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Sleep disorders and changes in melatonin concentrations in pregnant women with preeclampsia

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ABSTRACT

Melatonin plays a significant role in the development of normal pregnancy, in particular, it contributes to the successful implantation of the fertilized egg, affects the act of childbirth, is actively produced by the trophoblast and placenta, reduces oxidative stress, in particular, with pre-eclampsia. In addition, melatonin is one of the essential hormones in the protection of the endothelium and stem cells from the oxidative stress.

***OBJECTIVE** – to study the mechanisms of development, terms of manifestation, and types of sleep disorders, as well as changes in the concentrations of melatonin in the blood of pregnant women with preeclampsia.*

***METHODS.** 50 pregnant women at a mean age of 29.1 ± 3.4 years who had preeclampsia in the 3rd pregnancy trimester were examined (experimental group). All women in the research group had a gestation term of 30-32 weeks of pregnancy. The control group consisted of 33 women with a mean age of 31.2 ± 6.6 years who had an uncomplicated pregnancy. The presence of sleep disorders was established using a questionnaire: pregnant women were asked about the term of pregnancy in which complaints of sleep disorders appeared, the nature of sleep disorders, the frequency of episodes of sleep disorders (how many times a week such a condition was noted), etc. The concentration of melatonin in the venous blood of the examined pregnant women was determined by ELISA. Blood was taken at 9:00 a.m., on an empty stomach, and all patients were analyzed at the same time of a day.*

***RESULTS.** The study showed that sleep disorders in pregnant women with pre-eclampsia, which complicates the pregnancy in the 3rd trimester, occurred earlier, compared to women with an uncomplicated pregnancy: pregnant women with pre-eclampsia were more likely to notice worsening of sleep, starting from 22-30 weeks of pregnancy (in 26.0 % of cases), while in pregnant women with a physiological pregnancy, similar complaints appeared mainly after 30 weeks. In the third trimester of pregnancy women with preeclampsia were more likely to wake up 2 or more times per night (in 68.0 % of cases) compared to controls (in 23.3 % of cases, $p < 0.001$) and 3 or more times per night per week (in 54.0 % of cases, in controls – in 16.7 % of cases, $p < 0.001$), which may be a consequence of a disorder of the function of the pineal gland. Women with preeclampsia were more likely (56.0 % vs. 13.3 % in the control group, $p < 0.01$) to use gadgets (electronic devices, mainly smartphones) for more than 2 hours after 9:00 p.m., which also negatively affects the function of the pineal gland. In pregnant women whose pregnancy was complicated by preeclampsia in the 3rd trimester, a significant (1.8-fold) decrease in the level of melatonin in venous blood taken at 9 a.m. was observed, compared to women with an uncomplicated pregnancy ($p = 0.029$).*

***CONCLUSIONS.** Sleep disorders in pregnant women with preeclampsia occur earlier and are more expressed compared to women with an uncomplicated pregnancy. The appearance of complaints of insomnia in the second trimester of pregnancy, in our opinion, can be considered a diagnostic sign of pineal gland dysfunction in preeclampsia. A decrease in the level of melatonin in pregnant women with preeclampsia, established against the background of minimal daily activity of the pineal gland (at 9 a.m.), indicates a decrease in the melatonin-producing function of the placenta which might have an impact on the condition of stem cells of fetus and placenta.*

***KEY WORDS:** pregnancy; placenta; preeclampsia; pineal gland; melatonin; sleep disorders*

At this stage of the development of Obstetrics and Gynecology, the fact that the favorable course of pregnancy and its outcome directly depends on the mother's health, particularly her endocrine system, is generally accepted. One of the important components of this system is the pineal gland. The endocrine function of the pineal gland is to secrete melatonin and serotonin. Melatonin (5-methoxy-N-acetyltryptamine) is

a compound belonging to the indole class. The biological precursor of melatonin is the essential amino acid tryptophan. Unlike serotonin, melatonin easily penetrates through the blood-brain barrier [1, 2]. It is known that melatonin plays a significant role in the development of normal pregnancy, in particular, it contributes to the successful implantation of the fertilized egg [3], affects the act of childbirth [4], is actively produced by the trophoblast and placenta [3, 5], reduces oxidative stress [6], in particular, with preeclampsia [2, 7, 8], etc. At the same time, the relationship between the pineal gland and the placenta, as a producer of melatonin, remains not fully understood. It is also unknown whether the placenta secretes melatonin in a circadian mode or not [8].

