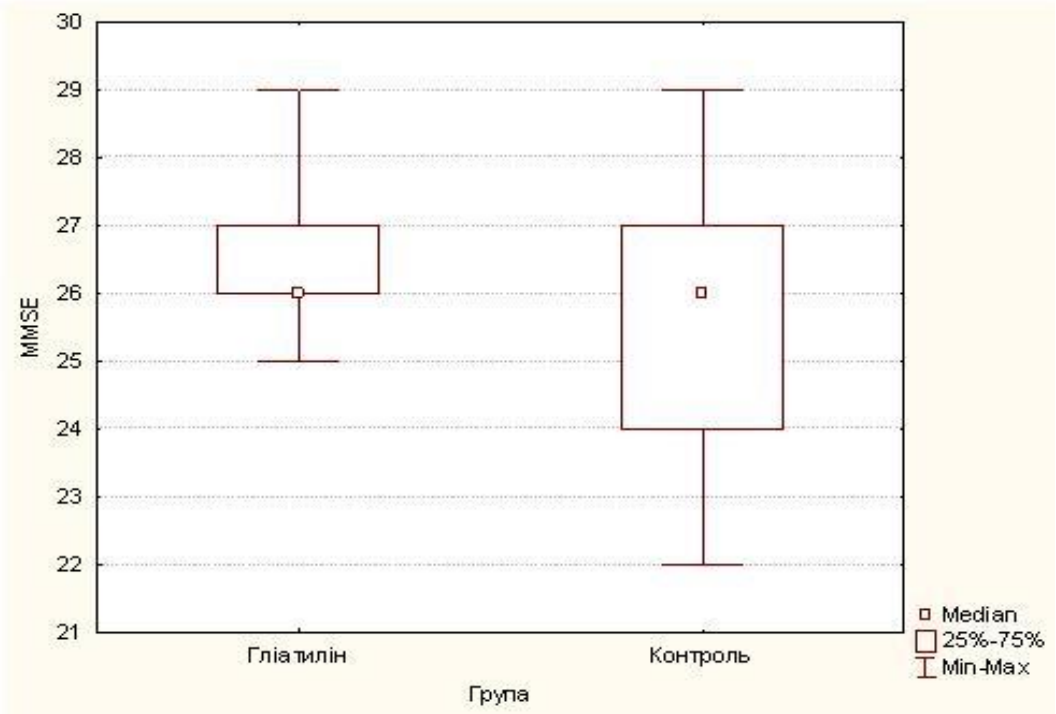

Figure 1. Distribution of results of cognitive function on a scale MMSE before surgery in the study and control groups.

All patients had been performed hysterectomy for cancer of the body or cervix under general inhalation anesthesia sevoflurane. Its depth controlled targets MAC (1,5-2) and BIS-monitoring (40-60). For postoperative analgesia was used combined NSAIDs and opioid analgesics. From time to stop inhalation anesthetic to wake the patient and to Extubation in Group 1 in the averaged 8,2 [CI 95%: 7.6, 8.8] and 14 [CI 95%: 13.4, 14.9] minutes respectively. In Group 2 (control) from time stopping inhalation anesthetic to wake the patient and to extubation average was 16,5 [CI 95%: 14.7, 18.2] and 22,8 [CI 95%: 21.1, 24,4], respectively. The authentic difference between the groups for a time of awakening and extubation time ($p = 0.0001$). At 3 days after surgery all patients re-tested with a MMSE. The odds ratio (OR) indicates that the risk of POCD in the control group was significantly higher than the risk in the treatment group POCD 8.5 times.

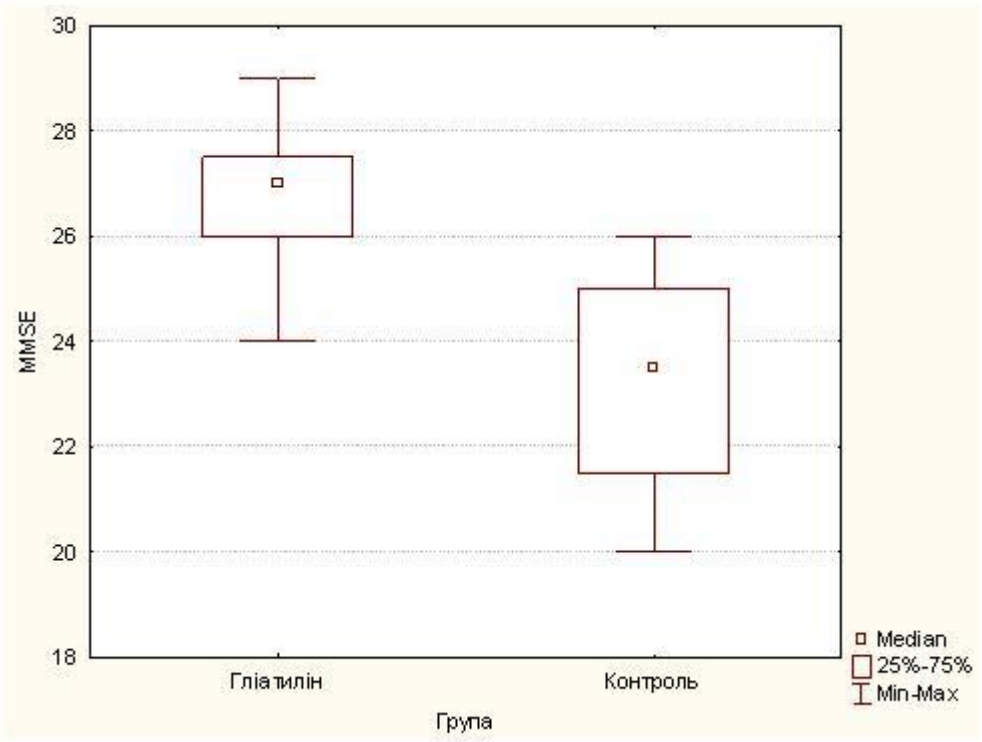

Figure 2. Distribution of results of cognitive function on a scale MMSE at 3 days after surgery in the study and control groups.

