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Genotoxic and Reprotoxic Effects of Afabazole Tobacco Smoke

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ABSTRACT

The harms of smoking are well known. Smokers are more likely to develop lung cancer and other malignant tumors, cardiovascular pathologies and chronic respiratory diseases. The genotoxic and reprotoxic effects of Afabazole tobacco smoke are discussed in detail in this article.

KEYWORDS: *Harm of smoking, lung cancer and other malignant tumors in smokers, cardiovascular pathology*

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Pathogenetic significance of genotoxic lesions

In the current ecological situation, the emergence of pathological processes in the human body is often associated with the effects of genotoxicants, most of which are characterized by anthropogenic origin. The ability of environmental factors to influence the genetic structures of cells can lead to poorly predictable medical and biological consequences, which highlights the need to pay more attention to the study of mutagenesis.

Hereditary diseases

One of the identified consequences of genotoxic lesions of the human body is to increase the burden of these hereditary diseases. This group of diseases includes more than 4,500 pathologies based on genetic mutational changes in the genome [191]. Approximately 1% of the genetic load is due to gene mutations, 0.5% to chromosomal mutations, and about 3–3.5% to multifactorial diseases with a clear genetic component [87]. It should be noted that, as always, not all mutations in structural genes are directly related to the occurrence of a particular genetic pathology. A wide group of late-onset hereditary diseases has been identified that cause a special type of condition called dynamic mutations, the effects of which occur in the adult state. Examples of this group of pathologies are neurodegenerative diseases, in particular schizophrenia and manic-depressive psychosis [38, 204].

Carcinogenesis

One of the leading causes of death and one of the most common diseases is malignant neoplasms. According to some estimates, about 6 million people on the planet are diagnosed with cancer each year.

contributes to the development and progression of carcinogenesis, pregnancy and fetal development disorders.

Pathogenic effects of smoking

There are more than 1.1 billion smokers worldwide, with the proportion of male and female smokers being about 60% and 20% in the Russian Federation, 30% and 28% in the UK, and 28% and 24% in the United States.]. In other words, at least a quarter of the population in developed countries is a smoker. Russia is the world leader in the number of smokers. In 2009, there were 44 million tobacco users in the country, representing about 40 percent of the population.

The genotoxic potential of smoking

The ability of tobacco smoke to have a genotoxic effect on the human body is unquestionable, it contains more than 4,000 chemical compounds, at least 250 of which are dangerous to health and more than 50 have mutagenic properties [120, 188] 234] polycyclic aromatic hydrocarbons (PAH), a. as well as N-nitrosamines; Aromatic amines and aldehydes in the solid and gaseous phases of cigarette smoke. [200]

Effects of smoking on pregnancy and reproductive development

The first report on the negative effects of tobacco smoke on pregnancy and offspring was published more than 50 years ago [196]. To date, an impressive amount of data has been collected from experimental studies on this issue, as well as from clinical and epidemiological observations.

Experimental observations

Before directly reviewing the results of experimental studies evaluating the effects of smoking on embryonic or fetal development, attention should be paid to the suitability of the conditions for modeling the effects of smoking on the body. experience. Many studies only study individual components common in tobacco smoke - nicotine, PAH, carbon monoxide (CO), or using tobacco smoke condensate as an object of study [79]. The prevalence of these approaches is explained by the simplicity of modeling in the experiment, but they lose the main thing - the complexity of the effects of different tobacco combustion products and the way it enters the body. In this regard, the results of such studies are not taken into account in considering this case.

Epidemiological and clinical observations

Despite the various difficulties encountered in attempting to determine the cause-and-effect relationship between the effects of tobacco smoke on the mother's body and the presence of pathologies in the newborn, numerous epidemiological and clinical observations suggest active and / or genotoxic and reprotoxic effects of tobacco smoke 'reveals the secret. passive smoking. They are listed in the relevant meta-comments [79, 119, 194].

Prevention of genotoxic and teratogenic effects

Factors that have genotoxic and teratogenic effects are common in the human environment. Their effects on pregnant women lead to defects in physical and mental development in the postpartum period [139]. The impossibility of completely eliminating contact with potentially toxic xenobiotics of the environment actualizes the task of finding compounds with antigenotoxic (antimutagenic) and antiteratogenic properties and ways to use them to prevent various pathologies.

Mechanisms of teratogenesis

In a broad sense, teratogenesis refers to the occurrence of morphological, metabolic, and functional disorders that occur during intrauterine development. The main role in their emergence is played by factors of exogenous / endogenous origin - infectious diseases, ionizing radiation, co-morbidities and bad habits of the pregnant woman, industrial and domestic pollutants, as well as some medicinal substances.