Preeclampsia is a systemic disorder of the "mother-placenta-fetus" system, which is specific to human pregnancy [9, 10]. Preeclampsia is characterized by the appearance of hypertension first detected in the period of pregnancy after 20 weeks, as well as damage to other organs, primarily the kidneys, liver function disorders, changes in the state of the blood, and – often – fetal growth retardation [9, 11, 12]. Thus, the key link in the pathogenesis of preeclampsia is placental dysfunction.

It is noted that in pregnant women with preeclampsia, a decrease in night-time melatonin concentrations is noted, compared to healthy pregnant women [13], which may indicate a disorder of the functioning of the pineal gland in preeclampsia. However, the decrease in melatonin levels in this pathology is caused not only by changes in the work of the pineal gland: it is known that the expression of the two most important enzymes necessary for the synthesis of melatonin, namely, aralkylamine-N-acetyltransferase and hydroxyindole-O-methyltransferase, is significantly reduced in placenta tissue in women, having preeclampsia, as well as the expression of melatonin receptors of both types (M1 and M2); therefore, insufficient synthesis of melatonin by the placenta in preeclampsia has been quite accurately confirmed [13, 14].

An endothelial dysfunction against the background of poor remodeling of the spiral arteries in case of preeclampsia is reported to damage the vascular component in the maternal organism; this condition provokes massive oxidative stress the antioxidant therapies and vitamin supplementation (e.g., vitamin E, vitamin C, carotenoids, coenzyme Q10, and selenium) have only marginal effect on. It is now evident that the placenta contains a reservoir of mesenchymal stem cells (MSCs), and these cells could be of major clinical importance. The rapid development of allogeneic and autologous MSC-based therapies to combat various chronic diseases, including oxidative stress-related pathologies, is reported nowadays [15]. However, significant changes in the regenerative potential of placental stem cells, obtained on the background of preeclampsia, should be expected. That might be a precaution from the application of such therapeutic strategies in some cases.

Taking this into account, it can be assumed that melatonin plays a significant role in establishing the physiological relationships between the mother's endocrine system and pregnancy, both at the implantation stage and at later stages of gestation. However, this part of the pathogenesis of normal and complicated pregnancy needs further study.

THE OBJECTIVE of the study – to determine the mechanisms of development, terms of manifestation, and types of sleep disorders, as well as changes in the concentrations of melatonin in the blood of pregnant women with preeclampsia, since melatonin is one of the essential hormones in the protection of the endothelium and stem cells from the oxidant stress.

MATERIALS AND METHODS

An examination of 50 pregnant women at a mean age of 29.1 ± 3.4 years (aged from 21 to 36 years) who had preeclampsia hospitalized at the Chernivtsi Regional Perinatal Centre was conducted. The presence of preeclampsia was diagnosed by systolic blood pressure ≥ 140 mmHg and diastolic blood pressure ≥ 90 mm Hg when measured twice with an interval of more than 4 hours, or ≥ 160 mm Hg and diastolic blood pressure ≥ 110 mm Hg, with a single measurement, as well as the presence of proteinuria ≥ 300 mg per 24-hour urine collection [16]. All women in the study group had a gestational age of 30-32 weeks of pregnancy, confirmed by calculating the due date based on the first day of the last menstruation, and ultrasound of the first trimester of pregnancy (11-13 weeks). The control group for our study consisted of 33 women with a mean age of 31.2 ± 6.6 years (aged from 21 to 38 years) who had an uncomplicated pregnancy, they were observed in the women's consultation department of the Chernivtsi Regional Perinatal Centre; the gestation period was also 30-32 weeks. Patients with extragenital diseases (chronic arterial hypertension, obesity, pregestational and gestational diabetes, endocrine diseases, significant anemia, etc.) were not included in either the main or control groups. We also did not involve in the study patients who were known to have received prevention of preeclampsia with aspirin (required by Order of the Ministry of Health of Ukraine No. 151 of 24.01.2022). This was applied to both the experimental and control groups.

