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**Editor**

**Komarytskyy M.L.**

*Ph.D. in Economics, Associate Professor*

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**e-mail: [berlin@sci-conf.com.ua](mailto:berlin@sci-conf.com.ua)**

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## TABLE OF CONTENTS

### AGRICULTURAL SCIENCES

1. *Калинка А. К., Дроник Г. В., Лесик О. Б., Саранчук І. І., Похивка М. В., Меленко К. М.* 16  
ДОСЯГНЕННЯ НАУКОВЦІВ ДЛЯ ФЕРМ БУКОВИНИ
2. *Ліскович В. А.* 26  
ЕФЕКТИВНІСТЬ ГАЛУЗІ КОНЬАРСТВА В УКРАЇНІ

### BIOLOGICAL SCIENCES

3. *Бочарова А. О.* 30  
РЕКОМЕНДАЦІЇ ЩОДО ВИБОРУ МОЛОЧНОЇ ПРОДУКЦІЇ ТА ВИКОРИСТАННЯ ХАРЧОВИХ ДОБАВОК У ЇЇ СКЛАДІ
4. *Вишинська О. Л.* 36  
ФОРМУВАННЯ СУЧАСНОЇ СВІТОГЛЯДНОЇ ПОЗИЦІЇ УЧНІВ В ПИТАННЯХ ЄВРОПЕЙСЬКОГО ЗЕЛЕНОГО КУРСУ

### MEDICAL SCIENCES

5. *Abdukarimov U. G., Ikhtiyarova Gu. A.* 43  
PILOT BREAST SCREENING IN THE CITY OF KAGAN, BUKHARA REGION OF THE REPUBLIC OF UZBEKISTAN
6. *Obolonska O., Chupryna K., Soichenko P.* 47  
FEATURES OF THE COURSE OF ACUTE KIDNEY INJURY IN CHILDREN WITH TUBULOINTERSTITIAL NEPHRITIS. ANALYSIS OF A CLINICAL CASE
7. *Puchkov V. A., Deinichenko O. V., Bohomolova O. A.* 51  
INFLUENCE OF COMBINED NEUROPROTECTIVE THERAPY ON OBSTETRICAL RESULTS OF BIRTH IN FETES WITH EARLY FORM OF FETAL GROWTH RESTRICTION
8. *Valovina Yu. D., Halii Z. I., Valovina N. Yu.* 54  
SURGICAL TREATMENT IN WOUNDED WITH GUNSHOT TIBIA FRACTURES
9. *Акімова Л. С.* 56  
КЛІНІЧНІ ЗМІНИ НИРКОВОГО РЕЗЕРВУ У ХВОРИХ НА ХРОНІЧНЕ ОБСТРУКТИВНЕ ЗАХВОРЮВАННЯ ЛЕГЕНЬ II-III СТАДІЇ У ПОЄДНАННІ З ГІПЕРТОНІЧНОЮ ХВОРОБОЮ II СТАДІЇ
10. *Бельмасова М. С., Макаров В. В., Феськов В. М.* 59  
ТУРНИКЕТНИЙ СИНДРОМ: ПАТОГЕНЕЗ ТА ШЛЯХИ УНИКНЕННЯ
11. *Герцен Г. І., Гапон О. М., Білоножкін Г. Г.* 63  
ПОКАЗАННЯ ДО ІНТРАМЕДУЛЯРНОГО ОСТЕОСИНТЕЗУ ПЕРЕЛОМІВ ТІЛА КЛЮЧИЦІ КОМПРЕСІЙНИМ СТРИЖНЕМ

# INFLUENCE OF COMBINED NEUROPROTECTIVE THERAPY ON OBSTETRICAL RESULTS OF BIRTH IN FETES WITH EARLY FORM OF FETAL GROWTH RESTRICTION