Genotoxic mechanisms of teratogenesis

Comparative analysis of genotoxic cross-linking; and> the teratogenic activity of xenobiotics appears to be one of the most effective ways to determine the role of genetic damage in reproductive toxicity.

Genotoxic and reprotoxic effects of tobacco smoke

Harmful effect on DNA

The evaluation was carried out according to the methodological recommendations of A.D. Durnev by the method of alkali gel electrophoresis of individual cells ("DNA comet" method). and others (2006) [18], in the head and body tissues of the placenta and embryo.

In the placental cells of animals in the control group, the rate of spontaneous DNA damage, estimated at% of "tail DNA", was 2.2 ± 0.2%. In the cells of the head and body of the embryo, the index was 2.8 ± 0.6 and 3.6 ± 0.9, respectively. The use of cyclophosphamide in animals in the positive control group resulted in a statistically significant increase in DNA damage in placental cells (23.7 ± 3.1% "tail DNA") and embryonic cells (16.0 ± 3.8% "DNA"). tail ").

The data presented are similar to the negative and positive control results previously established in O.V.'s dissertation research. Shreder (2008).

A statistically significant increase in placental DNA damage in animals exposed to tobacco smoke was found to be 14.9 ± 2.9% of "tail DNA". Similarly, smoking in animals resulted in a 4.2-fold (11.6 ± 0.9% "tail DNA") and 3.4-fold (12.4 ± 1.5% "tail DNA") increase in DNA damage in embryonic head and body cells. came "), respectively. Increased DNA damage under the influence of tobacco smoke or tobacco combustion products has been previously reported, but this is the first time it has been reported in placental and embryonic tissues.

In estimating the percentage of apoptotic DNA comets in the embryonic tissues of animals in the control group, this figure was 3.0 ± 1.2, 1.1 ± 0.2, and

1.9 ± 0.8%, respectively, in satellite, head, and trunk cells. formed. embryo. After the introduction of cyclophosphamide into placenta and embryonic cells, the proportion of apoptotic DNA comets increased to 40.3 ± 3.4 and 8.5 ± 3.6%, respectively. Significant increases in the level of apoptotic DNA comets in animals exposed to smoking were observed in all studied samples: up to 21.8 ± 6.4% in the placenta, up to 10.9 ± 3.0% in the head, and 11.7 ± 3, 3% each. in the body of the embryo.

Examples of DNA damage detected by the DNA comet method and apoptotic DNA comet are shown.

The data obtained prove the ability of tobacco smoke to destroy DNA in satellite cells and rat embryos.

Afobazole is a characteristic of pharmacological properties

Selective anxiolytic afobazole (2- [2- (morpholino) ethyltio]] -5-ethoxybenzimidazole hydrochloride with broad-spectrum cytoprotective effect was developed under the guidance of the VV Zakusov Research Institute of Pharmacology of the Russian Academy of Medical Sciences. Academician S. B. Seredenin. Extensive research has been conducted at the Pharmacological Research Institute named after

Evaluation of the genotoxic effects of tobacco smoke

DNA comet method

The study of the effect of afobazole on DNA damage caused by tobacco smoke was performed by the method of DNA comets in the alkaline version in placenta and embryonic cells. To this end, the method was first used in the works of O.V. Schroeder and co-authors (2008-2009) worked in the Laboratory of Drug Toxicology of the Pharmacological Research Institute. V. V. Zakusova RAMS.

Description of the method

The experiments were performed according to methodological recommendations [18].

On the 13th day of gestation, 30 minutes after the smoking process, the animals were excluded from the experiment with dislocation of the cervical spine [30]. After autopsy, 4 placentas and 4 embryos were obtained from each woman, each divided into head and trunk (excluding embryos from the positive control group). The obtained material was placed in test tubes containing 1 mL of cooled phosphate-buffer saline solution containing 20 mM EDTA-Na2 and 10% DMSO, pH = 7.4, intended for cell suspension. After that, the embryonic tissue and placenta were pulverized with a glass rod to obtain cell suspension. After 5 min, after precipitation of large tissue fragments, 60 µl of cell suspension was obtained from each tube, 240 µl 1% low-solubility type 4 agarose (0000099222), trying not to trap tissue debris. placed in eppendorfs with agarose gel prepared using. , "PB Rapgeas, Spain), preheated in a thermoblock at t = 42 ° C. Subsequently, the contents of the eppendorphs were re-suspended 7 times with an automatic pipette and applied to a pre-prepared type 1 agarose using type 1 universal agarose (29637,). . DiaeM, Spain) and gel slides heated to t = 40–50 ° C were covered with a coating and placed on ice for 1 min.

