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Research of lipid metabolism disorders in female combatants

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The objective: to find out the peculiarities of stress-induced changes in lipid metabolism indicators in women who have experienced concussion during combat operations. Study the state and morphostructure of adipose tissue. To analyze the relationship between lipid metabolism disorders and changes in reproductive health of female combatants.

Materials and methods. The research was conducted at the Department of Obstetrics, Gynecology and Reproductology of the Ukrainian State Institute of Reproductology of the Shupyk National Healthcare University. 118 women participated in the study. Group I consisted of examination data of women who suffered concussion during combat operations with PTSD, group II – control, it consisted of healthy women. Average age of women who participated in hostilities and suffered contusion 27.08±4.23 years.

Results. The influence of stress factors associated with military service in women servicemen on the development of lipid metabolism disorders is obvious. In the main group (118 women), blood cholesterol levels were significantly higher than in the control group. In parallel, a very low level of anti-atherogenic lipoprotein fractions was detected. Lipid metabolism in women who experienced concussion during combat with PTS was characterized by a high frequency of hyperlipidemia of types IIa and IIb, higher serum concentrations of atherogenic lipids fractions (CL, CL-LDL) and low anti-atherogenic fractions (CL-HDL), which were observed in all age subgroups and progressed with age.

Conclusions. As a result of lipid metabolic disorders, the prerequisites for the development of hyperproliferative diseases of the female reproductive system, early and severe atherosclerosis are created.

Keywords: reproductive system, women veterans, contusion, PTSD, carbohydrate metabolism, lipid metabolism disorders.

Дослідження порушень ліпідного обміну у жінок-учасниць бойових дій *A.B. Сербенюк*

Мета дослідження: з'ясувати особливості стресіндукованих змін показників ліпідного обміну у жінок, що зазнали контузії під час бойових дій, стан та морфоструктуру жирової тканини. Проаналізувати взаємозв'язок між порушеннями ліпідного обміну та змінами репродуктивного здоров'я жінок-учасниць бойових дій.

Матеріали та методи. У дослідженні взяли участь 118 жінок. До І групи увійшли дані 82 обстежених жінок, що зазнали контузії під час бойових дій, з ПТС, до ІІ групи (контрольної) — 36 здорових жінок. Середній вік пацієнток, що брали участь у бойових діях та зазнали контузії, становив 27,08±4,23 року.

Результати. Вплив стрес-факторів, пов'язаних з військовою службою, у жінок-віськовослужбовиць на розвиток порушень ліпідного обміну очевидний. В основній групі рівень холестерину в крові був значно вище, ніж у контрольній групі. Паралельно з цим виявлено дуже низький рівень антиатерогенних фракцій ліпопротеїнів. Стан ліпідного обміну у жінок з ПТС, що зазнали контузії під час бойових дій, характеризувався високою частотою гіперліпідемії Па та Пб типів, вищими показниками вмісту у сироватці крові атерогенних фракцій ліпідів (ХС, ХС-ЛПНШ) та низькими показниками антиатерогенних фракцій (ХС-ЛПВШ), які спостерігалися у всіх вікових підгрупах і прогресували з віком. Висновки. Внаслідок порушень ліпідного обміну створюються передумови для розвитку гіперпроліферативних захворювань жіночої репродуктивної системи, раннього та тяжкого перебігу атеросклерозу.

Ключові слова: репродуктивне здоров'я, жінки-ветеранки, контузія, посттравматичний стресовий розлад, вуглеводний обмін, порушення ліпідного обміну.

Prolonged stress resulting from adverse environmental factors or psycho-emotional stress can cause the development of pathological processes. Chronic psycho-emotional stress in female combatants develops as a result of the continuous or periodic action of stress factors that have arisen as a result of military service. Stress provokes changes not only in mental, but also in physical health. Women veterans develop menstrual disorders (menstrual irregularities, secondary amenorrhea, hypomenstrual syndrome, acyclic uterine bleeding), carbohydrate metabolic disorders (impaired glucose tolerance, impaired fasting glycemia, type II diabetes mellitus). Changes in lipid metabolism indicators are also typical outcomes of the stress influence.