The study was approved by the Commission on Biological and Medical Ethics of the Bukovinian State Medical University (Minutes No. 4 dated December 22, 2020). It was conducted in strict accordance with the Code of Ethics of the World Medical Association Declaration of Helsinki for experiments involving people. All engaged patients agreed to participate in the study and signed an informed consent form.

A questionnaire we used was developed by Berbets A. and co-authors [17, 18]. Pregnant women were asked about the period of pregnancy in which complaints of sleep disturbances appeared (earlier than 12 weeks of pregnancy, 12-22 weeks of pregnancy, 22-30 weeks of pregnancy, from 30 weeks of pregnancy to the date of delivery), the nature of sleep disorders ("difficult to fall asleep", waking up at night 2 or more times, "fatigue and tiredness in the morning"), the frequency of episodes of sleep disturbances (how many times per week a similar condition was noted), etc. The questionnaires also separately asked questions about the conditions in the room for sleeping at home, in particular, about the presence or absence of energy-saving lamps. All 50 pregnant women from the experimental group and 30 women included in the group with an uncomplicated pregnancy took part in the survey.

A quantity assessment of melatonin levels in the blood of 32 women, randomly selected from the group of surveyed pregnant women with preeclampsia, was also carried out. All 33 patients with an uncomplicated pregnancy, who were included in the study, were in the control group. Blood sampling was performed by puncture of the cubital vein at 9 a.m. on an empty stomach and was performed in all patients of the experimental and control groups at the same time of the day. Blood melatonin levels were determined by ELISA using the Melatonin ELISA diagnostic kit (*IBL*, Germany).

For mathematical calculation of the results of the survey, we used the tool "Comparison of Proportions" of the MedCalc software package (*MedCalc Software Ltd*, Belgium). Statistical processing of the biochemical results was carried out using the "Comparison of Means" tool using the Welch test for unequal samples, included in the MedCalc software package; the data is represented as the mean value with a 95 % confidence interval for it. The statistical difference was considered significant in the case of $p < 0.05$.

RESULTS AND DISCUSSION

The results of a survey of pregnant women regarding the quality of their sleep are shown in **Table 1**.

Table 1. Results of a survey of pregnant women with preeclampsia regarding sleep quality.

	Group with preeclampsia (n = 50)	Control group (n = 30)
The presence of sleep disorders before pregnancy	16 (32.0 %)*	3 (10.0 %)
Deteriorations of sleep during pregnancy	44 (88.0 %)*	21 (70.0 %)

