International Journal of Biomedicine 13(2) (2023) 292-295
http://dx.doi.org/10.21103/Article13(2)_OA17

ORIGINAL ARTICLE

Adolescent Health

INTERNATIONAL JOURNAL OF BIOMEDICINE

The Level of Lipid Peroxidation Products and Medium-Molecular-Weight Peptides in Adolescents with Obesity

Marina A. Darenskaya*, Lyubov V. Rychkova, Dolgor B. Balzhirova, Natalya V. Semenova, Olga A. Nikitina, Anastasia Lesnaya, Natalya Yuzvak, Maria A. Rashidova, Lyubov I. Kolesnikova

Scientific Centre for Family Health and Human Reproduction Problems, Irkutsk, Russian Federation

Abstract

Background: The aim of this research was to study the plasma content of lipid peroxidation products and MMWP in obese adolescents.

Materials and Results: The studies were conducted on 19 adolescent girls and 18 adolescent boys with an established diagnosis of exogenous constitutional obesity of the first degree. Twenty-four adolescent girls and 20 adolescent boys made up control groups. All adolescents were subjected to general clinical examination, including anamnestic data collection, physical examination, anthropometric data analysis, and nutritional status assessment. The content of primary, secondary, and final lipid peroxidation (LPO) products was evaluated, as well as medium-molecular-weight peptides (MMWP) absorbing at wavelengths 238, 254, and 280 nm by the spectrophotometric method.The group of obese adolescent girls, compared to the control, showed lower values of secondary LPO (thiobarbituric acid reactants) (P=0.022) and elevated levels of MMWP-238 (P<0.0001) and MMWP-280 (P=0.03). The group of obese adolescent boys, compared to the control, showed higher values of secondary LPO products (ketodienes and conjugated trienes) (P=0.042) and elevated levels of MMWP-238 (P=0.03).

Conclusion: The obtained data demonstrate the presence of activation of lipid peroxidation processes at the stage of secondary products in adolescent boys and endogenous intoxication in obese adolescents, regardless of gender. The need to monitor and correct these indicators in adolescent patients with obesity should be an important component of pathogenetic treatment.(**International Journal of Biomedicine. 2023;13(2):292-295.**)

Keywords: lipid peroxidation • medium-molecular peptides • adolescents • obesity

For citation: Darenskaya MA, Rychkova LV, Balzhirova DB, Semenova NV, Nikitina OA, Lesnaya A, Yuzvak N, Rashidova MA, Kolesnikova LI. The Level of Lipid Peroxidation Products and Medium-Molecular-Weight Peptides in Adolescents with Obesity. International Journal of Biomedicine. 2023;13(2):292-295. doi:10.21103/Article13(2)_OA17

Abbreviations

BMI, body mass index; **CD**, conjugated dienes; **KD-CT**, ketodienes and conjugated trienes; **LPO**, lipid peroxidation; **MMWP**, medium-molecular-weight peptides; **OS**, oxidative stress; **ROS**, reactive oxygen species; **SB**, Schiff bases; **TBARs**, thiobarbituric acid reactants.

Introduction

The study of the pathogenetic mechanisms of the formation of childhood obesity is becoming increasingly important due to the high prevalence and risk of developing numerous complications in adulthood.[1] The most common type of obesity is the exogenous-constitutional form, manifested by an imbalance between calories consumed and expended.[3] It has been established that obesity is associated with chronic inflammation of adipose tissue, activation of pro-inflammatory factors, dyslipidemia, the development of oxidative stress (OS), and other elements.[4-6] The progression of OS is accompanied by the formation and accumulation of cytotoxic compounds, which act as mediators of damage and provoke characteristic metabolic shifts.[7-9] At the same time, lipid peroxidation (LPO) processes are

activated in the biological membranes of cells, against which endogenous intoxication of the body develops.[10-12] In this case, the damaging agents are unbalanced biologically active substances circulating in the blood and acquiring the properties of endogenous toxins.[13] The level of medium-molecular-weight peptides (MMWP) is recognized as a universal biomarker of endogenous intoxication.[14] The composition of the MMWP includes various combinations of regulatory peptides, including peptide hormones and their fragments and non-regulatory oligopeptides.[15] Determination of the level of MMWP in biological fluids with a molecular weight of 300-5000 D makes it possible to characterize the severity of intoxication during the development of the pathological process.[14,15]

The aim of this research was to study the plasma content of lipid peroxidation products and MMWP in obese adolescents.