After exposure to stressors, early (increased levels of lipidoproteins, triglycerides) and remote consequences manifested by metabolic disorders develop. Chronic psycho-emotional stress causes prolonged lipid peroxidation, activation of lipases and phospholipases, determine high cholesterol levels. The main plasma lipids are free fatty acids, triglycerides, phospholipids and cholesterol esters. Lipids are part of cell membranes and are also the main source of energy, solvents of vitamins, and are involved in the synthesis of steroid hormones. Disruption of lipid metabolism leads to changes in their functions and the development of pathological processes, such as: dislipoproteinemia (DLP), hyperlipoproteinemia and

АКТУАЛЬНІ ТЕМИ

hyperlipidemia. Dyslipidemia includes an increase in lipids and lipoproteins, as well as possible reductions in high-density lipoproteins (HDL). Hyperlipidemia (HLP) is characterized by an increase in blood lipids (cholesterol and triglycerides) above optimal values.

To characterize the HLP, the classification by D. Fredrickson is used:

- Phenotype I is characterized by an isolated increase in chylomicrons (one of the lipoprotein species). This HLP phenotype is rarely observed and is usually not associated with the development of pathological processes in the body;
- 2. Phenotype IIa shows an increase in LDL and CL concentration, TG level is within the normal range. This phenotype is quite common, it is associated with the development of atherosclerosis;
- 3. Phenotype IIb is characterized by an increase in the concentration of LDL and LDLD, sometimes determine elevated levels of CL and TG, this is an atherogenic type;
- 4. Phenotype III is manifested by an increase in intermediate density lipid proteins (IDLP), CL and TG. It is usually found in metabolic disorders, in particular in metabolic syndrome and diabetes mellitus;
- 5. Phenotype IV is characterized by an increase in the concentration of LDLD and hypertriglyceridemia. This type of dyslipidemias is found in 40% of patients with lipid metabolism disorders.

An essential role belongs to the influence of stress, as one of the causes of the development of metabolic disorders with the subsequent development of obesity, which are risk factors for the development of hyperplastic processes of the endometrium and cancer of the female genital organs.

Estrogens are synthesized in the ovaries and adipose tissue, the substrate for their synthesis is CL and LDL. Most of the estrogens bind to proteins and only a small part of the estrogens are in the free state. Due to the influence of chronic stress factor, CL and LDL cannot be adequately used for the synthesis of estrogens, which, accordingly, leads to an increase in their level in the blood with a subsequent increase in adipose tissue in women. Adipose tissue accumulates female sex hormones in the body. The reason for this is that adipose tissue contains a large amount of aromatase, which converts adrenal androgens into estrogens. Modern evidence suggests that women combatants are more likely to develop hyperplastic processes that are directly associated with impaired lipid metabolism.

The objective: to find out the peculiarities of stressinduced changes in lipid metabolism indicators in women who have experienced concussion during combat operations. Study the state and morphostructure of adipose tissue. To analyze the relationship between lipid metabolism disorders and changes in reproductive health of female combatants.

MATERIALS AND METHODS

The research was conducted at the Department of Obstetrics, Gynecology and Reproductology of the Ukrainian State Institute of Reproductology of the Shupyk National Healthcare University. 118 women participated in the study. Group I consisted of examination data of women who suffered concussion during combat operations with PTSD, group II – control, it consisted of healthy women. Average age of women who participated in hostilities and suffered contusion 27.08±4.23 years.

To achieve this goal, a comprehensive clinical and laboratory examination was carried out. Complaints, obstetric and gynecological and somatic history were studied in detail when examining women. Height, body weight, circumference of waist, hips and hands, determination of body mass index were carried out. The state of the lipid profile was studied, determination of: total cholesterol: (LDL, HDL, LDLD), CL, TG.

Laboratory methods: studies of LDL, HDL, LDLD, triglycerides. The examination was carried out according to generally accepted rules. The examination was carried out according to generally accepted rules. Venous blood was sampled on the empty stomach, fatty food was excluded from the diet the day before sampling.

