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The effect of vitamin D_3 deficiency and its correction on endothelial function in experimental preeclampsia

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Vitamin D_3, widely recognized for its key role in maintaining calcium-phosphate homeostasis, also has a multifaceted effect on the regulation of immune, inflammatory and vascular processes, including the maintenance of proper endothelial function. Disruption the endothelial regulation during pregnancy can lead to the development of serious complications, including preeclampsia and fetoplacental insufficiency. The aim of this study was to evaluate the effect of 25(OH)D_3 deficiency on endothelial function parameters in pregnant female rats and to determine its role in the development of endothelial dysfunction in physiological pregnancy and experimental preeclampsia. The experiment was conducted on 35 female Wistar rats divided into three groups: control, vitamin D_3 deficient, and vitamin D_3 deficient with cholecalciferol supplementation. PE was induced by L-NAME administration. The levels of 25(OH)D_3, endothelial nitric oxide synthase (eNOS), endothelin-1, nitric oxide (NO), malondialdehyde (MDA) and superoxide dismutase (SOD) were measured in serum and tissues. In rats with vitamin D_3 deficiency, there was a decrease in eNOS and NO levels, an increase in endothelin-1, and an increase in markers of oxidative stress. Vitamin D_3 supplementation partially restored these parameters, attenuated oxidative stress, and reduced vasoconstriction. Preeclampsia worsened endothelial dysfunction regardless of vitamin D_3 levels, but the changes were more pronounced in the deficient group. These results confirm the important role of vitamin D_3 in maintaining endothelial function during pregnancy and confirm its potential use in the prevention of vascular and placental complications.

Key words: vitamin D_3; oxidative stress; endothelial dysfunction; preeclampsia; pregnancy; pregnancy complications.

INTRODUCTION

Vitamin D_3 is a fat-soluble secosteroid hormone that is traditionally recognized for its role in maintaining calcium–phosphate homeostasis and ensuring normal bone mineralization and skeletal health [1, 2]. Its classical function involves regulating the intestinal absorption of calcium and phosphate, maintaining normal serum concentrations of these minerals, and supporting bone remodeling processes. However, over the past two decades, a substantial body of evidence has emerged demonstrating numerous extra-skeletal effects of vitamin D_3, encompassing a wide range of physiological processes [3, 4]. These include modulation of the immune system, regulation of inflammatory responses, effects on the cell cycle and apoptosis, as well as preservation of vascular endothelial function [5, 6]. Such properties make vitamin D_3 an important factor in maintaining systemic homeostasis and preventing the development of chronic inflammatory and vascular diseases.

The endothelium, which lines the inner surface of blood vessels, is a dynamic tissue performing multiple critical functions to sustain vascular homeostasis [7]. It regulates vascular tone through the synthesis of vasodilators, such as nitric oxide (NO), and vasoconstrictors, maintaining a balance between pro-inflammatory and anti-inflammatory signals. The endothelium also controls coagulation, vascular cell proliferation, and interactions with immune components. Impaired endothelial function is considered an early step in the development of vascular pathology, including arterial hypertension, atherosclerosis, and numerous complications associated with

altered blood flow [8, 9]. Endothelial function is of particular importance during pregnancy, when adequate vascular adaptation ensures optimal uteroplacental blood flow, which is essential for normal fetal development and the maintenance of gestation [10].

Vitamin D_3 deficiency during pregnancy has become the focus of intensive research due to its established association with an increased risk of gestational complications. In particular, low vitamin D_3 levels are associated with preeclampsia (PE), gestational diabetes, fetal growth restriction, preterm birth, and other obstetric complications [11, 12]. The main mechanisms are multifactorial and include a weakening of the vasoprotective effect of vitamin D_3, manifested in a decrease in the synthesis of NO, a key vasodilator and anti-inflammatory mediator in the vascular system [13]. In addition, vitamin D_3 deficiency contributes to oxidative stress, increases the production of active oxygen species that damage cell structures, and enhances the expression of pro-inflammatory cytokines, further impairing endothelial function [14].