	Group with preeclampsia (n = 50)	Control group (n = 30)
Significant deteriorations of sleep during pregnancy (except for a single awakening at night after 30 weeks)	36 (72.0 %)**	7 (23.3 %)
Taking treatment for sleep disorders before pregnancy	3 (6.0 %)	3 (10.0 %)
Manifestations of sleep disorders:		
- no sleep disorders	6 (12.0 %)*	9 (30.0 %)
- waking up at night	41 (82.0 %)*	17 (56.7 %)
- difficulty in falling asleep and waking up at night	15 (30.0 %)*	0
- waking up at night and tiredness in the morning	26 (52.0 %)**	0
- only difficulty in falling asleep	0	1 (3.3 %)
- only tiredness in the morning	0	3 (10.0 %)
- other	0	0
Bedtime:		
- earlier than 22:00	3 (6.0 %)	2 (6.7 %)
- 22:00 – 00:00	41 (82.0 %)	26 (86.7 %)
- 00:00 – 02:00	4 (8.0 %)	2 (6.7 %)
- later than 02:00	2 (4.0 %)	0
Daytime sleep during pregnancy:		
- no	24 (48.0 %)	16 (53.3 %)
- yes, once a day	25 (50.0 %)	14 (46.7 %)
- yes, twice a day	1 (2.0 %)	0
- other	0	0
From what period of pregnancy night awakenings appeared:		
- no awakenings	6 (12.0 %)*	9 (30.0 %)
- up to 12 weeks of pregnancy	2 (4.0 %)	2 (6.7 %)
- 12-22 weeks of pregnancy	4 (8.0 %)**	0
- 22-30 weeks of pregnancy	13 (26.0 %)*	2 (6.7 %)
- after 30 weeks of pregnancy	25 (50.0 %)	17 (56.7 %)
Reasons for waking up at night:		
- no night awakenings	6 (12.0 %)*	9 (30.0 %)
- baby's movements	3 (6.0 %)	6 (20.0 %)
- the desire to go to the toilet	15 (30.0 %)	15 (50.0 %)
- for no apparent reason	26 (52.0 %)**	0
Number of nights with awakenings, per week:		
- no awakenings	6 (12.0 %)*	9 (30.0 %)
- 1 time a week	9 (18.0 %)	8 (26.7 %)
- 2-3 times a week	8 (16.0 %)	8 (26.7 %)
- more than 3 times a week	27 (54.0 %)**	5 (16.7 %)
Number of awakenings at night, per 1 night:		
- no awakenings	6 (12.0 %)*	9 (30.0 %)
- 1 time per night	10 (20.0 %)*	14 (46.7 %)
- 2 or more times a night	34 (68.0 %)**	7 (23.3 %)
Time of first awakening at night:		
- no awakening	6 (12.0 %)*	9 (30.0 %)
- 23:00 - 01:00	9 (18.0 %)	6 (20.0 %)
- 01:00 - 03:00	32 (64.0 %)*	12 (40.0 %)
- 03:00 - 05:00	3 (6.0 %)	3 (10.0 %)
Using gadgets (smartphone, tablet, computer) after 21:00:		
- no	3 (6.0 %)	0
- less than 30 min	8 (16.0 %)	3 (10.0 %)
- 30 minutes - 1 hour	11 (22.0 %)**	23 (76.7 %)
- 2 or more hours	28 (56.0 %)**	4 (13.3 %)
Availability of energy-saving lamps at home:		
- no such lamps at home	8 (16.0 %)**	24 (80.0 %)
- outside the sleeping room	11 (22.0 %)	2 (6.7 %)
- in the room for sleeping	31 (62.0 %)**	4 (13.3 %)
Sleep changes after hospitalization (only in the preeclampsia group):		
- deterioration	10 (20.0 %)	-
- improvement	11 (22.0 %)	-
- unchanged	29 (58.0 %)	-
Taking drugs for sleep improvement:		
- no	24 (48.0 %)*	24 (80.0 %)
- yes	26 (52.0 %)*	6 (20.0 %)

*Note: * – $p < 0.05$, ** – $p < 0.001$, compared to pregnant women with a physiological pregnancy.*

One-time awakenings related to going to the toilet, which appeared after the 30th week of pregnancy, we considered as the norm.

In women whose pregnancy was complicated by preeclampsia, in comparison with women with an uncomplicated pregnancy, sleep disorders were noted in the anamnesis before the onset of pregnancy more often (16 cases, 32.0 %), than in the group of healthy pregnant women (3 cases, 10.0 %, $p = 0.0261$). This fact can be considered as the evidence of the presence of a violation of the pineal gland function in the examined women, included in the research group, even before the onset of pregnancy.

There was also a significant difference between the groups in the occurrence of complete absence of sleep disturbances during pregnancy: in the group with a complicated pregnancy, namely, in the presence of preeclampsia, women were less likely to note the complete absence of sleep disturbances during pregnancy (12.0 % versus 30.0 % in the control group, $p < 0.05$).

We found no significant difference in bedtime between groups, as well as in the frequency of daytime sleep episodes. On the contrary, our questionnaire showed that pregnant women who developed preeclampsia in the 3rd trimester of pregnancy began to notice sleep deterioration quite early, namely in the period of 12-22 weeks of pregnancy (4 cases, 8.0 %, while in the control group in this period of gestation, no sleep disturbances were noted) and at 22-30 weeks of pregnancy (13 cases, 26.0 %, while in the control group, 2 cases were present, 6.7 %, $p < 0.05$ in both cases). In pregnant women of the control group, similar complaints appeared mainly after 30 weeks (56.7 %, 17 cases out of 30).