Based on data on total cholesterol and HDL, an atherogenic index (AI) is calculated, an indicator that enables to establish lipid metabolic disorders. This indicator is considered a key criterion in the assessment of lipid-lowering therapy. Calculation of AI: high-density lipoproteins are subtracted from the total cholesterol, and then divided by their amount; AI = (CL – HDL) / HDL. The higher the index is, the higher is the risk of developing atherosclerosis and the more significant disorders of lipid metabolism.

Symptoms of the effects of concussion at the time of examination were determined by the Cicero questionnaire. At the same time, patients performed self-assessment of their own symptoms in view of the present. For PTSD screening, a PCL-m (Military Version) questionnaire was used. The study of the state of vegetative regulation was carried out by filling out a questionnaire for the subjective assessment of dystonia (according to the questionnaire of A.M. Wein, 1998).

Statistical processing of the research results was performed using Statistica 6.0 software package and Microsoft Office software package using standard descriptive statistics methods (Mintzer O.P., 2016).

RESULTS AND DISCUSSION

The state of lipid metabolism was studied in 118 women, 82 women who experienced concussion during combat operations with PTSD and 36 women from the comparison group. The content of CL in patients with PTS at all ages was significantly higher than in the comparison group.

At the age of 25 mmol/L 45 years, the level of cholesterol in group I was 4.52 ± 0.02 mmol/L (in group II -3.62 ± 0.74 mmol/L; p=0.007); at the age of 46-55-4.83*1.22 mmol/L (in group II -2.62 ± 0.59 mmol/L; p<0.001; at the age over 55 years -4.72*0.64 mmol/L (in group II -4.41*0.37 mmol/L; p<0.001).

33*0.81 mmol/L (p=0.008), no statistically significant difference was found between the groups for the other age subgroups. In group I, CL-HDL were significantly lower than in group II: 25-46 years -1.01 ± 0.27 and 1.43*0.82 mmol/L (p=0.021); in women over 55

АКТУАЛЬНІ ТЕМИ

Lipid metabolism disorders in women

Type of hyperlipidemia	Group	Aged 26-45	Aged 46-55	Aged >55	P (age)
		Abs (%)	Abs (%)	Abs (%)	
lla	I	8 (27,6)	9 (25,7)	2 (11,1)	0,384
	II	0	1 (8.3)	1 (8.3)	0.589
Р		0,024	0,115	0,402	
IIb	I	10 (44,8)	20 (57,1)	14(77,8)	0,013
	II	0	0	2(16.7)	0.336
Р		0,004	<0,001	<0,001	
Norm	I	8 (27,6)	6 (17,1)	2 (11,1)	0,343
	II	12 (100)	11 (91,7)	9 (75,0)	0,140
Р		<0,001	<0,001	<0,001	

Page: influence of age on the incidence of hyperlipidemia.

years -0.83 ± 0.16 mmol/L and 1.18 ± 0.09 mmol/L (p<0.001). In women aged $26-45-2.55\pm0.66$ mmol/L and 1.6 ± 0.4 mmol/L; aged $46-55-3.11\pm1.04$ and 1.8 ± 0.8 mmol/L; in patients over 55 years old -2.7 ± 0.33 and 1.9 ± 0.09 mmol/L, respectively (p<0.001). The levels of CL - LDLD were not statistically significantly different between the groups of all ages.

AI in women of group I was also significantly higher at all ages than in group II: in women aged $26-45-3.51\pm1.92$ and 1.57 ± 0.41 mmol/L (p=0.001); 46-55 years old -3.53 ± 1.53 and 2.30 ± 0.81 mmol/L (p=0.010); in women over 55 years -4.88 ± 1.39 and 3.40 ± 0.62 mmol/L (p<0.001). In group I, there was a statistically significant influence of the patient's age on the following indicators of lipid metabolism: CL-HDL (p<0.001), CL-LDL (p=0.013) and AI (p=0.009); in group II: on the content of CL (p = 0.005), LDL-C (p = 0.002) and Ka (p<0.001). In the group was 4.52 ± 1.02 mmol/L (group II -3.62 ± 0.74 mmol/L; p=0.007).