Experimental animal models are used to better understand the pathogenic mechanisms of vitamin D_3 effect on endothelial function during pregnancy. Pregnant female rats are a widely used model due to their physiological and metabolic similarities to humans in terms of reproduction and vitamin D_3 metabolism [15]. These models allow the study of molecular and cellular vascular changes, including endothelial nitric oxide synthase (eNOS) activity, oxidative stress levels, and the expression of endothelial dysfunction markers under different vitamin D_3 conditions. Experimental studies have shown that vitamin D_3 deficiency reduces eNOS activity, leading to decreased NO production, impaired vasodilation, an imbalance of oxidants and antioxidants, and increased expression of pro-inflammatory markers and adhesion molecules — signs of endothelial dysfunction [16].

Given the high prevalence of vitamin D_3 deficiency among pregnant women worldwide and its potential impact on obstetric complications, particularly those related to vascular pathology, there is an urgent need for further research into the role of vitamin D_3 in regulating endothelial function during pregnancy. Such research will not only improve our understanding of the molecular mechanisms underlying pregnancy complications, but also contribute to the development of preventive and therapeutic strategies aimed at optimising vitamin D_3 levels to improve perinatal outcomes.

The aim of this study to determine the effect of 25(OH)D_3 deficiency on endothelial function parameters in pregnant female rats and to assess the role of impaired vitamin D_3 status in the development of endothelial dysfunction during normal pregnancy and under conditions of experimental preeclampsia.

METHODS

The study was carried out in accordance with the principles of bioethics and international regulations governing the care and use of laboratory animals (EU Directive 2010/63/EU and Commission Implementing Decision (EU) 2020/569), including the provisions of the European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes (Strasbourg, 1986), as well as the national guidelines "Bioethical Expertise of Preclinical and Other Scientific Research Conducted on Animals" (Kyiv, Ukraine, 2006). The study protocol was approved by the Bioethics Committee of Bogomolets National Medical University (Protocol No. 123 dated 04 November 2024).

A total of 35 female Wistar rats, aged 8 weeks with a mean body weight of 174 ± 12 g, were included in the study. Animals were housed in the vivarium under controlled environmental conditions (temperature 22 ± 2°C, relative humidity 55-60%, 12 h light/12 h dark cycle) with ad libitum access to standard chow and drinking water.

The females were randomly allocated into three experimental groups (Table 1): Group I (n = 10, control): received a standard laboratory diet containing vitamin D_3 throughout the

experiment. Group II (n = 12, vitamin D_3 deficiency): for 60 days prior to mating, were fed a rachitogenic diet (wheat flour – 89.5%, $CaCO_2$ – 3%, NaCl – 2%, dried brewer's yeast – 0.01%, vitamin A – 0.01%, vitamin E – 0.01%, water-soluble vitamins (Complevit) – 0.02%) completely devoid of vitamin D_3 to induce a deficient state. Group III (n = 13, vitamin D_3 supplementation): initially received the rachitogenic diet for 60 days, followed by transition to a standard diet supplemented with cholecalciferol ("Sigma", USA) at a dose of 1000 IU/kg body weight. The preparation was dissolved in sunflower oil and administered orally via gastric gavage at 0.2 ml once daily for 14 days prior to mating [17]. The limited sample size, although consistent with the principles of Directive 2010/63/EU and Commission Implementing Decision (EU) 2020/569 aimed at minimising the use of laboratory animals, inevitably limits the statistical significance of the analysis and increases the risk of error. Therefore, the conclusions presented should be considered preliminary [18].

To prevent endogenous synthesis of vitamin D_3, animals in Groups II and III were housed without access to direct sunlight. Vitamin D_3 deficiency was induced by feeding a rachitogenic diet for 60 days prior to mating. Serum 25-hydroxyvitamin D_3 [$25(OH)D_3$] concentrations were determined twice—before mating and at the end of the experiment. Blood samples were collected from the tail vein under light inhalation anesthesia. Quantification was performed using the General 25-Hydroxyvitamin D_3 ELISA kit (UNDL00047, "Assay Genie", USA), and sample concentrations were calculated with the Gain Data® software (arigo's ELISA Calculator).