In our opinion, such an early appearance of complaints about sleep disturbances in women with preeclampsia diagnosed in the 3rd trimester indicates a decrease in the level of melatonin in their body. The reason for this is the placental dysfunction itself, which accompanies preeclampsia, and in which the placenta produces less melatonin, but also disorders on the part of the pineal gland. Research that supports this hypothesis is outlined below.

Regarding the reasons for night awakenings: for example, such an answer as "the desire to go to the toilet" was found in 30.0 % of surveyed pregnant women from the group with preeclampsia and in 50.0 % of pregnant women from the control group, which did not make a statistically significant difference. However, we noted that more than half of the pregnant women (26 out of 50 patients, 52.0 %) with preeclampsia noted that awakening occurred "for no apparent reason." Such complaints were not observed at all in women with an uncomplicated pregnancy ($p < 0.01$).

We did not find a difference in the frequency of complaints of waking up because of the "feeling of the baby's movements" between the preeclampsia group and the normal pregnancy group.

Women from the main group were significantly more likely to wake up 2 or more times per night (68.0 % of positive responses – 34 of 50 cases) compared to controls (7 cases of 30, which is 23.3 %, $p < 0.001$). In addition, pregnant women with preeclampsia probably woke up 3 or more times a week, compared to women with a normal pregnancy, according to the questionnaire data collected by us (54.0 % positive answers, in the control – 17.0 %, $p < 0.001$).

There were no statistically significant differences in daytime sleep between groups of pregnant women, as well as in the time of going to bed in the evening: the majority of interviewed pregnant women fell asleep between 22:00 and 00:00. The first awakening of the night occurred, as usually reported by women, between 01:00 and 03:00 in both the preeclampsia group and the control group. However, the frequency of awakening between 01:00 and 03:00 was probably higher in the group of women with preeclampsia, which complicated the pregnancy in the third trimester, compared to women with a physiological gestation. Such a difference indicates discrepancies in the functional activity of the pineal gland between the examined groups. The near-normal endocrine activity of the pineal gland was noted in women with a normal pregnancy, whereas melatonin secretion was likely reduced in women with preeclampsia, as demonstrated below.

Women in study groups (both experimental and control), of course, used gadgets (electronic devices, mostly smartphones), but women with preeclampsia, which complicated the pregnancy in the 3rd trimester, probably more often (56.0 % vs. 13.3 % in the control group, $p < 0.01$) used gadgets for more than 2 hours after 9:00 p.m. Some studies indicate that the blue light emitted by a computer or gadget screen greatly suppresses the hormonal activity of the pineal gland [19]. In addition, pregnant women with preeclampsia, which complicated the pregnancy in the 3rd trimester, probably more often (in 62.0 % of cases, 31 out of 50 respondents) had energy-saving lamps of "white" light in the bed room at home, while pregnant women of the control group – only in 13.0 % of cases ($p < 0.01$).

The fact that pregnant women of the main group in 22.0 % of cases noted an improvement in sleep after hospitalization attracts our attention. Usually sleep normalized on the 3rd day after hospitalization, which was manifested by a decrease in the number of night awakenings (no more than 1 time per night) and the absence of complaints of "fatigue and tiredness" in the morning.

Regarding the determination of melatonin concentrations: in the results of the studies conducted, a significant decrease in melatonin concentrations was found in the blood of women whose pregnancy was complicated by preeclampsia in the 3rd trimester, compared to patients with an uncomplicated pregnancy.

As can be seen from **Fig. 1**, the level of melatonin in venous blood taken from women whose pregnancy was complicated by preeclampsia in the 3rd trimester was significantly lower, compared to healthy pregnant women: 31.0 pg/mL (95 % confidence interval for the mean value 19.8-42.2 pg/mL) against 55.2 pg/mL (95 % confidence interval for the mean value 36.2-74.2 pg/mL, $p = 0.029$). Thus, we can affirm that in the presence of such a complication of pregnancy as preeclampsia, the level of melatonin in the venous blood of women during pregnancy significantly decreases (1.8 times) compared to women with an uncomplicated pregnancy. As a reminder: the blood sampling was carried out at 9 a.m., when the activity of the pineal gland, according to some authors, was minimal.

