UDC: 618.111 -6 15.009-06-92

MORPHOBIOCHEMICAL PARAMETERS OF RATS INTRODUCED TO TITANIUM DIOXIDE (experimental study)

Mavlonova G.Sh., Tokhirov Zh. Ya.
Bukhara Medical University named after Abu Ali Ibn Sina. Uzbekistan.

Аннотация. Due to the widespread use of titanium dioxide nanoparticles (NPs-TiO2) in completely different areas of human activity, the question arises about the safety of this nanomaterial. Of particular interest is the study of the problem of the influence of nanoparticles on the body, since the substance in nanoform has completely new properties. The toxic properties of TiO2 NPs have not yet been sufficiently studied, so this topic is relevant. The study assessed the morphological and biochemical parameters of the blood of Wistar rats after intraperitoneal injection of titanium dioxide nanoparticles (TiO2 NPs) at doses of 13.3 and 133.3 mg/kg. The selected concentrations of nanoparticles did not exceed the maximum tolerated dose (MTD) for a given metal. The size of the nanoparticles used was 90 nm. On the first, seventh and fourteenth days, blood was taken from the tail vein for further analysis. The results showed an increase in serum levels of aspartate aminotransferase, alanine aminotransferase, urea and creatinine activity against the background of general leukocytosis. During the experiment, the dose-dependent nature of the effects was not established, but their manifest manifestations were noted on the first day of the experiment, followed by leveling off by the seventh day, which indicates the presence of adaptive reactions in the body. The identified toxic effects of TiO2 NPs indicate a potential risk to women's health.
Keywords: titanium dioxide (NP-TiO2), white male rats, tail vein.
Relevance. Due to their unique physicochemical properties (pigment, sensor, adsorption, optical, electrical and catalytic), titanium dioxide nanoparticles (TiO2 NPs) have acquired a wide range of uses. Approximately 60% of TiO2 NPs are used in construction (in paint and varnish products, cement, facing tiles), 30% in the production of plastics, about 13% in paper production and 3% in electronics, catalysts, cosmetics (sunscreen, dental paste), as well as in the production of ceramics, printing ink, welding fluxes, self-cleaning glass, mirrors and other surfaces [1,15,16 ,17,18,19,20]. Of great interest is the study of the photocatalytic (PC) properties of this material, which make it possible to increase the efficiency of technological FC processes for purifying water and air from toxic impurities. All

these processes are aimed at solving global energy saving problems [1,29,30,31,32]. In addition, this property is also used in medicine – photodynamic therapy, which has found application in oncology [1,2,3,4,5,6,7]. The main producers of TiO2 today are: Du Pont (USA), Crystal Global (Saudi Arabia), Kronos (Germany), Tronox (USA), whose shares account for more than 60% of global TiO2 production, which in 2014 amounted to about 6, 5 million tons [1,8,9,10,11,12,13,14]. Due to the widespread use of TiO2 NPs in completely different areas of human activity, the question arises about the safety of this nanomaterial. The toxic properties of TiO2 NPs have not yet been sufficiently studied, although extensive research is being conducted in different countries of the world to assess their safety [1,21,22,23,24,25,26,27,28]. TiO2 NPs can enter the body through the mucous membranes of the respiratory tract and digestive tract, as well as transdermally when using cosmetics. According to Professor G.M. Balan, the main target organs of TiO2 NPs are the tissues of the respiratory, digestive, immune, and skin systems, and the critical ones in terms of the consequences of their action are the brain, spinal cord, reproductive and excretory organs.

Purpose of the study: To evaluate the influence of TiO2 NPs on the morpho-biochemical parameters of the rat body.

Research methods. The studies were carried out in the experimental biological clinic of the Bukhara State University named after Abu Ali Ibn Sina on 30 white male Wistar rats weighing 150-180 g, kept under standard vivarium conditions and a diet for laboratory animals, in accordance with the rules of laboratory practice when conducting preclinical studies in UzR (GOST 3 51000.3-96 and GOST 51000.4-96).

Experimental studies on animals were carried out in accordance with the instructions recommended by the Uzbek Regulations, 1987 and “The Guide for the Care and Use of Laboratory Animals (National Academy Press Washington, D.C. 1996).” Efforts were made during the research to minimize animal suffering and reduce the number of samples used.