Following the assessment of vitamin D_3 status, females were paired with sexually mature males at a ratio of 2:1 (male:female). The presence of spermatozoa in a vaginal smear the following morning was designated as gestational day 1 (GD1).

Within each dietary group, animals were further divided into two subgroups: Subgroup A – continued the assigned diet without additional interventions. Subgroup B – received Nω-nitro-L-arginine methyl ester (L-NAME) to induce preeclampsia-like features. L-NAME, a non-selective inhibitor of nitric oxide synthase, reduces the bioavailability of endogenous NO, causing systemic vasoconstriction, endothelial dysfunction, gestational hypertension, proteinuria, and foetal growth restriction — key features of preeclampsia in rats [19]. Initiation of treatment on gestational day (GD) 5 targets the period of implantation/early placentation, and exposure through GD15 coincides with spiral artery remodelling, thereby maximising the likelihood of developing a preeclampsia-like phenotype. We combined subcutaneous boluses (100 mg/kg on GD5 and GD7) to achieve rapid systemic inhibition of NOS with continuous administration in drinking water (40 mg/kg/day, GD5–GD15) to maintain a more stable effect while minimising the stress of manipulation and injection-related factors.

L-NAME is highly soluble in water and remains chemically stable in neutral aqueous solution at room temperature when protected from light. To ensure accurate dosing and avoid

Table 1. Experimental timeline for rat groups

Group	Days 0–60	Days 61–74	Days 75–78	Days 79–100	GD5–GD15
Control (Group I)	Standard diet	Vehicle treatment	Mating	Pregnancy	A B + L-NAME
D3 Hypovitaminosis (Group II)	Rachitogenic diet	Vehicle treatment	Mating	Pregnancy	A B + L-NAME
D3 Hypovitaminosis and Vitamin D3 (Group III)	Rachitogenic diet	Vitamin D_3 treatment	Mating	Pregnancy	A B + L-NAME

microbial growth, solutions were prepared fresh and replaced every 24 h, stored in light-protected bottles and kept at standard room temperature. The target concentration in water was adjusted based on the average daily intake and current body weight of pregnant rats, with verification of actual consumption to prevent under- or overdosing [19].

The concentration of nitric oxide (NO) in blood serum and total nitric oxide synthase (NOS) activity were assessed in blood samples collected at the end of the experiment. NO levels were measured using a commercial Nitric Oxide Assay Kit (MAK454, "Sigma-Aldrich", USA), while NOS activity was determined with a NOS Assay Kit (MAK532-1KT, "Sigma-Aldrich", USA), both according to the manufacturers' instructions. Antioxidant enzyme activity—superoxide dismutase (SOD)—and the concentration of malonic dialdehyde (MDA) were determined according to previously described methods [17]. Endothelin-1 (ET-1) levels were quantified using the Rat Endothelin-1 ELISA Kit (R1458, "Elabscience", USA) following the manufacturer's protocol.

Statistical analysis was performed using standard methods of variation statistics. For each parameter, the arithmetic mean (M) and the standard error of the mean (±m) were calculated. Distribution normality was assessed using the Shapiro–Wilk test. For comparison of more than two groups, one-way analysis of variance (ANOVA) was applied, followed by Bonferroni post hoc correction to account for multiple comparisons. For each significant intergroup difference, the mean difference (Δ) and its 95% confidence interval (95% CI) were calculated. In cases of non-normal data distribution, non-parametric alternatives were additionally considered to validate the results. Statistical significance was set at $P < 0.05$. All analyses were performed using Origin Lab software, version 8.5.

RESULTS

The results of our study demonstrate a significant impact of vitamin D_3 deficiency on endothelial function and oxidative stress parameters in pregnant female rats (Table 2). Vitamin D_3 status was assessed by serum 25-hydroxyvitamin D_3 [$25(OH)D_3$], a widely accepted biomarker of vitamin D_3 bioavailability.

In the D_3 hypovitaminosis group (II A), serum $25(OH)D_3$ concentrations were significantly lower than in controls (I A) by $\Delta = 32.8$ ng/ml; 95% CI 25.9–39.7; $P < 0.001$, confirming a marked deficiency. This finding aligns with prior evidence linking low vitamin D_3 during gestation to dysregulated calcium-phosphate metabolism, impaired NO synthesis, and elevated preeclampsia risk.