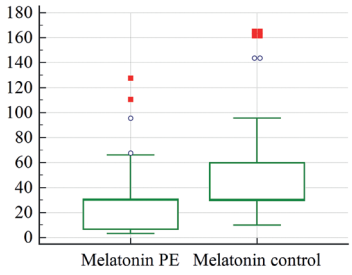

Fig. 1. Graphical comparison of melatonin concentrations in venous blood collected from pregnant women diagnosed with preeclampsia in the 3rd trimester (Melatonin PE) and control group with an uncomplicated pregnancy (Melatonin control).

It is known that the placenta actively produces melatonin starting from the early stages of pregnancy [19]. Thus, the appearance of complaints about insomnia in the second half of pregnancy, in our opinion, can serve as an early diagnostic sign of the formation of placental dysfunction, which is realized, in particular, in the form of preeclampsia in the 3rd trimester of pregnancy. In addition, there is no doubt about the presence of violations in the functioning of the pineal gland in pregnant women with preeclampsia, which was confirmed by our survey.

In the case of preeclampsia and associated placental dysfunction, there is insufficient synthesis of melatonin by the placenta. Given that the body's requirements for hormones, including melatonin, increase during pregnancy, these requirements should be covered, in our opinion, by a higher secretory activity of the pineal gland. This does not happen in the group of women with preeclampsia, as a result of which there is a higher frequency, compared to healthy pregnant women, of the complaints listed in **Table 1**, which is caused by poorer sleep quality. We believe that such a situation is caused, along with other factors, by pregnant women's non-observance of sleep hygiene, namely: the use of gadgets, the presence of energy-saving lamps in the room for sleeping, falling asleep late, the lack of an established bedtime routine (falling asleep at different times), etc.

The decrease in the level of melatonin in the blood of the pregnant women of the research group that we found is caused, in our opinion, by the manifestations of placental dysfunction, which accompany such a complication of pregnancy as preeclampsia in the 3rd trimester of pregnancy, and the appearance of which is caused by insufficient trophoblast invasion at the end of the first and the beginning of the second trimester of pregnancy. It is known that due to melatonin deficiency, the oxidative stress that accompanies preeclampsia increases, which leads to the appearance of a higher amount of circulating reactive oxygen species and reactive nitrogen species; both types of molecules play an important role as secondary messengers in many intracellular signaling cascades, but they can also have a critical impact on pathological processes occurring in the body of a pregnant woman [20]. In addition, studies have shown the stimulating effect of melatonin on the activity, growth, and differentiation of various types of stem cells, in particular, mesenchymal and neural [21], which is extremely important both for the growth and development of the fetus, primarily its nervous system, and for the recovery of mother's body after pregnancy and childbirth.

In modern regenerative medicine, possibilities of clinical application of placenta-derived stem cells are being actively researched [22]. The diagnosis of sleep disorders can be an additional marker for comprehensive scrutiny of the potential risks of further use of mesenchymal stem cells obtained from the placenta or decidua with the background of preeclampsia, as they can be damaged due to dysfunction of the niche of stem cells. This substantiates the relevance of further studies.

CONCLUSION

1. ***Sleep disorders in pregnant women with preeclampsia occur earlier and are more expressed compared to women with an uncomplicated pregnancy.***
2. ***The appearance of complaints of insomnia in the second trimester of pregnancy, in our opinion, can be considered a diagnostic sign of pineal gland dysfunction in preeclampsia.***
3. ***A decrease in the level of melatonin in pregnant women with preeclampsia, established against the background of minimal daily activity of the pineal gland (at 9 a.m.), indicates a decrease in the melatonin-producing function of the placenta which might have an impact on the condition of stem cells of fetus and placenta.***
4. ***Prospective for further research includes the study of the changes in melatonin concentrations during the day in pregnant women, in particular, in those whose pregnancy was complicated by preeclampsia, as well as in tracking the course of pregnancy, childbirth, and the state of the fetus in women, depending on the concentration of melatonin in their biological fluids, namely, saliva and blood.***