In women of group I aged over 55, there was a statistically significant increase in AI (p<0.001), mainly due to an increase in CL (p=0.005), an increase in TG (p<0.001), CL-LDL (p=0.013) compared to women aged 26–45. In group II, women over 55 years old demonstrated a significant increase in CL-LDLD (p=0.009) and AI (p=0.009) compared to women aged 26–45, mainly due to a decrease in CL-HDL (p<0.001). The conducted studies show that normal indicators of lipid metabolism were observed in Group I much less frequently than in Group II (p<0.001) (Table).

In patients of group I aged 26–45, type II hyperlipidemia was found in 27.6%, in group II it was absent. Hyperlipidemia of type IIb in women of group I was observed significantly more often than in group II in all age groups. Group I participants demonstrated a statistically significant correlation between age and the development of type II hyperlipidemia (p=0,013). In group II, the impact of age on the frequency and nature of lipid metabolism disorders was not significant (RC >0.05).

CONCLUSIONS

The influence of stress factors associated with military service in women servicemen on the development of lipid metabolism disorders is obvious. In the main group (118 women), blood cholesterol levels were significantly higher than in the control group. In parallel, a very low level of anti-atherogenic lipoprotein fractions was detected.

Lipid metabolism in women who experienced concussion during combat with PTS was characterized by a high frequency of hyperlipidemia of types IIa and IIb, higher serum concentrations of atherogenic lipids fractions (CL, CL-LDL) and low anti-atherogenic fractions (CL-HDL), which were observed in all age subgroups and progressed with age.

As a result of these lipid metabolic disorders, the prerequisites for the development of hyperproliferative diseases of the female reproductive system, early and severe atherosclerosis are created.

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АКТУАЛЬНІ ТЕМИ

REFERENCES

- 1. Menegetti A. Psikhosomatika. Moskva: NF «Antonio Manegetti»; 2015. 334 p.
- 2. Dubossarskaya ZM, Dubossarskaya YUA. Metabolicheskiy sindrom i ginekologicheskiye zabolevaniya. Medix Anti-Aging. 2009;2(8):42-51.
- 3. Astahov VM, Batsyileva OV, Puz IV. Psihodiagnostika v reproduktivnoy medit-sine. Vinnitsa: OOO Nilan-LTD; 2016. 380 p.
- World Health Organization WHO Consultation: definition, diagnosis and classification of diabetes mellitus and its complications: Report of a WHO Consultation. Part I: Diagnosis and classification of diabetes mellitus [Internet]. Geneva: WHO; 1999. 59 p. Available from: https://apps.who.int/iris/handle/ 10665/66040
- American Diabetes Association; American Diabetes Association Professional Practice Committee; Draznin B, Aroda VR, Bakris G, Benson G, et al. Comprehensive Medical Evaluation and Assessment of Comorbidities: Standards of Medical Care in Diabetes. Diabetes Care. 2018;41(Suppl.1):28-37.
- 6. American Diabetes Association. Introduction: Standards of Medical Care in Diabetes. Diabetes Care.2019;42(Suppl.1):46-60. doi: 10.2337/dc22-Sint.
- 7. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders: DSM-5 [Internet]. American Psychiatric Association; 2013. Available from: https://dsm.psychiatryonline.org/doi/epdf/10.1176/appi.book s.9780890425596.

- 8. Avogaro P, Crepaldi G, Enzi G, Tiengo A. Metabolic aspects of essential obesity. Epatologia. 1965;11(3):226-23.
- 9. Bader JE, Enos RT, Velázquez KT, Carson MS, Sougiannis AT, McGuinness OP, et al. Repeated clodronate-liposome treatment results in neutrophilia and is not effective in limiting obesity-linked metabolic impairments. Am J Physiol Endocrinol Metab. 2019;316:E358-E372. doi: 10.1152/aipendo.00438.2018.
- 10. Chen J, Yu J. Sex Differences in Genetic and Environmental Influences on Adolescent Depressive Symptoms: A Meta-Analytic Review. Depress Res Treat. 2015;2015:476238. doi: 10.1155/2015/476238.
- 11. Dessì A, Marincola FC, Fanos V. Metabolomics and the great obstetrical syndromes-GDM, PET, and IUGR. Best Pract Res Clin Obstet Gynaecol. 2015;29(2):156-64. doi: 10.1016/j.bpobgyn.2014.04.023.
- 12. Druz OB, Syropiatov OH, Badiuk ML, et al. Udoskonalennia likuvannia ta reabilitatsiiviis ko vo sluzhbov tsiv Zbroinykh Syl Ukrainy iz boiovoiu psykhichnoiu travmoiu: metodychni rekomendatsii. Kyiv: MP Lesia; 2015. 52 p.
- 13. Dunlop BW, Rothbaum BO, Binder EB, Duncan E, Harvey PD, Jovanovic T, et al. Evaluation of a corticotropin releasing hormone type 1 receptor antagonist in women with posttraumatic stress disorder: study protocol for a randomized controlled trial. Trials. 2014;15:240. doi: 10.1186/1745-6215-15-240.
- 14. Guffanti G, Galea S, Yan L, Roberts AL, Solovieff N, Aiello AE, et al. Genome-