**Puchkov Volodymyr Anatoliyovych**

Doctor of Medicine, Associate Professor

**Deinichenko Olena Valeriivna**

PhD., Associate Professor

**Bohomolova Oksana Andriivna**

Assistant

Zaporizhzhia State Medical and Pharmaceutical University,

Zaporizhzhia, Ukraine

**Introductions.** Fetal growth restriction (FGR) is often associated with the fetus not reaching its genetic and biological growth potential and can be the result of several causes, but one of the most common causes is placental dysfunction. Although the highest mortality occurs in fetuses with a birth weight below the 2.3rd percentile, an increased perinatal risk exists even if the fetal weight is above the 10th percentile [Lees, C. C., Romero, 2022]. Hypoxia and oxidative stress, caused by an increase in reactive oxygen species and/or a lack of availability and activity of antioxidants, have long been associated with FGR. Changes in oxygen concentration can cause sterile inflammation of the placenta, possibly exacerbating placental dysfunction and impairing fetal development during pregnancy with FGR [Nüsken, E., Appel, S., 2024]. The brain of the fetus is especially sensitive to the disturbance of growth conditions in the mother's womb. It has been shown that in newborns with FGR, changes in brain structure that occur during the prenatal period persist until adolescence. Such changes alter brain connectivity and are associated with neurodevelopmental disorders [Wixey, J. A., 2021].

**Aim.** To evaluate the effectiveness and impact of complex neuroprotective therapy in fetuses with fetal growth retardation on the obstetric outcomes of delivery.

**Materials and methods.** The case-control study involved 63 women with a singleton pregnancy between 24 and 34 weeks of gestation who were treated at the

Zaporizhzhia Regional Perinatal Center from 2018 to 2021. The study participants were divided into 2 groups. Group I included 30 pregnant women with early fetal growth retardation who were prescribed neuroprotective therapy by prescribing melatonin (12 mg/day) in combination with citicoline (1000 mg/day). Group II included 33 pregnant women with an early form of FGR, whose pregnancy and childbirth management was provided for by the current Order of the Ministry of Health of Ukraine. FGR was diagnosed according to current clinical protocols. Statistical analysis was performed using the "STATISTICA®" program. The statistical significance of differences between groups was determined using Fisher's exact test for qualitative indicators, and Student's T-test for quantitative ones.

**Results and discussion.** The average age of pregnant women, parity, term of pregnancy at inclusion, as well as clinical and anamnestic characteristics in the study groups, did not reveal a statistically significant difference ( $p > 0.05$ ). Among somatic pathologies, hypertensive disorders during pregnancy prevailed, the frequency of which was 7.6% and 10.2% in groups I and II, respectively, and had no statistically significant differences ( $p > 0.05$ ).

Peculiarities of the course of childbirth in the research groups showed that the average term of childbirth in the I group was statistically greater ( $p < 0.05$ ) and was 35.7 weeks, compared to 33.0 weeks in the II group. The frequency of premature births in group I was 2 times lower than in group II, and amounted to 41.3% versus 81.8%, respectively. The most frequent indication for premature birth was signs of fetal distress during pregnancy, which in the II group amounted to 66.7%, which was 2 times higher than the corresponding indicator of the I group (22.6%) ( $p < 0.001$ ). The frequency of premature detachment of the normally located placenta occurred in 12.1% in the II group and was not in any case in the women of the I group ( $p > 0.0001$ ). Delivery by caesarean section was also higher in group II compared to group I (81.8% versus 46.7%). The average birth weight in group I was statistically significantly higher ( $p < 0.05$ ) (1988.0 g) compared to group II (1470.0 g). Apgar score  $< 7$  points at 5 minutes in the II group was 3.6 times higher than the corresponding indicator in the I group and was 48.5% and 13.3%, respectively

( $p < 0.001$ ). The need to stay in the intensive care unit in group I was 46.7%, which is 1.5 times less than in group II (69.7%) ( $p < 0.001$ ). The total duration of hospitalization of newborns in the hospital in the I group was statistically shorter (15.2 days) compared to the II group (26.2 days) ( $p < 0.001$ ).

**Conclusion.** The proposed complex neuroprotective therapy, which includes the combined use of melatonin with citicoline in fetuses with an early form of growth retardation, allowed to improve the obstetric outcomes of delivery.