After the agarose had solidified (1-2 min.), The lid slips were carefully removed from the micropreparations obtained and placed in the Schifferdijker cuvette.Then the room was darkened and subsequent manipulations were performed only under yellow light. Working lysis solution (10 mM Tris-HCL (3600C201, Helicon, Russia) [pH 10], 2.5 MNaCL (4103520801, Helicon, Russia), 100 mM EDTA-Na2 1% Triton X-100 (00240078, SpaRSge)) , 10% DMSO), cover the slides with micropreparations and incubate at 4 ° C for at least 1 h.

After the lysis solution is removed, the micropreparations are washed with distilled water4 and placed back in the chamber with a rough surface for horizontal electrophoresis and filled with the working solution. electrophoresis, covering the slides 2-3 mm: 300 niM NaOH (7609300/02/098; DiaeM, Germany), G hM EDTA-Na2, pH> 13 and left for 20 minutes. Electrophoresis was performed for 20 minutes; 1. At a field strength of V / cm and a current of ~ 300 mA. After graduation; During electrophoresis, the micropreparation slides were carefully removed with tweezers, dried with filter paper, placed in Schifferdijker cuvettes, and fixed in a 70% ethanol solution for 15–20 min. After drying, the ethanol solution (1-2 hours) was stained with SYBR Green I (1: 10000 in TE buffer) (689961 Invitrogen, USA) for 20 minutes in a dark room. The dye was applied to the micropreparations in an amount of 200 µl. The obtained micropreparations were analyzed using a high-resolution digital camera (VEC-335, EVS, Russia) at a magnification of * 200 using a Mikmed-2 12T epifluorescent microscope (Lomo, Russia). Digital images of DNA damage in the form of comets were analyzed using the GASP v program. 1.2.2.

At least 100 DNA comets were analyzed from each sample of the placenta, head, and body of the embryo. The percentage of “tail DNA” (% “tail DNA”) of DNA comets was used as an indicator of DNA damage. DNA comets with a “tail DNA” index of more than 50% were separated as a separate category, as a rule, common tail and almost headless DNA comets classified as apoptotic were isolated and their percentage was calculated visually.

To study the reprotoxic effects of tobacco smoke

In this study, the general principles and methods of embryotoxicity analysis, the study of prenatal and postnatal development of rats were carried out in accordance with the requirements of methodological recommendations for assessing the teratogenic activity of pharmacological substances. [19, 36].

Evaluation of embryotoxic effects

The general condition and behavior of the animals were observed during the study. Rats were weaned on days 1, 7, 14, and 20 of gestation.

The animals were excluded from the experiment with dislocation of the cervical spine on the 20th day of gestation. After the opening of the abdomen, the condition of the female genitals was examined: the number of yellow bodies in the ovaries; in the uterus, the number of living and dead fetuses, as well as the sites of implantation and resorption. embryos. Based on the data obtained, the post-implantation mortality rate of the embryos was calculated (the difference between the number of implantation sites and the living fetus refers to the number of implantation sites assumed to be 100%).

Fetal weight (g) was determined, cranio-caudal size (cm) was measured, and external macroscopic examination of the fetus was performed to detect visible developmental abnormalities, as well as the presence of hyperemia, bleeding, and hematomas. Subsequently, the status and presence of abnormalities in the development of internal organs in some fetuses were examined using the Wilson microanatomical method.

Another part of the fetus was fixed in 960 ethanol, stained with alizarin and alcia blue to assess the condition of bone and cartilage tissue by the Peters method. Anomalies in connective tissue development were noted, and the average number of ossification points1 of individual skeletal bones and different skeletal bones (skull, sternum, pelvis, spine, limbs) was calculated. Separately, the formation of bone tissue in the cranial region, the condition of the brain sutures, and the fontanelles were assessed.

Effects of afobazole on genotoxic and reprotoxic effects of tobacco smoke

DNA-damaging modification using afobazole

Afobazole at a dose of 1 mg / kg in female rats significantly reduced DNA damage caused by tobacco smoke in both the placenta and head and body cells when the animals were excluded from the experiment on the 13th day of gestation. from embryos. However, in embryonic tissues,% of DNA in the tail was reduced to negative control values: in embryonic head cells - 3.7 ± 0.7 compared to the control 2.8 ± 0.6; in body cells - 4.1 ± 1.0, in controlled 3.6 ± 0.9. DNA damage caused by tobacco smoke in placental cells was significantly reduced by 2.9 times under the influence of afobazole.

REFERENCES:

[1] Abramchenko, V. V. Pregnancy and high-risk childbirth [Text] / V. V. Abramchenko.-M.: MPA., 2009.-400 p.

[2] Alekperov, U.K. Antimutagenesis. Theoretical and practical aspects [Text] 7U. K. Alekperov;.- Mi: Nauka, 1984. - P. 100.