Vitamin D_3 supplementation (III A) effectively restored $25(OH)D_3$ levels in deficient rats, increasing them by roughly 1.5-fold compared with the hypovitaminosis group (II A). In III B, where preeclampsia was induced, $25(OH)D_3$ declined slightly, by about 15% compared with III A, likely reflecting increased metabolic consumption during systemic inflammatory activation. Similarly, in the control preeclampsia group (I B), $25(OH)D_3$ decreased by $\Delta = 9.0$ ng/ml; 95% CI 2.1–15.9; $P < 0.05$ vs I A, indicating that preeclampsia adversely affects vitamin D_3 status independently of baseline sufficiency.

Endothelial nitric oxide synthase activity in D_3 hypovitaminosis rats (II A) was reduced by $\Delta = 17.6$ a.u.; 95% CI 8.2–27.0; $P = 0.002$ vs I A, signifying impaired NO-mediated vasodilation and endothelial dysfunction. Mechanistically, vitamin D_3 deficiency downregulates eNOS expression and disrupts calcium-calmodulin signaling, decreasing NO production. Correction of vitamin D_3 deficiency (III A) partially restored eNOS activity ($P = 0.01$ vs II A). In III B, preeclampsia reduced eNOS by $\Delta = 21.3$ a.u.; 95% CI 10.1–32.5; $P < 0.05$ vs III A, indicating persistent endothelial impairment despite sufficient vitamin D_3. Similarly, in the control preeclampsia group (I B), eNOS declined by $\Delta = 20.5$ a.u.; 95% CI 10.2–30.8; $P < 0.05$ vs I A, highlighting the systemic impact of preeclampsia on vascular tone.

Endothelin-1 a potent vasoconstrictor, was

Table 2. Biochemical parameters and markers of endothelial function in the study groups

Indicator	Control(Group I; n = 10)		D_3 Hypovitaminosis (Group II; n = 12)	D_3 Hypovitaminosis and Vitamin D_3 (Group III; n = 13)	
	without preeclampsia (I A; n = 5)	preeclampsia (I B; n = 5)	without preeclampsia (II A; n = 6)	without preeclampsia (III A; n = 7)	preeclampsia (III B; n = 6)
25(OH)D_3, ng/ml	49.8 ± 2,6	40.8 ± 3.7*	17.0 ± 1.1	35.3 ± 2.2**	30.5 ± 1.2*,**
Endothelial nitric oxide synthase, a.u.	72.8 ± 4.8	52.3 ± 3.7*	55.2 ± 4.3	68.4 ± 5.0**	47.1 ± 4.5*,**
Endothelin-1, pg/ml	54.1 ± 4.6	87.4 ± 7.2*	78.5 ± 6.7	60.3 ± 5.8**	98.7 ± 8.3*,**
Nitric oxide, μmol/l	37.9 ± 3,4	26.0 ± 2.1 *	28.7 ± 2.4	35.4 ± 3.0**	22.8 ± 2.2* **
Malonic dialdehyde, nmol/ml	2.7 ± 0.3	4.4 ± 0.4*	3.5 ± 0.3	2.9 ± 0.4**	5.1 ± 0.5*,**
Superoxide dismutase, U/mg protein	20.7 ± 1.3	14.6 ± 1.0*	15.8 ± 1.2	19.4 ± 1.5**	13.5 ± 1.1*,**

Note: *statistically significant difference compared to control Group I A, $P < 0.05$; **statistically significant difference compared to Group II A, $P < 0.05$.

elevated in D_3 hypovitaminosis rats (II A) by Δ = 24.4 pg/ml; 95% CI 10.3–38.5; P = 0.004 vs I A, suggesting a compensatory vasoconstrictive shift. Vitamin D_3 supplementation (III A) partially normalized ET-1 levels, reducing them by nearly one-third compared with the hypovitaminosis group (II A). Preeclampsia markedly increased ET-1 in III B to more than twice the level of the supplemented group, and in I B to approximately twice the level of controls, reflecting progressive endothelial dysfunction.