On day 7 after surgery all patients re-tested on a scale assessment of mental status Folsteyn. POCD diagnosed in 3 (15%) patients from Group 1 and 8 (40%) patients of group 2, the difference between POCD incidence in groups was not statistically significant, but the trend toward greater incidence POCD in the control group persisted (P = 0.078, OR = 3,78 [CI 95%: 0.69, 25.86]).

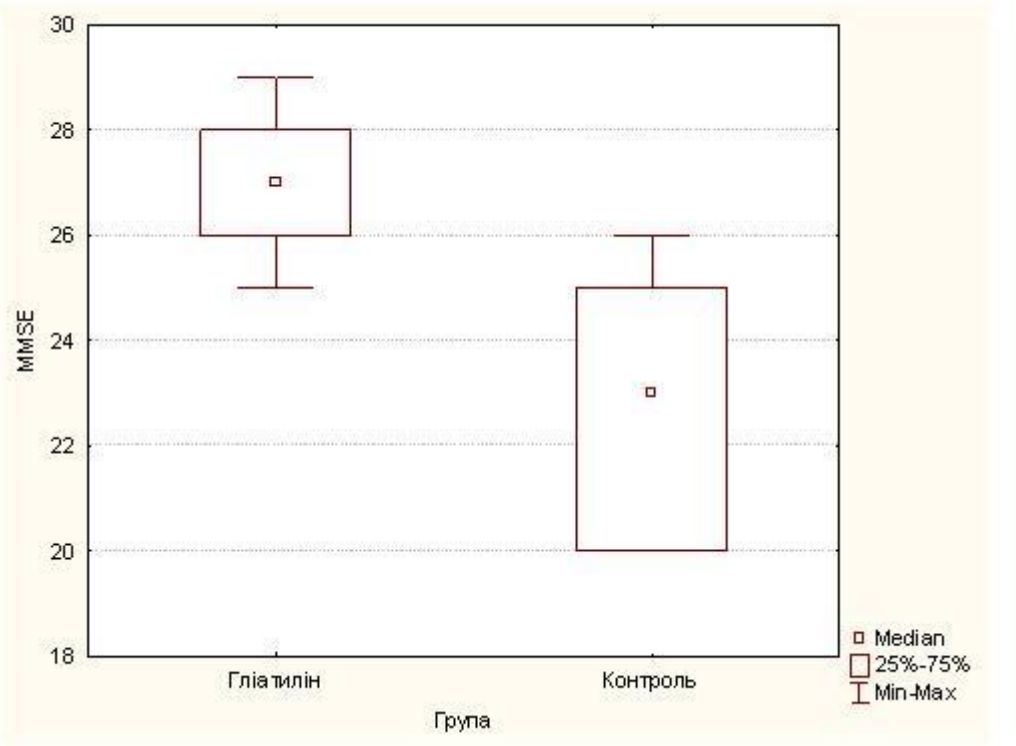

Figure 3. Distribution of results of cognitive function on a scale MMSE on day 7 after surgery in the study and control groups.

Blood glucose levels were not statistically different in groups. After 6 hours after surgery mean blood glucose in group 1 amounted to 5.5 mmol/l (CI 95%: 4.6, 6.8), in group 2 - 6.2 mmol/l (CI 95%: 5.2, 6.9). Within 24 hours after the operation the average level of glucose in group 1 was 5.9 mmol/l (CI 95%: 4.68, 6.8), in group 2 - 6.0 mmol/l (CI 95%: 4.9, 6.9), p> 0,05. The average duration of surgery did not differ statistically in the groups, and was in group 1 - 132 minutes (CI 95%: 122, 178), in group 2 - 140 minutes (CI 95%: 125, 180), p> 0.05 .

Discussion and conclusions: the problem of cognitive dysfunction after surgery scheduled oncogynecology department is important for middle-aged women. The incidence of POCD, the results of our research can be up to 60% in women after oncogynecology operations. According to foreign authors in non-cancer patients of all ages POCD incidence is 31-40% [2]. Most patients improve cognitive function within the next three months [2], but there is a direct relationship between the development POCD and increased mortality in the first year after major noncardiologic operations [21].

Risk factors POCD are advanced age, low education level, acute cerebrovascular accident or transient ischemic attack in history, repeated surgery, intraoperative hypoxia or large blood loss (2). In this study, we studied the effect of applying gliatylin on the incidence of POCD, our goal was to eliminate factors-co-founders that could affect the study results (factors that distort the impact assessment study factor on the outcome, because both have a causal relationship and with the result, and the factors). Groups did not differ in age, education,

neurological history, type of surgery, anaesthesia and postoperative analgesia. In all patients was performed primary surgery group were not statistically different between the duration transaction volume of blood loss, with the exception of periods of intraoperative hypoxia. On the development of stress reactions can indirectly judge the dynamics of blood glucose in both groups, based on proven correlation between the level of blood glucose and levels of stressors (cortisol, proinflammatory mediators) [26]. Dynamics of blood glucose did not differ statistically in the studied groups.

One of methods of prevention of perioperative POCD is neuroprotectors purpose, including derivatives of exogenous choline (gliatylin). In this study gliatylin was associated with a significant reduction risk of POCD, reducing wake time and time to extubation patients. Therefore, perioperative administration of gliatylin potentially could be the prevention of POCD. However, definitive conclusions necessary to conduct further research on large selections patients with placebo control.

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