[3] Anisimov, V.N., Aging and carcinogenesis1 [Tskst] / V. 1-1. Anisimov // Achievements of gerontology. - 2002. - Issue 10. -Pages 99-925.

[4] Bochkov, N.P. Medical genetic counseling on mutagenic and teratogenic effects, [Text] / N. P. Bochkov, T. A. Roslova, I; I. Yakushina // Medical genetics; - 2009. - No 1. - S. - 3-8.

[5] Bochkov, N.P.Human Heredity and Environmental Mutagens [Text] / N. P. Bochkov, A. N-Chebotarev. -Mi: Medicine; 1989. - 272 p.

[6] Burlev, V. A. Regulation of angiogenesis of pregnancy (literature review) [Text] / V. A. Burlev, 3. S. Zaidieva, N; A. Ilyasova // Reproductive problems. -2008. -T.14j # 3. - BILAN. 18-22.

[7] Viglinskaya, A.O. Bioavailability of new * selective anxiolytic afobazole in rats [Text] / A. A: Viglinskaya, G. B. Kolyvanov, A. A. Litvin, O. IO. Kravtsova, V.P. Zherdev, S.B. Seredenin // Bulletin of Experimental Biology and Medicine. - 2007. - V. 143, № 5.-S. 529-530.

[8] Volodin, N. N. Perinatal neurology - problems and solutions [Text] / N. N. Vblodin // Journal of Neurology and Psychiatry. - 2009. -T.. 109, 10i-son - S. 4-8. !

[9] Gaynetdinova, D.; D. Genome instability in childhood patients cerebral palsy [Text] / D. D. Gainetdinova, V; V. Semenov, M; F. Ismagilov, I. A. Pakhalina, E. V. Kolochkova // Kaz: Med. Journal. - 2004; - No. 4. - P. 263-268.

[10] Ganshina, T.S. Effect of afobazole on cerebral blood supply in the hemorrhagic stroke model [Text] / T. S. Ganshina, I. N. Kurdyumov, A. I. Turilova, R; S. Mirzoyan, S. B. Seredenin // Chiq. and dagger, pharmacology. - 2009. - Issue 6. - P. 18-20 Gerasimenko, N. F. Regulation of legislation in the field of health

[Text] / N. F. Gerasimenko // Med. statements. -2001. - № 3. - S. 6.

[11] Global research on adult tobacco [Electronic resource] / country report, RF. - 2009. - P. 1-171. - http://www.who.int/tobacco/surveillance/ru_tfi_gatsrussian_countryreport.pdf

[12] Demikova, N. S. Computer reference and information system on research methods for hereditary metabolic diseases [Text] / N.S. Demikova // Ros. lead, perinat. and pediatrician. - 2001. - No 6. - P. 47-49.

[13] WHO Report "Women's Empowerment - Combating Tobacco Marketing in the WHO European Region" [Electronic resource] / WHO Regional Office for Europe. - Copenhagen. - 2011. - 40 p. - http://whodc.mednet.ru/rus.

[14] World Health Organization Global Tobacco Epidemic Report [Electronic resource] / B03 - Geneva. - 2009. - 340 p. - http://www.ismu.baikal.ru/docs/voz-2009-05.pdf.

[15] Durnev, A. D. Mutagens: screening and pharmacological prophylaxis! affects [Text] / A. D. Durnev, S. B. Seredenin. - M.: Medicine, 1998. -328 p.

[16] Durnev, A.D. Antimutagenic and antiteratogenic properties of afobazole [Text] / A.K.Janataev, O.V.Shreder, S.B.Seredenin // Experimental and clinical pharmacology. - 2009. - V. 72, No 1. - P. 46-51.

[17] Durnev, A.D. Application of the method of alkali gel electrophoresis of isolated cells to assess the genotoxic properties of natural and synthetic compounds [Text] / A. D. Durnev, A. K. Janataev, E. A. Anisina, E. S. Sidneva, V. A. Nikitina, L. A. Oganesyants, S. B. Seredenin // Methodical recommendations. - M, 2006. - 27 p.

[18] Dyban, A.P. Some current problems of experimental teratology [Text] / A. P. Dyban // Bulletin of the Academy of Medical Sciences of the USSR. - 1967. - No 1. - P. 18-30. Janataev, A.K. Study of the antimutagenic activity of afobazol in vivo [Text] / A. K. Janataev, A. D. Durnev, S. B. Seredenin // Expert. and clinical pharmacology. - 2000. - T. 63. - No 2. - P. 57-59.

[19] Janataev, A.K. Comparative study of antimutagenic activity of afobazol in different application methods [Text] / A.K. Janatayev, A.D. Durnev, S.B. Seredenin // Buqa. experimental biol. and Medical, 2000. - No. 11. - P. 539-542.