Experimental design. All experimental animals were divided into three groups (n=10). Animals of experimental groups I and II were administered a single dose of TiO2 NPs at a dose of 13.3 mg/kg and 133.3 mg/kg. The control group of animals was administered an isotonic solution of sodium chloride 0.9% in an equivalent volume. The selected concentrations of nanoparticles did not exceed the maximum tolerated dose (MTD) for a given metal. On the first, seventh and fourteenth days, blood was taken from the tail vein for morphological and biochemical studies.

Results. When comparing morphological blood parameters, it was revealed that the most significant changes were observed on the first day after intraperitoneal administration of NPs in experimental group I with an administered dose of NPs-TiO2 of 13.3 mg/kg (Table 1). In particular, an increase in the number of leukocytes (1.2 times; $p<0.05$), lymphocytes (1.3 times; $p<0.05$), monocytes (in 1.4 times; $p<0.05$), granulocytes (1.2 times; $p<0.05$), erythrocytes, hemoglobin and platelets. In experimental group II, on the seventh day, a tendency towards a decrease in all studied parameters was noted, with the exception of a slight increase in platelet levels.

By day 14, the experimental group was characterized by an increase in hemoglobin (1.3 times; $p<0.05$) and a decrease in platelets (1.5 times; $p<0.05$) compared to the control group. In experimental group II, no statistically significant differences with the control were detected. Analysis of biochemical blood parameters showed that a single intraperitoneal injection of TiO2 NPs leads to an increase in all studied parameters on the first day.

In the process of analyzing the results, it was noted that the greatest changes were observed in the indicators of ALaT, ASaT, creatinine and urea.

Thus, the highest ALaT activity was observed in experimental group I on the first (3.5 times; $p<0.05$) and seventh days (2.5 times); on the 14th day, the enzyme activity drops slightly, but remains higher than in control almost 2 times.

ACaT is also most active in group I and exceeds the data in the control on the first (2 times), seventh (4.8 times) and 14 days (2 times). Paradoxical, in our opinion, is the absence of changes in the levels of ACaT and ALaT on the first day at the maximum dose of NPs. However, by the seventh and 14th days in experimental group II there was a clear tendency towards an increase in data activity enzymes.

The level of LDH is characterized by high values throughout the experiment in experimental group II compared with the control and group I.

On the first (2.6 times) and especially on the seventh day (4 times) there was a sharp increase in the level of urea in group I, then by the 14th day this indicator began to level off to normal. In group II, despite the higher dose of TiO2 NPs, the indicators remained virtually unchanged.

As is known, the main sphere of action of leukocytes is the specific and nonspecific protection of the body from external and internal pathogenic agents, therefore it is absolutely natural that on the first day after a single administration of TiO2 NPs, leukocytosis was observed, which serves as an indicator of the inflammatory process. By the seventh day, the levels of leukocytes and its fractions had recovered, which probably indicates the normalization of homeostasis due to adaptive reactions in the body. At the end of the experiment, the "white blood" indicators were practically no different from the control, which is probably due to the removal of TiO2 NPs from the body.

Throughout the study, there was a trend toward an increase in the amount of hemoglobin with a fairly stable level of red blood cells. Our data are consistent with the results of a study examining the biological effects of intragastric administration of TiO2 NPs [2, 3]. There was a decrease in platelets in all experimental groups. It is interesting to note the fact that in experimental group II, against the background of the maximum dosage, there was an increase in platelet levels, while the overall dynamics of their decrease in experimental group I was observed.

ALaT and ACaT are metabolic enzymes of the liver; an increase in their activity in the blood serum indicates damage to liver cells and their membranes [4].

The results obtained indicate damage to hepatocytes by TiO2 NPs. Urea is formed in the body during the breakdown of proteins, is the end product of protein metabolism and is excreted along with urine. Its content level is used to judge the functioning of the kidneys [3]. An increase in urea in the blood may be a sign of kidney disease, and necrosis of the renal tubules is possible.

Creatinine is excreted from the body by the kidneys in the urine, so its amount in the blood is an important indicator of the functioning of this organ [1]. Its increase in experimental groups I and II may indicate moderate renal failure. As a result, serious disturbances of water-salt, acid-base and osmotic homeostasis can develop, which lead to secondary damage to all body systems.

The study of protein metabolism parameters showed that no significant differences were identified. However, on the first day, a sharp increase in this indicator was noted in experimental groups I (2 times) and II (2.5 times). By the seventh and 14th days, the level of protein in the body approached the levels of the control group.