Materials and Methods

The studies were conducted on 19 adolescent girls (mean age – 14.46±2.3 years) and 18 adolescent boys (mean age – 13.2±2.2 years old) with an established diagnosis of exogenous constitutional obesity of the first degree. Twenty-four adolescent girls (mean age – 13.76±1.26 years) and 20 adolescent boys (mean age – 13.89±1.41 years) made up control groups.

Criteria for inclusion in groups with exogenous-constitutional obesity of the 1st degree were excess body weight of more than the 95th percentile for a certain gender, height, and age; exclusion of acute or exacerbation of chronic diseases at the beginning of the examination or one month before it; permanent residence of a teenager on the territory of this municipality; signing by parents or legal representatives, as well as adolescents over 15 years of age informed consent to be included in the study. Height, body weight, and waist circumference were measured, body mass index (BMI) (kg/m^2) was calculated, and the puberty stage, according to Tanner, was determined. Overweight was considered at a BMI >85th percentile for a given gender and age, and obesity - at a BMI>95th percentile.[16] Exclusion criteria from the group: physical development delay, body weight deficiency, genetic and symptomatic forms of obesity, taking medications that potentially affect body weight, and the estimated biochemical characteristics.

All adolescents were subjected to general clinical examination, including anamnestic data collection, physical examination, anthropometric data (measurement of body weight, height, determination of BMI) analysis, nutritional status assessment, and determination of the concentration of total cholesterol and triglycerides in blood serum, glucose tolerance testing.

Biochemical measurements

Blood plasma was used as the material for the study. Plasma concentrations of primary/secondary/final products of LPO (conjugated dienes [CDs]/ketodienes and conjugated trienes [KD-CT]/Schiff bases [SB]) were estimated by I.A. Volchegorsky method.[17] TBARs (secondary LPO products) content was detected by fluorometry according to V.B. Gavrilov et al.[18]

The content of primary, secondary, and final LPO products was evaluated, as well as MMWP absorbing at wavelengths 238, 254, and 280 nm by the spectrophotometric method.

The MMP values (MMP 238, MMP 254, MMP 280) were evaluated by the spectrophotometric method.[19] Measurements were carried out on a spectrophotometer SF-2000 (Russia) and BTS350 Analyzer (BioSystems, Spain).

Statistical analysis was performed using STATISTICA 10.0 software package (Stat-Soft Inc, USA). The normality of distribution of continuous variables was tested by the Kolmogorov-Smirnov test with the Lilliefors correction and Shapiro-Wilk test. The F-test for equality of two variances was applied. For descriptive analysis, results are presented as median (Me), interquartile range (IQR; 25th to 75th percentiles). Differences of continuous variables departing from the normal distribution, even after transformation, were tested by the Mann-Whitney U-test. A probability value of $P \leq 0.05$ was considered statistically significant.

The study was carried out in accordance with the Helsinki Declaration of the World Medical Association (1964, ed. 2013) and approved by the Committee on Biomedical Ethics at the Scientific Center for Family Health and Human Reproduction (Extract from the meeting No. 5 as of 16.05.2016).

Results and Discussion

The group of obese adolescent girls, compared to the control, showed lower values of secondary LPO (TBARs) (P=0.022) and elevated levels of MMWP-238 (P<0.0001) and MMWP-280 (P=0.03) (Table 1). The group of obese adolescent boys, compared to the control, showed higher values of secondary LPO products (KD and CT) (P=0.042) and elevated levels of MMWP-238 (P=0.03) (Table 1).

Table 1.

Parameters of LPO products and MMWP in adolescents with obesity (Me (25%;75% quartiles)).

Parameters	Girls		Boys		Statistics
	Control (1)	Obesity (2)	Control (3)	Obesity (4)	
CDs, μmol/L	0.86 [0.64;1.08]	0.98 [0.82;1.15]	0.96 [0.8;1.45]	0.89 [0.8;1.11]	
KD and CT, units	0.32 [0.13;0.60]	0.40 [0.30;0.56]	0.46 [0,23;0.66]	0.58 [0.24;0.48]	P_{3-4}=0.042
TBARs, μmol/L	1.54 [1.28;2.15]	1.23 [0.82;1.44]	1.44 [1.28;1.69]	1.18 [0.92;1.44]	P_{1-2}=0.022
SB, μmol/L	0.04 [0.03;0.04]	0.04 [0.03;0.05]	0.04 [0.03;0.05]	0.04 [0.03;0.05]	
MMWP 238, units	0.09 [0.05;0.15]	0.26 [0.22;0.28]	0.01 [0.08;0.02]	0.25 [0.10;0.28]	P_{1-2}<0.0001 P_{3-4}=0.03
MMWP 254, units	0.16 [0.12;0.18]	0.20 [0.14;0.23]	0.15 [0.14;0.20]	0.20 [0.17;0.23]	
MMWP 280, units	0.26 [0.24;0.28]	0.35 [0.25;0.38]	0.28 [0.22;0.34]	0.37 [0.30;0.38]	P_{1-2}=0.03