NO levels were significantly reduced in D_3 hypovitaminosis rats (II A) by Δ = 9.2 μmol/l; 95% CI 4.3–14.1; P = 0.01 vs I A. Correction of vitamin D_3 partially restored NO levels, whereas preeclampsia caused a marked reduction in NO in both the supplemented group (III B) and the control preeclampsia group (I B), lowering levels to roughly half of the normal values. These results underscore NO critical role in maintaining vascular homeostasis during gestation.

Oxidative stress, a pivotal pathogenic mechanism in preeclampsia and vitamin D_3 deficiency, was quantified by malonic dialdehyde levels, an indicator of lipid peroxidation, and by superoxide dismutase activity, reflecting the enzymatic neutralization of reactive oxygen species. Malonic dialdehyde a marker of lipid peroxidation, was elevated in D_3 hypovitaminosis rats (II A) by Δ = 0.8 nmol/ml; 95% CI 0.3–1.3; P = 0.02 vs I A. In rats with vitamin D_3 deficiency, supplementation led to a reduction in MDA levels, whereas in the preeclampsia group with supplementation MDA increased again; a similar rise was observed in the control preeclampsia group, indicating enhanced lipid peroxidation under pathological conditions.

Superoxide dismutase activity was decreased in D_3 hypovitaminosis rats (II A) by Δ = 5.0 u/mg; 95% CI 2.6–7.4; P = 0.005 vs I A. Vitamin D_3 supplementation increased SOD (P = 0.01 vs II A), whereas preeclampsia reduced it in III B and in I B. In general, decreased SOD activity combined with elevated MDA levels indicates insufficient antioxidant protection and increased formation of reactive oxygen species, which

contributes to endothelial dysfunction, eNOS inhibition, and excessive ET-1 production.

DISCUSSION

This study demonstrates that vitamin D_3 deficiency significantly impairs endothelial function in pregnant Wistar rats, manifested by decreased endothelial nitric oxide synthase activity and nitric oxide levels, accompanied by increased concentrations of the vasoconstrictor endothelin-1. These changes disrupt vascular tone, contributing to the development of hypertension and vascular dysfunction, which are key pathogenic mechanisms of preeclampsia [19, 20]. Elevated MDA levels and decreased SOD activity in vitamin D_3 deficiency indicate increased oxidative stress, which further damages the endothelium and creates favourable conditions for vascular complications [21]. These results suggest that vitamin D_3 is a critical modulator of vascular homeostasis during pregnancy, and its deficiency causes both functional and structural vascular disorders.

Vitamin D_3 supplements in this study improved key parameters of endothelial function. In particular, they increased eNOS activity and NO production, decreased endothelin-1 concentration, reduced MDA lipid peroxidation, and enhanced SOD activity. This highlights the key role of optimal vitamin D_3 levels in maintaining endothelial integrity and preventing oxidative stress during pregnancy. The observed protective effects are consistent with data from Ma et al. [22], who reported that vitamin D_3 treatment of rats with LPS-induced preeclampsia significantly reduced blood pressure and proteinuria in mothers, improved placental morphology and cognitive abilities in offspring. In addition, vitamin D_3 inhibited the toll-like receptor 4/ nuclear factor kappa-light-chain-enhancer of activated B cells (TLR4/NF-κB) signalling pathway in the placenta, indicating a combined endothelial and anti-inflammatory effect.

Comparisons with other recent studies provide a broader picture of the role of vitamin D_3 during pregnancy and preeclampsia. Poniedziałek-Czajkowska et al. [23] highlighted the preventive potential of vitamin D_3 against preeclampsia, emphasising its effect on placental implantation, regulation of angiogenic factors, and immune modulation. Similarly, Nema et al. [24] demonstrated that prenatal vitamin D_3 supplementation normalized vascular endothelial growth factor (VEGF) and Fms-like tyrosine kinase-1 (Flt-1) levels in the placenta and attenuated hypertension in experimental models of preeclampsia, suggesting an influence of vitamin D_3 on both maternal vascular function and placental angiogenesis. These studies support the conclusion that vitamin D_3 plays a multifaceted role in maintaining vascular homeostasis and alleviating the severity of preeclampsia.

