International Science Group

ISG-KONF.COM

# SCIENCE AND PRACTICE OF TODAY

# IX

# SCIENTIFIC AND PRACTICAL CONFERENCE

16-19 November

Ankara, Turkey

DOI 10.46299/ISG.2020.II.IX

ISBN 978-1-63649-920-8

# ELECTRON MICROSCOPIC FEATURES OF THE HIPPOCAMPAL FORMATION DEVELOPMENT IN POSTERITY OF FEMALE RATS AFTER PGE2 INJECTION FOR LABOR INDUCTION

**Hryhorieva Olena**
MD, PhD, DSc, Professor, Head of the Department of Normal Anatomy, Operative Surgery and Topographic Anatomy
Zaporizhzhia State Medical University, Zaporizhzhia, Ukraine

**Mamai Irina**
Post-graduate student of the Department of Normal Anatomy, Operative Surgery and Topographic Anatomy
Zaporizhzhia State Medical University, Zaporizhzhia, Ukraine

**Relevance.** Induction of labor is a fairly widespread medical intervention that is performed on every fourth or fifth women in the UK, Europe and the USA. Data from the WHO Global Survey on Maternal and Perinatal Health, which included 373 clinics in 24 countries and almost 300,000 births, shows that induction of labor occurs in 9.6% of cases [1]. At the same time, this indicator tends to grow. In the United States, between 1990 and 2006, the rate of induction of labor increased from 9.5% to 22.5% [2]. In 2012, in the United States, already 23.3% of singleton births were induced [3].

Despite the large number of possible complications associated with labor hyperstimulation, there are still no universal standards on criteria that should be used to determine unsuccessful induction and methods for accurately determining the time intervals for re-induction [4].

A meta-analysis by W Chen et al (2016), that included 96 studies (17,387 women), showed that vaginal misoprostol is most effective for inducing labor within 24 hours, but has the highest frequency of uterine hyperstimulation with changes in heart rate [5]. In a study by Jane Thomas et al. (2014), which included 70 studies involving 11,487 women, it was found that vaginal prostaglandins can stimulate too strong uterine contraction, which can cause the slowing down fetal heart rate [6]. In a study by Yi-Ran Liu et al. (2018), based on data from five randomized trials (603 women), dinoprostone injection was associated with a higher incidence of uterine hyperstimulation (RR 0.17, 95% CI 0.06-0.54) and a decrease in the arterial blood pH of the newborns umbilical cord <7.1 (RR 0.36, 95% CI 0.15-0.84) [7].

For the fetus, induction can lead to jatrogenic prematurity, physical injury and hypoxia (due to increased contractile activity of the uterus). Respiratory disorders are the most common complication caused by labor induction [8]. Children who have undergone a hypoxic-ischemic state in the neonatal period show an increased risk of speech and communication impairments due to the ongoing morphogenesis of certain neuronal populations [9, 10]. In newborns, pyramidal cells of the hippocampus are still

migrating to the corresponding layers CA1, CA2 and CA3, and are vulnerable to hypoxic-ischemic conditions [11, 12]. Hippocampus damage leads to cognitive deficits that may replicate some phenotypes of children with neurological disorders [13].

Thus, it is important to study the ultrastructural features of the hippocampal formation development in posterity of female rats after PgE2 injection for labor induction.

**Aim.** To determine the ultrastructural features of the hippocampal formation development in laboratory rats in the first two weeks of life after intravaginal injection of prostaglandin E2 for labor induction.

**Methods.** The changes in the ultrastructural of hippocampal formation in posterity of white syngenic rats in the first two weeks of life have been studied. The beginning of pregnancy was established using the method of vaginal smears stained with methylene blue; the presence of sperm in smears was the evidence of the 0 day of pregnancy. Pregnant females of the experimental group were injected PgE2 in the form of a gel intravaginally to stimulate labor on the 22th day of pregnancy. The duration of the experimental rats pregnancy amounted to 23 day, in the intact group - 23-24 day after conceiving. We were guided by the "European Convention for Working with Experimental Animals", as well as scientific and practical recommendations for keeping laboratory animals and working with them [14]. Brain tissue from experimental animals of the 1st, 7th and 14th days of life after grinding in a drop of 2.5% glutaraldehyde in 0.1 M phosphate buffer with pH 7.4 were fixed in a similar solution for 2 hours at t + 4C. After washing the fixing solution in phosphate buffer, the material was treated for two hours in 1% OsO4 solution. Subsequently, the pieces were dehydrated in an ascending battery of ethyl spirits up to 100% acetone with additional contrasting for two hours with 2.5% uranyl acetate on 70% ethyl spirit; pouring into the block was carried out by gradually soaking the tissue with a compound of acetone and Epon (2: 1, 1: 1, 1 : 2) and poured into pure Epon. Epon polymerization was carried out in two stages at 36 ° C (12 h) and 56 ° C (24 h).