During the study, we monitored changes in blood glucose levels. On the first, seventh and 14th days in experimental groups I and II we saw a slight increase in glucose levels within normal limits. This shows that the introduction of NPs did not disrupt carbohydrate metabolism [2].

Conclusion. The studies carried out reveal the negative impact of TiO2 NPs on the body, which may cause the development of pathological conditions, in particular the liver and kidneys. During the experiment, the dose-dependent nature of the effects was not established, but their manifest manifestations were noted on the first day of the experiment, followed by leveling off by the seventh day, which indicates the presence of adaptive reactions in the body. The identified toxic effects of TiO2 NPs indicate a potential risk to women's health, as well as to environmental biota.

Literature

1. Алимбетова Г.З., Гайнуллина М.К. Профессиональный риск нарушения репродуктивного здоровья женщин-работниц производства искусственных кож // Успехи современного естествознания. 2014. № 12. С. 31–32.
2. Артамонова В.Г., Мухин Н.А.Профессиональные болезни. – М.: Медицина, 2004. 480 с.
3. Байдюк О.Н. Гигиена и физиология труда женщин, занятых в современном производстве суперфосфатов: автореф. дисс…. канд. мед. наук. – Омск, 2015. 24 с.
4. Данилин В.А. Особенности влияния на организм комплекса токсических веществ производства СКИ-3 в малых концентрациях (клинико-экспериментальное исследование): автореф. дисс.... докт. мед. наук. – Горький, 2021. 36 с.
5. Khamdamov I.B. Clinical evaluation of the effectiveness of the traditional approach to the treatment of hernias of the anterior abdominal wall in women of fertile age // Doctor's Bulletin. –Samarkand 2022. No. 2.2 (104).-P.65-70.
6. Khamdamov I.B., Mirkhodzhaev I.A. Khakimov M.Sh. Khamdamov B.Z. Evolution of the use of polymer implants for hernioplasty // Tibbiyotda Yangi kun. – Tashkent; 2021,- No. 2 (34) P.-107-111.
7.Khamdamov I.B., Khamdamov A.B. Differentiated approach to the choice of hernioplasty method in women of fertile age (Clinical and experimental study) // Tibbiyotda Yangi kun. – Bukhoro, 2021.-No. 6 (38/1).-P. 112-114.
8. Khakimov M.Sh., Urmanova N.M., Khudoiberdiev S.S., Khamdamov I.B. Possibilities of allohernioplasty in women of fertile age // Nazariy va clinic tibbiyot journals. Tashkent.-2022.-No.3.P.89-93.
9. Khamdamov I.B., Khamdamov A.B. Fertil yoshdagi ayollarda endovideo surgeon hernioplasty // Tibbiyotda yangi kun. Bukhoro, 2021.-№6 (38/1) -S. 25-27.
10. Khamdamov I.B. Experimental determination of the extensibility of the anterior abdominal wall tissues at different times of pregnancy using various approaches to hernioplasty // Academicia: An International Multidisciplinary Research Journal Vol. 12, Issue 04, April 2022 SJIF 2022 = 8.252 R.193-201 (Scopus).
11. Khamdamov I.B. Improving tactical approaches in the treatment of hernias of the anterior abdominal wall in women of fertile age // Tibbiyotda Yangi kun. Bukhoro, 2022.-№10(48)- pp. 338-342.
12. Khamdamov I.B. Morphofunctional features of the abdominal press in women of reproductive age // Tibbiyotda Yangi kun. Bukhoro, 2022.-№3(41)- pp. 223-227.
13. Khamdamova M.T. Ultrasound features of three-dimensional echography in assessing the condition of the endometrium and uterine cavity in women of the first