However, some studies report conflicting results. Ali et al. [25] found that vitamin D_3 deficiency in pregnant rats did not cause classic signs of preeclampsia, such as elevated blood pressure or proteinuria, nor did it affect the mother's angiogenic or vasculogenic factors. These discrepancies can be explained by differences in experimental models, the duration and severity of vitamin D_3 deficiency, the genetic background of the animals, or the presence of additional stressors and inflammatory factors. Such differences emphasise the context-dependent nature of vitamin D_3 effect on preeclampsia development, indicating that deficiency alone may not always be sufficient to cause the full spectrum of pathological changes associated with preeclampsia.

From a pathogenetic aspect, it is believed that vitamin D_3 deficiency causes an imbalance between mediators that dilate and constrict blood vessels. A decrease in eNOS and NO levels limits endothelial vasodilation, while an increase in endothelin-1 levels enhances vasoconstriction. At the same time, oxidative stress is exacerbated by a decrease in antioxidant defence, reflected in a decrease in SOD activity and an increase in MDA levels. These changes are associated with endothelial dysfunction, placental hypoperfusion, and vascular inflammation. In addition,

vitamin D_3 deficiency may potentiate proinflammatory signals via the TLR4/NF-κB pathway, leading to increased levels of cytokines such as TNF-α, IL-6, and IL-1β, which further impair endothelial function [26]. Conversely, vitamin D_3 supplementation appears to modulate these pathways by enhancing anti-inflammatory and antioxidant mechanisms, restoring eNOS activity, and promoting the expression of angiogenic factors (VEGF, PlGF), thereby providing a comprehensive protective effect on the maternal vascular system and placental function.

An important aspect of this study is that even with vitamin D_3 supplementation, the presence of experimental preeclampsia induced by L-NAME led to severe endothelial dysfunction and redox imbalance [24]. This indicates that although vitamin D_3 has a protective effect, severe pathological stress factors may outweigh its ability, highlighting the multifactorial and complex nature of preeclampsia. Importantly, the complete lack of survival in the group with combined vitamin D_3 deficiency and preeclampsia highlights the synergistic toxicity of these factors, illustrating that vitamin D_3 deficiency may exacerbate disease severity in the presence of additional stressors.

The results of the study are also consistent with epidemiological data linking vitamin D_3 deficiency in mothers with an increased risk of preeclampsia and adverse pregnancy outcomes. Observational studies show that low vitamin D_3 levels in mothers are associated with placental development disorders, increased inflammation, and an increased incidence of hypertensive disorders during pregnancy [23]. Recent experimental data obtained using this model confirm the view that maintaining adequate vitamin D_3 levels is important not only for the mother's blood vessels, but also for normal placental function and fetal growth.

Despite the convincing results, this study has some limitations. The sample size was relatively small, which may affect the statistical significance and generalisability of the results. In addition, only one experimental model of preeclampsia was used, limiting the ability to extrapolate the results to other forms of the disease. The period and timing of vitamin D_3 deficiency and supplementation may also influence the results, requiring further investigation in future studies. Furthermore, molecular targets of oxidative stress and inflammation, such as nicotinamide adenine dinucleotide phosphate (NADPH) oxidase or specific cytokine signalling pathways, were not explored in detail, which could provide additional knowledge.

Future research directions should include: Dose-response studies to determine optimal levels of vitamin D_3 supplementation for vascular and placental protection in various preeclampsia models. Longitudinal studies evaluating the impact of vitamin D_3 levels prior to conception and throughout pregnancy on maternal, placental, and foetal outcomes. Molecular studies of the TLR4/NF-κB and VEGF/PlGF signalling pathways, as well as interactions with oxidative stress mediators and immune responses. Multimodal preeclampsia models combining vitamin D_3 deficiency with other risk factors, such as inflammation or metabolic disorders, to better model the disease in humans. Translational studies to assess whether maternal vitamin D_3 supplementation can prevent or mitigate preeclampsia in humans, including randomised controlled trials stratified by baseline vitamin D_3 status.