OS is an important component of the pathogenesis of obesity and its possible complications.[20,21] Preclinical studies in vitro and in vivo have shown a stimulating effect of OS on the proliferation and differentiation of preadipocytes, as well as an increase in the size of adipocytes.[22] It is known that in a healthy body, reactive oxygen species (ROS) are involved in the activation of hypothalamic neurons involved in the regulation of eating behavior. In conditions of obesity, due to increased oxidative processes, the production of ROS increases, the hunger center is activated, the depot of white adipose tissue increases, and appetite increases.[23] In addition, the following factors associated with obesity that stimulate OS reactions can be distinguished: hyperglycemia, elevated lipid levels, bioelement deficiency, chronic inflammation, hyperleptinemia, increased activity of muscle tissue to maintain excess body weight in obesity, endothelial dysfunction, impaired respiratory function of mitochondria, etc.[24,25] Metabolic disorders in obesity include developing insulin resistance and hyperglycemia. Intracellular increase in glucose levels leads to activation of glycolysis and the tricarboxylic acid cycle, which leads to hyperproduction of oxidized forms of dehydrogenase coenzymes — nicotinamide adenine nucleotide phosphate (NADP) and flavin adenine dinucleotide (FAD), disruption of the mitochondrial respiratory chain and, as a consequence, hyperproduction of ROS.[4] Glucose autooxidation products serve as additional sources of hydroxyl radical and superoxide-anion radical production. (26) Obesity is accompanied by an increase in the level of free fatty acids in the blood, which stimulates the production of superoxide-anion radicals.[4]

LPO products formed at various stages of the chain process serve as significant markers of OS in the body.[27] We found higher values of secondary lipid peroxidation products (KD and CT) in obese adolescent boys. These products can damage the cell's structural components by induction of apoptotic and mutational processes, inhibition of DNA synthesis, proliferation, etc.[4] A significant contribution to the accumulation of lipid peroxidation products can be made by the deficiency of vitamins and minerals observed in obesity. In addition, in obese patients, there is a decrease in the activity of antioxidant enzymes (superoxide dismutase, glutathione peroxidase) and a decrease in the overall antioxidant status of blood plasma, as well as a positive relationship between the level of these OS markers and BMI.[28,29] There is a close relationship between the accumulation of LPO products and the development of endogenous intoxication in obesity, which is also noted in our study.

MMWPs belong to the products of cellular disorganization, incomplete decomposition, and non-enzymatic transformation of proteins, the so-called fragments of endogenous proteins. The main source of MMWP formation is non-enzymatic proteolysis, including blood proteins (fibrinogen, albumin, thrombin), as a result of which products of high functional activity are formed.[15,30] Several MMWP fractions are determined depending on the wavelength. In our study, the fraction with the intensity of ultraviolet absorption at 238 nm was the most indicative. As a rule, substances of catabolic origin, xenobiotics, decay products of tissue cells, and particles of microbial origin are registered in this range. In a healthy person's biological fluids, such substances might be found in small quantities (i.e., below the threshold of sensitivity of the method). Therefore, the appearance of high extinction values at a wavelength of 238 nm always indicates pathological processes in the body. As a rule, an increase in the values of this indicator may indicate an increase in catabolic processes and stimulation of the LPO processes.[14] Due to the direct effect of MMP on biomembrane lipids, one can expect the development of pathological phenomena of a disconnecting nature: microcirculation disorders, disconnection of oxidative phosphorylation processes, inhibition of carbohydrate and energy metabolism enzymes, etc.[31]

Conclusion

The obtained data demonstrate the activation of lipid peroxidation processes at the stage of secondary products in adolescent boys and endogenous intoxication in obese adolescents, regardless of gender. Monitoring and correcting these indicators in adolescent patients with obesity should be an important component of pathogenetic treatment.

Sources of Funding

This study was supported by the RF Grant (NSh-3382.2022.1.4).

Competing Interests

The authors declare that they have no competing interests.

This work was carried out using the equipment of the Center for the Development of Advanced Personalized Health Technologies at the Scientific Centre for Family Health and Human Reproduction Problems (Irkutsk).

