EMBRYONIC ORGANOGENESIS UNDER THE EFFECT OF DUAL GLP-1/GIP RECEPTOR AGONIST

Omirgul Bakenova[1,2], Galiya Akylzhanova[2], Arslan Umarov [3], Danysh Abetov[2], Zhanna Mussaeva[3], Ainur Akilzhanova[2], Dos Sarbassov[1,2]

[1]Nazarbayev University, School of Science and Humanities, Astana, Kazakhstan, 010000 [2] Center for Life Sciences, National Laboratory Astana, Nazarbayev University, Astana, Kazakhstan, 010000
[3]Nazarbayev University, School of Engineering and Digital Sciences, Astana, Kazakhstan, 010000
[4]Eurasian National University, Faculty of Biology, Astana, Kazakhstan, 010000

Corresponding authors: akilzhanova@nu.edu.kz, dos.sarbassov@nu.edu.kz

Background: Glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP) are incretin hormones that regulate glucose metabolism and cardiovascular health. Tirzepatide, a dual GLP-1/GIP receptor agonist, has demonstrated cardioprotective and metabolic benefits, but its safety during pregnancy remains unexplored.

Materials and methods: Pregnant C57BL/6J mice were assigned to control and tirzepatide groups. Maternal blood was collected before and after pregnancy to assess systemic changes. Embryos were harvested for morphological and molecular analyses, including transcriptomics and proteomics.

Results: Control mice exhibited steady maternal weight gain throughout pregnancy and produced embryos with normal size and morphology, indicating healthy maternal–fetal metabolic support. In contrast, tirzepatide-treated dams showed a progressive reduction in body weight over the treatment period. Gross examination of maternal livers revealed pale, mottled tissue with irregular texture, consistent with hepatic metabolic disturbance. Embryos from the tirzepatide group were noticeably smaller and showed growth restriction, suggesting that the drug compromised nutrient transfer across the placenta.

Conclusion: These findings demonstrate that tirzepatide exposure during pregnancy disrupts maternal metabolism, leading to impaired hepatic function and reduced nutrient availability to the developing fetus. The resulting restricted embryonic growth highlights potential reproductive risks associated with dual GLP-1/GIP receptor agonists during gestation. Further investigations—encompassing molecular, transcriptional, and proteomic analyses—are warranted to elucidate the specific pathways and mechanisms underlying these adverse effects and to determine whether similar outcomes might occur in other mammalian models or in clinical contexts.

Acknowledgement: Supported by the Committee of Science of the Ministry of Science and Higher Education of Republic of Kazakhstan (BR24993023).

Key words: GLP-1, GIP, tirzepatide, embryogenesis, pregnancy, organogenesis