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Розлади сну та зміни концентрацій мелатоніну у вагітних з прееклампсією

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РЕЗЮМЕ

Мелатонін відіграє значну роль у перебігу нормальної вагітності, зокрема, сприяє успішній імплантації запліднені яйцеклітини, впливає на акт пологів, активно виробляється трофобластом і плацентою, знижує оксидативний стрес, зокрема, при прееклампсії. Крім того, мелатонін є одним із основних гормонів у захисті ендотелію та стовбурових клітин від оксидативного стресу.

***МЕТА РОБОТИ** – встановити механізми розвитку, терміни прояву та типи розладів сну, а також зміни концентрації мелатоніну в крові вагітних з прееклампсією.*

***МЕТОДИ.** Проведено обстеження 50-ти вагітних із середнім віком 29,1 ± 3,4 років з прееклампсією в III триместрі (дослідна група), які мали термін вагітності в межах 30-32 тижнів. Контрольну групу склали 33 жінки із середнім віком 31,2 ± 6,6 років, які мали неускладнений перебіг вагітності. Наявність розладів сну встановлювалася шляхом анкетування: вагітним ставилися питання про термін вагітності, в якому з'являлися скарги на порушення сну, характер розладів сну, частоту епізодів порушень сну (скільки разів на тиждень відмічався подібний стан) тощо. Концентрацію мелатоніну у венозній крові обстежених вагітних визначали методом ІФА. Кров брали о 9 годині ранку натщесерце, аналіз проводили всім пацієнтам в один і той же час доби.*

***РЕЗУЛЬТАТИ ТА ЇХ ОБГОВОРЕННЯ.** Анкетування показало, що розлади сну у вагітних з прееклампсією, що ускладнює перебіг вагітності в III триместрі, наступали раніше порівняно з жінками з неускладненим перебігом вагітності: вагітні з прееклампсією вірогідно частіше відмічали погіршення сну, починаючи з терміну вагітності 22-30 тижнів (у 26,0 % випадків), тоді як у вагітних з фізіологічним перебігом гестації подібні скарги з'являлися переважно після 30 тижнів. У третьому триместрі вагітності жінки з прееклампсією частіше прокидалися 2 і більше разів за ніч (у 68,0 % випадків) порівняно з контрольною групою (у 23,3 % випадків, $p < 0,001$) та 3 і більше разів за ніч за тиждень (у 54,0 % випадків, у контролі – у 16,7 % випадків, $p < 0,001$), що може бути наслідком порушення функції епіфіза. Жінки з прееклампсією частіше (56,0 % проти 13,3 % у контрольній групі, $p < 0,01$) користувалися гаджетами (електронними пристроями, переважно смартфонами) більше 2 годин після 21:00, що також негативно позначається на функції епіфіза. У вагітних жінок, чия вагітність ускладнилася прееклампсією в III триместрі, спостерігалося вірогідне (в 1,8 рази) зниження рівня мелатоніну у венозній крові, взятій о 9-й годині ранку, порівняно з жінками з неускладненим перебігом вагітності ($p = 0,029$).*

***ВИСНОВКИ.** Розлади сну у вагітних з прееклампсією виникають раніше і носять більш виражений характер порівняно з жінками з неускладненим перебігом гестації. Поява скарг на безсоння в другому триместрі вагітності, на нашу думку, може слугувати діагностичною ознакою дисфункції епіфіза при прееклампсії. Зниження рівня мелатоніну у вагітних з прееклампсією, встановлене на тлі мінімальної добової активності епіфіза (о 9-й годині ранку), свідчить про зниження мелатонін-продукуючої функції плаценти, що може впливати на стан стовбурових клітин плода і плаценти.*

***КЛЮЧОВІ СЛОВА:** вагітність; плацента; прееклампсія; епіфіз; мелатонін; розлади сну*