REVIEW ARTICLE

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Environmental exposure to formaldehyde and effects on human health

Narażenie środowiskowe na formaldehyd i jego wpływ na zdrowie człowieka

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Abstract

Introduction and Objective. Formaldehyde is a common toxic substance in the environment, formed both naturally and as a result of human activity. Due to its widespread use, it can pose a threat to a significant portion of the population. The aim of this study was to analyze scientific research on environmental exposure to formaldehyde and its effects on human health.

Brief description of the state of knowledge. The concentration of formaldehyde in indoor air of buildings reaches much higher values than in the open air. It most often enters the human body through the respiratory tract, less often through the skin. Formaldehyde can be one of the causes of sick building syndrome or non-specific building-related health symptoms. Occupational exposure to formaldehyde most often affects workers in the health care, factory, construction and garment industries.

Results. The results of the study analysis suggest that formaldehyde exposure may be associated with a higher risk of cancer, especially nasopharyngeal cavity cancer and leukemia. Formaldehyde exposure can also cause the development of asthma in both children and adults, as well as some brain diseases.

Summary. Many workers, by virtue of their occupation, are exposed to concentrations of formaldehyde that exceed permissible levels. This can become the cause of the development of many diseases. Adequate education of workers, provision of protective measures, and exposure prevention systems can reduce the risk of adverse health effects.

Key words

cancer, asthma, formaldehyde, toxic

Streszczenie

Wprowadzenie i cel pracy. Formaldehyd jest powszechnie występującą w środowisku substancją toksyczną, powstającą zarówno w sposób naturalny, jak i w wyniku działalności człowieka. Ze względu na powszechne zastosowanie może stanowić zagrożenie dla znacznej części populacji. Celem niniejszego badania była analiza badań naukowych dotyczących środowiskowego narażenia na formaldehyd oraz jego wpływu na zdrowie człowieka.

Opis stanu wiedzy. Stężenie formaldehydu w powietrzu w pomieszczeniach i budynkach osiąga znacznie wyższe wartości niż na otwartej przestrzeni. Najczęściej dostaje się on do organizmu człowieka przez drogi oddechowe, rzadziej przez skórę. Formaldehyd może być jedną z przyczyn syndromu chorego budynku lub niespecyficznych objawów zdrowotnych związanych z budynkiem. Zawodowe narażenie na formaldehyd najczęściej dotyczy pracowników służby zdrowia oraz osób pracujących w fabrykach, a także zatrudnionych w branży budowlanej i zakładach przemysłu odzieżowego. Wyniki analizy badań sugerują, że narażenie na formaldehyd może wiązać się z wyższym ryzykiem zachorowania na raka, zwłaszcza raka jamy nosowo-gardłowej, i białaczkę. Narażenie na formaldehyd może również powodować rozwój astmy, zarówno u dzieci, jak i dorosłych, a także niektóre choroby mózgu.

Podsumowanie. Wiele osób, ze względu na wykonywany zawód, jest narażonych na stężenia formaldehydu przekraczające dopuszczalne poziomy. Może stać się to przyczyną rozwoju licznych chorób. Odpowiednia edukacja pracowników, zapewnienie im środków ochronnych i wprowadzenie systemów zapobiegania narażeniu na formaldehyd może zmniejszyć ryzyko wystąpienia negatywnych skutków zdrowotnych.

Słowa kluczowe

nowotwór, astma, toksyczność, formaldehyd

INTRODUCTION

Carbonyl compounds are one of the most common environmental pollutants. One of them is formaldehyde (CH_2O). It is a common toxic substance found in the

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environment, formed both naturally (e.g. emitted by vegetation, a component of organic compounds emitted by plants) and as a chemical compound of anthropogenic origin (e.g. formed as a result of industrial emissions, smoke, exhaust emissions, or chemical production). Carbonyls like acetaldehyde or formaldehyde are involved in photochemical reactions that produce airborne pollutants [1–3]. The European Chemicals Agency (ECHA) classifies formaldehyde as skin sensitizing, carcinogenic, and suspected to be a mutagenic factor. Additionally, formaldehyde is toxic if swallowed or inhaled, can cause eye damage and severe skin burns (according to the ATP06 – harmonized classification and labelling, validated by the European Union). Due to its wide use, formaldehyde is used in, among other things, in cosmetics, laundry and cleaning products, biocides, pastes, waxes, building materials, particle board, paints, adhesives, plasters and fuels.