- wide association study implicates a novel RNA gene, the lincRNA AC068718.1, as a risk factor for post-traumatic stress disorder in women. Psychoneuroendocrinol. 2013;38(12):3029-38. doi: 10.1016/j. psyneuen.2013. 08.014.
- 15. Hyde CL, Nagle MW, Tian C, Chen X, Paciga SA, Wendland JR, et al. Identification of 15 genetic loci associated with risk of major depression in individuals of European descent. Nat Genet. 2016;48(9):1031-6. doi: 10.1038/ng.3623.
- 16. Karam EG, Friedman MJ, Hill ED, Kessler RC, McLaughlin KA, Petukhova M, et al. Cumulative traumas and risk thresholds: 12-month PTSD in the World Mental Health (WMH) surveys. Depress. Anxiety. 2014;31(2):130-42. doi: 10.1002/da.22169.
- 17. Lai Q, Xiang W, Li Q, Zhang H, Li Y, Zhu G, et al. Oxidative stress in granulosa cells contributes to poor oocyte quality and IVF-ET outcomes in women with polycystic ovary syndrome. Front Med. 2018;12(5):518-24. doi: 10.1007/s11 684-017-0575-y.
- 18. Mallinson RJ, De Souza MJ. Current perspectives on the etiology and manifestation of the «silent» component of the Female Athlete Triad. Int J Womens Health. 2014;6:451-67. doi: 10.2147/ JWH.S38603.
- Stebliuk V, Pronoza-Stebliuk K. Postconcussion Syndrome in Ukrainian Veterans: Physical and Mental Manifestations.
 J Educ Health Sport. 2018;8(2):349-54.

- 20. Trzaskowski M. et al. Quantifying between-cohort and between-sex genetic heterogeneity in major depressive disorder. Am J Med Gent B Neuropsychiatr Genet. 2019;180(6):439-47. doi: 10.1002/ajmg.b.32713.
- 21. Wang M, Liang Q, Li H, Xia W, Li J, Peng Y, et al. Normal pregnancy-induced amino acid metabolic stress in a longitudinal cohort of pregnant women: novel insights generated from UPLC-QTOFMS-based urine metabolomic study. Metabol. 2016;12(8):131. doi: 10.1007/s11306-016-1067-9.
- 22. Walsh K, Nugent NR, Kotte A, Amstadter AB, Wang S, Guille C, et al. Cortisol at the emergency room rape visit as a predictor of PTSD and depression symptoms over time. Psychoneuroendocrinol. 2013;38(11):2520-8. doi: 10.1016/j.psyneuen.2013.05.017.
- 23. Zaporozhan VM. Akusherstvo. Akusherstvo ta hinekolohiia: nats. pidruchnyk. Kyiv: VSV Medytsyna; 2013. 1032 p.
- 24. Zannas AS, Provencal N, Binder EB. Epigenetics of posttraumatic stress disorder: current evidence, challenges, and future directions. Biol Psychiatr. 2015;78(5):327-35. doi: 10.1016/j.bio-psych.2015.04.003.
- 25. Zuo J, Lan Y, Hu H, Hou X, Li J, Wang T, et al. Metabolomics-based multidimensional network biomarkers for diabetic retinopathy identification in patients with type 2 diabetes mellitus. BMJ Open Diabetes Research Care. 2021;9(1):e001443. doi: 10.1136/bmjdrc-2020-001443.

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