Ultrathin (50-60 nm) sections were obtained on a PowerTome RMC Boeckeler ultratome. Ultrathin sections were contrasted with lead citrate according to the E. Reynolds method for 30 minutes at room temperature. Ultrathin sections were studied in a PEM-100 electron microscope with an accelerating voltage 60 kV.

**Results.** The earliest changes were revealed in the synaptic apparatus in posterity of female rats after PgE2 injection for labor induction. On the first day of life, the neuropil of the hippocampal formation in the experimental group is characterized by edema of astrocytic processes, pre- and postsynaptic processes, damage to the mitochondrial apparatus, and intercellular edema. Changes in the presynaptic terminals in the group of experimental animals include edema of the presynaptic endings, aggregation of synaptic vesicles in the center of the presynaptic processes with their distancing from the presynaptic membrane, swelling and destruction of mitochondria, the appearance of large vacuoles in the presynaptic processes, perforations at the contact points of pre- and postsynaptic seals.

Changes in the synaptic apparatus were combined with changes in other structural components of the nervous tissue. Ultrastructural changes in oligodendroglia were observed at all periods in the experimental group: hypertrophied, fragmented nuclei of

oligodendrocytes, stratification of the myelin sheath of the axons of the hippocampal formation.

The severity of ultrastructural changes in the neuropil is in direct proportion to the severity of microcirculation disorders in the structures of the hippocampal formation. In the brain of animals of the control group, the lumen of the capillaries and blood vessels is smooth with tight intracellular contacts between endothelial cells. On the contrary, in the brain of experimental rats, characteristic microvilli on the endothelial surface, disruption of contacts between entothelial cells and fragmentation of the cytoplasm of endothelial cells with the formation of villi in the lumen of the capillary were found.

The study revealed changes in the CA1 and CA2 neurons of the hippocampus, dentate gyrus and entorhinal cortex.

The images showed that the ultrastructure of mitochondria in the control group had a clear structure of mitochondrial cristae, but the mitochondria of neurons in the hippocampal formation of experimental animals became swollen, vacuolated with rupture and destruction of the cristae.

In most cases, mitochondria had an irregular shape, and mitochondria with damaged internal structures and a reduced number of cristae were observed.

Conclusions.

1. In posterity of female rats after receiving PgE2 for labour induction microcirculatory changes are observed in the form of a violation of contacts between entothelial cells and fragmentation of the cytoplasm of endothelial cells with the formation of villi in the lumen of capillaries in the first two weeks of life;

2. In the experimental group of animals at all periods, changes in the synaptic apparatus are observed: edema of the presynaptic endings, synaptic vesicles aggregation in the center of the presynaptic processes with its distance from the presynaptic membrane, swelling and destruction of mitochondria, the appearance of large vacuoles in presynaptic processes, perforations at the sites of contact of pre- and postsynaptic seals.

3. Oligodendroglia changes in experimental rats presented by hypertrophy, fragmentation of oligodendrocyte nuclei, stratification of the myelin sheath of axons on the 1st, 7th and 14th days of life in the CA1, CA2 and dentate gyrus regions.

4. In experimental rats in the CA1, CA2 regions and the dentate gyrus, ultrastructural changes in neurons were observed on the 1st, 7th, and 14th days of life: edema and vacuolization of mitochondria with rupture and destruction of cristae, massive granular vesicles and microtubules formation, Golgi apparatus hypertrophy.

**References:**

1. WHO Global Survey on Maternal and Perinatal Health. Induction of labour data. Geneva, World health Organization, 2010.