CONCLUSIONS

Vitamin D_3 deficiency in pregnant Wistar rats was associated with a significant decrease in plasma $25(OH)D_3$ concentration and the development of severe endothelial dysfunction. Endothelial dysfunction in vitamin D_3 deficiency was manifested by decreased eNOS activity, decreased NO levels, increased endothelin-1 concentration, and impaired oxidative-antioxidant balance, namely increased MDA levels and decreased SOD activity. Cholecalciferol supplements increased plasma $25(OH)D_3$ levels to 35.3 ± 2.2 ng/ml, restored

eNOS activity, and partially alleviated oxidative stress, confirming the important role of optimal vitamin D_3 levels in maintaining vascular function during pregnancy. In experimental preeclampsia, even with vitamin D_3 supplementation, severe endothelial dysfunction persisted, characterised by decreased eNOS activity and increased endothelin-1 levels. These results demonstrate the multifactorial nature of vascular damage and the limited compensatory potential of vitamin D_3 therapy in severe pregnancy pathology.

From a clinical perspective, these findings underscore the importance of maintaining optimal vitamin D_3 levels during pregnancy to preserve endothelial function, maintain the balance between vasodilatory and vasoconstrictive pathways, and counteract oxidative stress—key pathogenic mechanisms underlying preeclampsia. Timely assessment and correction of vitamin D_3 deficiency may serve as an effective preventive and therapeutic strategy to reduce the risk of severe pregnancy complications, including endothelial dysfunction, impaired uterine and placental perfusion, and fetal growth restriction. Furthermore, these findings provide a pathogenetic rationale for the development of scientifically sound clinical protocols for monitoring and individualized vitamin D_3 supplementation in pregnant women, especially those at high risk, in order to optimise maternal and fetal vascular function and reduce the incidence of preeclampsia and related vascular complications.

The authors of this study confirm that the research and publication of the results were not associated with any conflicts regarding commercial or financial relations, relations with organizations and/or individuals who may have been related to the study, and interrelations of co-authors of the article.

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ВПЛИВ ДЕФІЦИТУ ВІТАМІНУ D_3 ТА ЙОГО КОРЕКЦІЇ НА ЕНДОТЕЛІАЛЬНУ ФУНКЦІЮ ПРИ ЕКСПЕРИМЕНТАЛЬНІЙ ПРЕЕКЛАМПСІЇ

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Вітамін D_3 бере участь у регуляції кальцієво-фосфорного обміну та чинить багатоаспектний вплив на імунні та запальні механізми, сприяючи підтриманню нормальної функції судинного ендотелію. Порушення ендотеліальної регуляції під час вагітності здатне спричиняти розвиток тяжких ускладнень, включно з прееклампсією та фетоплацентарною недостатністю. Метою нашого дослідження було оцінити вплив дефіциту $25(OH)D_3$ на параметри ендотеліальної функції у вагітних самиць щурів і визначити його роль у формуванні ендотеліальної дисфункції за фізіологічної вагітності та за умов експериментальної прееклампсії. Експеримент проведено на 35 самицях щурів Вістар, розподілених на три групи: контроль, гіповітаміноз D_3 та гіповітаміноз із корекцією холекальциферолом. Прееклампсію моделювали введенням L-NAME. Визначали вміст $25(OH)D_3$, активність ендотеліальної NO-синтази (eNOS), вміст ендотеліну-1, NO, малонового діальдегіду та супероксиддисмутади у плазмі та тканинах. У щурів з дефіцитом вітаміну D_3 знижувався вміст NO,активність eNOS , підвищувався вміст ендотеліну-1, а також спостерігалися ознаки оксидативного стресу. Корекція вітаміном D_3 частково відновлювала показники, зменшувала оксидативний стрес і вазоконстрикцію. Прееклампсія поглиблювала ендотеліальні порушення незалежно від вмісту вітаміну D_3 проте у разі дефіциту зміни були значно вираженими. Отримані результати підтверджують важливу роль вітаміну D_3 у збереженні ендотеліальної функції під час вагітності та обґрунтовують його використання для профілактики судинних і плацентарних ускладнень.

Ключові слова: вітамін D_3; оксидативний стрес; ендотеліальна дисфункція; прееклампсія; вагітність; ускладнення вагітності.

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