period of middle age using intrauterine contraceptives // Biology va tibbyot muammolari. - Samarkand, 2020. - No. 2 (118). - P.127-131.
14. Khamdamova M. T. Ultrasound assessment of changes in the endometrium of the uterus in women of the first and second period of middle age when using intrauterine and oral contraceptives // Биомедицина ва амалиёт журнали. – Ташкент, 2020. - №2. - 8 часть. - С.79-85.
15.Khamdamova M. T. Anthropometric characteristics of the physical status of women in the first and second period of middle age // A new day in medicine. Tashkent, 2020. - № 1 (29). - C.98-100.
16. Khamdamova M.T. Age-related and individual variability of the shape and size of the uterus according to morphological and ultrasound studies // News of dermatovenereology and reproductive health. - Tashkent, 2020. - No. 1-2 (88-80). - P.49-52.
17.Khamdamova M. T. Anthropometric characteristics of the physical status of women in the first and second period of middle age // Тиббиётда янги кун. Ташкент, 2020. - № 1 (29). - С.98-100.
18. Khamdamova M.T. Age-related and individual variability of the shape and size of the uterus according to morphological and ultrasound studies // News of dermatovenereology and reproductive health. - Tashkent, 2020. - No. 1-2 (88-80). - P.49-52.
19. Khamdamova M.T. Ultrasound features of three-dimensional echography in assessing the condition of the endometrium and uterine cavity in women of the first period of middle age using intrauterine contraceptives // Biology va tibbyot muammolari. - Samarkand, 2020. - No. 2 (118). - P.127-131.20.Khamdamova M. T. Ultrasound assessment of changes in the endometrium of the uterus in women of the first and second period of middle age when using intrauterine and oral contraceptives // Biomedicine va amaliyot journals. – Tashkent, 2020. - No. 2. - Part 8.- C.79-85.
21. Khamdamova M.T. Features of ultrasound parameters of the uterus in women of the first and second period of middle age using injection contraceptives // Tibbiyotda yangi kun. - Tashkent, 2020. - No. 2/1 (29/1). - pp.154-156.
22. Khamdamova M.T. Features of ultrasound images of the uterus and ovaries in women of the second period of middle age using combined oral contraceptives // Tibbiyotda yangi kun. - Tashkent, 2020. - No. 2 (30). - pp. 258-261.
23. Khamdamova M.T. Individual variability of the uterus and ovaries in women who use and do not use various types of contraceptives // Tibbiyotda yangi kun. - Tashkent, 2020. - No. 3 (31). - pp. 519-526.24.Khamdamova M. T. Echographic features variability in the size and shape of the uterus and ovaries in women of the second period of adulthood using various contraceptives // Asian Journal of Multidimensional Research - 2020. – N9 (5). - P.259-263.
25.Khamdamova M. T. Somatometric characteristics of women of the first and second period of adulthood using different contraceptives with different body types

// The american journal of medical sciences and pharmaceutical research - 2020. – N8 (2). - P.69-76.
26. Хамдамова М.Т., Жалолдинова М.М.,Хамдамов И.Б. Состояние оксида азота в сыворотке крови у больных кожным лейшманиозом // Тиббиётда янги кун. - Бухоро, 2023. - № 5 (55). - С. 638-643.
27. Хамдамова М.Т., Жалолдинова М.М.,Хамдамов И.Б. Значение церулоплазмина и меди в сыворотки крови у женщин носящих медьсодержащих внутриматочной спирали // Тиббиётда янги кун. - Бухоро, 2023. - № 6 (56). - С. 2-7.
28. Khamdamova M. T. Bleeding when wearing intrauterine contraceptives and their relationship with the nitric oxide system // American journal of pediatric medicine and health sciences Volume 01, Issue 07, 2023 ISSN (E): 2993-2149. P.58-62
29. Khamdamova M. T. The state of local immunity in background diseases of the cervix // Eurasian journal of medical and natural sciences Innovative Academy Research Support Center.Volume 3 Issue 1, January 2023 ISSN 2181-287X P.171-175.
30. Хамдамова М.Т., Хасанова М.Т. Различные механизмы патогенез гиперплазии эндометрия у женщин постменопаузального периода (обзор литературы) // Тиббиётда янги кун. - Бухоро, 2023. - № 8 (58). - С. 103-107.
31. Khamdamova M. T., Khasanova Makhfuza Toyqulovna, Umidova Nigora Nabievna The role of genetic determinants in the occurrence of hyperplastic processes of the reproductive system of women's menopausal age // Journal of Advanced Zoology ISSN: 0253-7214 Volume 44 Issue Special Issue-2 Year 2023 Page 3724:3730
32. Измеров Н.Ф., Каспаров А.А. Медицина труда. Введение в специальность. – М.: Медицина, 2012. 392 с.
33. Косарев В.В., Бабанов С.А. Профессиональные болезни. – М.: ГЭОТАР-медиа, 2017. 368 с.