2. Lydon-Rochelle M. T., Cardenas V., Nelson J. C., Holt V. L., Gardella, C., Easterling T. R. Induction of labor in the absence of standard medical indications: incidence and correlates / M. T. Lydon-Rochelle, V. Cardenas, J. C. Nelson, V. L. Holt, C. Gardella, T. R. Easterling // Med Care 2007;45:505-512.

3. Osterman M. J. K. , Martin J. A. Recent declines in induction of labor by gestational age / Osterman M. J. K. , Martin J. A. // NCHS Data Brief 2014;155:1–8.

4. Rouse D. J., Owen J., Hauth J. C. Criteria for failed labor induction: prospective evaluation of a standardized protocol / D. J. Rouse, J. Owen, J. C. Hauth // Obstet Gynecol 2000;96:671-677.

5. Chen W., Xue J., Peprah M. K., Wen S. W., Walker M., Gao Y., Tang Y. A systematic review and network meta-analysis comparing the use of Foley catheters, misoprostol, and dinoprostone for cervical ripening in the induction of labour / W. Chen, J. Xue, M. K. Peprah, S. W. Wen, M. Walker, Y. Gao, Y. Tang // BJOG. 2016 Feb;123(3):346-54. doi: 10.1111/1471-0528.13456.

6. Thomas J., Fairclough A., Kavanagh J., Kelly A. J. Vaginal prostaglandin (PGE2 and PGF2a) for induction of labour at term / J. Thomas, A. Fairclough, J. Kavanagh, A. J. Kelly // 2014 Jun 19;2014(6):CD003101. doi: 10.1002/14651858.CD003101.pub3.

7. Liu Y. R., Pu C. X., Wang X. Y., Wang Double-balloon catheter versus dinoprostone insert for labour induction: a meta-analysis Y. R. Liu, C. X. Pu, X. Y. Wang, // Arch Gynecol Obstet . 2019 Jan;299(1):7-12. doi: 10.1007/s00404-018-4929-8.

8. Lydon-Rochelle M. T., Cardenas V., Nelson J. C., Holt V. L., Gardella, C., Easterling T. R. Induction of labor in the absence of standard medical indications: incidence and correlates / M. T. Lydon-Rochelle, V. Cardenas, J. C. Nelson, V. L. Holt, C. Gardella, T. R. Easterling // Med Care 2007;45:505-512.

9. Morales P., Bustamnte D., Espna-Marchant P. Pathophysiology of perinatal asphyxia: can we predict and improve individual outcomes? / P. Morales, D. Bustamnte, P. Espna-Marchant // EPMA J. 2011 Jun; 2(2): 211–230. doi: 10.1007/s13167-011-0100-3.

10. Martinez-Biarge M., Diez-Sebastian J., Rutherford M. A. Outcomes after central grey matter injury in term perinatal hypoxic-ischaemic encephalopathy / M. Martinez-Biarge, J. Diez-Sebastian, M. A. Rutherford // Early Hum Dev. 2010 Nov;86(11):675-82. doi: 10.1016/j.earlhumdev.2010.08.013.

11. Altman J., Bayer S. A. Development of layer I and the subplate in the rat neocortex / J. Altman, S. A. Bayer // Experimental Neurology January. 1990;107(1):48-62.https://doi.org/10.1016/0014-4886(90)90062-W.

12. Bayer S. A., Yackel J. W., Puri P. S. Neurons in the rat dentate gyrus granular layer substantially increase during juvenile and adult life / S. A. Bayer, J. W. Yackel, P. S. Puri // Science. 1982 May 21;216(4548):890-2. doi: 10.1126/science.7079742.

13. Lodygensky G. A., Seghier M. L., Warfield S. K., Tolsa C. B., Sizonenko S. Intrauterine growth restriction affects the preterm infant's hippocampus / G.A. Lodygensky, M.L. Seghier, S.K. Warfield, C.B. Tolsa, S. Sizonenko // Pediatric research 63 (4), 438-443.

14. Kozhem'yakin Y.M., Khromov O.S., Boldir'va N.Y., Dobrelya N.V., Sayfetdinova G.A. Scientific and practical recommendations for the establishment of laboratory creatures and robots for them Kiev: Interservice, 2017-182.