References

1. Spinelli A, Buoncristiano M, Kovacs VA, Yngve A, Spiroski I, Obreja G, et al. Prevalence of Severe Obesity among Primary School Children in 21 European Countries. Obes Facts. 2019;12(2):244-258. doi: 10.1159/000500436.
2. Balzhieva VV, Bairova TA, Rychkova LV, Ayurova ZhG, Kolesnikov SI. [Ethnogenetic aspects of obesity in children and adolescents]. Voprosy Detskoi Dietologii. 2017;15(5):29-34. doi: 10.20953/1727-5784-2017-5-29-34. [Article in Russian].
3. O'Connor TG, Williams J, Blair C, Gatzke-Kopp LM, Francis L, Willoughby MT. Predictors of Developmental Patterns of Obesity in Young Children. Front Pediatr. 2020 Mar 24;8:109. doi: 10.3389/fped.2020.00109.
4. Marseglia L, Manti S, D'Angelo G, Nicotera A, Parisi E, Di Rosa G, Gitto E, Arrigo T. Oxidative stress in obesity: a critical component in human diseases. Int J Mol Sci. 2014 Dec 26;16(1):378-400. doi: 10.3390/ijms16010378.

***Corresponding author:** Prof. Marina A. Darenskaya, PhD, ScD. Scientific Centre for Family Health and Human Reproduction Problems, Irkutsk, the Russian Federation. E-mail: marina_darenskaya@inbox.ru*

5. Darenskaya MA, Kolesnikova LI, Rychkova LV, Kravtsova OV, Semenova NV, Kolesnikov SI. Relationship between lipid metabolism state, lipid peroxidation and antioxidant defense system in girls with constitutional obesity. AIMS Molecular Science. 2021;8(2):117-126. doi: 10.3934/molsci.2021009
6. Zuo L, Prather ER, Stetskiv M, Garrison DE, Meade JR, Peace TI, Zhou T. Inflammaging and Oxidative Stress in Human Diseases: From Molecular Mechanisms to Novel Treatments. Int J Mol Sci. 2019 Sep 10;20(18):4472. doi: 10.3390/ijms20184472.
7. Darenskaya MA, Gavrilova OA, Rychkova LV, Kravtsova OV, Grebenkina LA, Osipova EV, Kolesnikov SI, Kolesnikova LI. The Assessment of Oxidative Stress Intensity in Adolescents with Obesity by the Integral Index. International Journal of Biomedicine. 2018; 8(1): 37-41. doi: 10.3390/ijms20184472
8. Kuleshova DK, Davydov VV. [Some peculiarities in the manifestation of oxidative stress and current status of antioxidant system in adolescents of different age groups with obesity, complicated by insulin resistance and without it]. Biomed Khim. 2014 Mar-Apr;60(2):264-74. doi: 10.18097/pbmc20146002264. [Article in Russian].
9. Kolesnikova LI, Darenskaya MA, Grebenkina LA, Labygina AV, Dolgikh MI, Natyaganova LV, Pervushina OA. [The ethnos in medical researches (literature review)]. Acta Biomedica Scientifica (East Siberian Biomedical Journal). 2013;4(92):153-159. [Article in Russian].
10. Darenskaya MA, Rychkova LV, Kolesnikov SI, Semenova NV, Nikitina OA, Brichagina AS, Mikhalevich IM, Kolesnikova LI. Biochemical Status of Obese Male Adolescents of Different Ethnicity: Discriminant Analysis in the Identification of the Most Informative Indicators. Bull Exp Biol Med. 2022 Aug;173(4):459-463. doi: 10.1007/s10517-022-05579-z.
11. Kolesnikova LI, Darenskaya MA, Grebenkina LA., Osipova EV, Dolgikh MI, Natyaganova LV. [The state of the antioxidant status of children of different ages]. Nutrition issues. 2013;82(4):27-33. [Article in Russian].
12. Kolesnikova LI, Bairova TA, Pervushina OA. Genes of antioxidant enzymes. Annals of the Russian Academy of Medical Sciences. 2013;68(12):83-88. doi: 10.15690/vramn.v68i12.865
13. Belskaya LV, Kosenok VK, Massard J, Zavyalov AA. [The state of indicators of lipid peroxidation and endogenous intoxication in patients with lung cancer]. Bulletin of the Russian Academy of Medical Sciences. 2016;71(4):313-322. doi: 10.15690/vramn712. [Article in Russian].
14. Vitkina TI. [Medium molecules in assessing the level of endogenous intoxication in chronic non-obstructive bronchitis]. Zdorovje. Meditsinskaia Ekologiia. Nauka. 2014;56 (2):70-72. [Article in Russian].
15. Karyakina EV, Belova SV. [Molecules of average weight as an integral indicator of metabolic disorders (review)]. Klinicheskaia Laboratornaia Diagnostika. 2004;3:3-8. [Article in Russian].
16. Styne DM, Arslanian SA, Connor EL, Farooqi IS, Murad MH, Silverstein JH, Yanovski JA. Pediatric Obesity-Assessment, Treatment, and Prevention: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2017 Mar 1;102(3):709-757. doi: 10.1210/jc.2016-2573.
17. Volchegorskiĭ IA, Nalimov AG, Iarovinskiĭ BG, Lifshits RI. [Comparison of various approaches to the determination of the products of lipid peroxidation in heptane-isopropanol extracts of blood]. Vopr Med Khim. 1989 Jan-Feb;35(1):127-31. [Article in Russian].
18. Gavrilov VB, Gavrilova AR, Mazhul' LM. [Methods of determining lipid peroxidation products in the serum using a thiobarbituric acid test]. Vopr Med Khim. 1987 Jan-Feb;33(1):118-22. [Article in Russian].
19. Gavrilov VB, Bidula MM, Furmanchuk DA. [Assessment of intoxication of the body by the imbalance between the accumulation and binding of toxins in the plasma]. Klinicheskaia Laboratornaia Diagnostika. 1999;2:13-17. [Article in Russian].
20. Povarova OV, Gorodetskaya EA, Kalenikova EI, Medvedev OS. Metabolic markers and oxidative stress in the pathogenesis of obesity in children. Russian Bulletin of Perinatology and Pediatrics. 2020;65(1):22-29.
21. Darenskaya MA, Rychkova LV, Kolesnikov SI, Kravtsova OV, Semenova NV, Brichagina AS, Kolesnikova LI. [Changes in lipid peroxidation system during standard therapy for exogenous constitutional obesity in adolescents of different sex]. Voprosy Detskoi Dietologii. 2022;20(1):5-11. doi: 10.20953/1727-5784-2022-1-5-11. [Article in Russian].
22. Smith MM, Minson CT. Obesity and adipokines: effects on sympathetic overactivity. J Physiol. 2012 Apr 15;590(8):1787-801. doi: 10.1113/jphysiol.2011.221036.
23. Kolesnikova LI, Darenskaya MA, Kolesnikov SI. [Free radical oxidation: a pathophysiologist's view]. Bulletin of Siberian Medicine. 2017;16(4):16-29. doi: 10.20538/1682-0363-2017-4-16–29. [Article in Russian].
24. Manna P, Jain SK. Obesity, Oxidative Stress, Adipose Tissue Dysfunction, and the Associated Health Risks: Causes and Therapeutic Strategies. Metab Syndr Relat Disord. 2015 Dec;13(10):423-44. doi: 10.1089/met.2015.0095.
25. Darenskaya MA, Rychkova LV, Semenova NV, Belkova NL, Kolesnikova LI. The Role of Oxidative Stress and Changes in the Composition of the Gut Microbiota in the Genesis of Adolescent Obesity. International Journal of Biomedicine. 2022;12(3):344-348. doi: 10.21103/Article12(3)_RA3
26. Vona R, Gambardella L, Cittadini C, Straface E, Pietraforte D. Biomarkers of Oxidative Stress in Metabolic Syndrome and Associated Diseases. Oxid Med Cell Longev. 2019 May 5;2019:8267234. doi: 10.1155/2019/8267234.
27. Darenskaya MA, Rychkova LV, Kolesnikov SI, Kravtsova OV, Semenova NV, Brichagina A, et al. Oxidative Stress Index Levels in Asian Adolescents with Exogenous-Constitutional Obesity. International Journal of Biomedicine. 2022;12(1):142-146. doi: 10.21103/Article12(1)_OA16
28. Kwaifa IK, Bahari H, Yong YK, Noor SM. Endothelial Dysfunction in Obesity-Induced Inflammation: Molecular Mechanisms and Clinical Implications. Biomolecules. 2020 Feb 13;10(2):291. doi: 10.3390/biom10020291.
29. How Effective Are Antioxidant Supplements in Obesity and Diabetes? Med Princ Pract. 2015;24(3):201-215.
30. Klisch IM, Myalyuk OP, Osinchuk RR, Marushchak MI. Endogenous intoxication in rats with nutritional obesity. Scientific review. Biological Sciences. 2016;1:57-59.
31. Bunyatyan ND, Vlasov AP, Nachkina EI, Kochkarova RR, Shibitov VA, Kargayeva TN, et al. [Functional-systemic reactions of the body in endotoxicosis and their correction]. Pharmacy. 2011;6:43-46. [Article in Russian].