A significant number of people are exposed to formaldehyde every day through the presence of this substance indoors. It can be found in building materials, furniture, carpets, floors, toys and electronic equipment, as well as in leather products – shoes, bags, accessories [4, 5]. In addition to external exposure, formaldehyde can pose a risk from internal exposure – the substance can also be found in water and food [6]. Indoor sources of formaldehyde in homes and apartments can be created by cooking, burning candles, incense and tobacco, among other things [7]. Due to the widespread distribution of formaldehyde and its various uses, millions of people around the world are exposed to this harmful substance [8]. Interestingly, small amounts of formaldehyde are produced endogenously in the human body. However, the human body has developed a defence mechanism, the enzyme alcohol dehydrogenase 5 (ADH5), which breaks down formaldehyde into less toxic forms. Estimating the prevalence of formaldehyde hypersensitivity in the population is difficult, although a number of studies suggest that it may affect more than 1% of the population. Studies suggest that formaldehyde may have negative effects on human health, increasing the risk of contracting certain diseases [9, 10].

OBJECTIVE

The aim of this review is to analyze environmental exposure to formaldehyde and assess its impact on human health. For this purpose, key publications were sought using search the engines Pubmed and Google Scholar, as well as other available recent materials on the subject, using the key words: 'formaldehyde', 'toxic', 'cancer', and 'asthma'. Forty-five publications were selectedd. The selection of cited literature focused on recent publications in order to select the most up-to-date information.

DESCRIPTION OF THE STATE OF KNOWLEDGE

Exposure to exogenous formaldehyde. In addition to endogenous production, exogenous formaldehyde enters the human body mainly through inhalation, hence the main factor influencing exposure to this substance is its concentration in the air. In European countries, as well as the USA, Canada and Japan, the levels of average formaldehyde concentration in residential facilities are usually in the range of 20–40 μg/m^3 (although some studies indicate a wider range – 10–80 μg/m^3), while in China, the average is as high as 240 μg/m^3. Indoor formaldehyde concentrations can be more than 200 μg/m3 when smoking a cigarette indoors [11]. Office and public buildings, unlike residential buildings, experience much lower FA concentrations. Mean outdoor formaldehyde concentrations are in the range of 1–4 μg/m^3, except in polluted cities, where levels can reach much higher values. The results of measurements of mean outdoor formaldehyde concentrations in metropolitan Houston, USA, were in the range of 4–9 μg/m^3, although the highest readings indicated concentrations as high as 45 μg/m^3. In rural areas, on the other hand, concentrations are much lower. In northern Michigan, USA, the maximum daytime and nighttime formaldehyde concentrations were 5 μg/m^3 and 0.6 μg/m^3, respectively. Formaldehyde concentrations in indoor and outdoor environments, measured in Strasbourg, France, varied depending on the room in which the measurement was taken, but concentrations in outdoor air were significantly lower than indoor air concentrations (Tab. 1).

Table 1. Formaldehyde concentrations (mg m^{-3}) in indoor and outdoor environments in Strasbourg, France

Sampling site	Formaldehyde concentration		
	Mean	Min.	Max.
City centre	5.7	4.4	7.1
Co Key words used were: 'formaldehyde', 'toxic›, 'cancer", 'asthma', 'commercial centre'			
Hall 1	28.2	28.0	28.3
Hall 2	15.0	13.2	16.5
Hall 3	21.9	18.7	24.3
Train station			
Hall	7.0	5.3	9.3
Counters	13.6	11.3	15.9
Outdoor	6.8	6.5	7.1
Airport			
Hall	10.8	8.8	13.0
Outdoor	6.8	6.5	7.1
Underground car park			
Normal	19.2	17.9	20.6
Car simulation	63.9	54.0	73.8
Car indoor?			
Parked car	13.9	12.2	15.7
Heavy traffic	26.8	23.3	30.2
Fluid traffic	16.6	12.1	21.2
Library 1	55.9	48.3	62.1
Library 2	33.7	31.3	
Cigarette experiment			
Before	20.2	–	–
After 5 cigarettes	217.1	213.0	221.1
After aeration	30.5	24.2	36.2

Source: own elaboration based on the study by C. Marchand et al. [11]

In 2010, the World Health Organization (WHO) developed guidelines for permissible indoor formaldehyde concentrations, setting the upper limit at 0.1 mg/m^3 (100

μg/m^3). This value must not be exceeded for any 30-min period of the day. However, formaldehyde can be felt and cause subjective sensory irritation already at concentrations below 0.1 mg/m^3 [12–14]. Interestingly, formaldehyde can enter the human body not only through absorption in the respiratory tract, but also through dermal absorption. This is how formaldehyde contained in cosmetics or other products is most often absorbed [15]. Due to the widespread use of formaldehyde in products and products used indoors, it seems important to comply with a withdrawal period for products containing formaldehyde – the time it takes for all hazardous substances to escape from these products. The withdrawal period can vary depending on the type of product. One way to reduce the concentration of released formaldehyde may be to ventilate rooms or create a protective barrier. In the case of furniture, the barrier may be to finish it properly, cover it with laminate, and avoid cracks. Safer products (e.g., adhesives, particleboard) that do not contain formaldehyde are increasingly available, as well as furniture made of solid wood, glass and metal [16].

Sick-building syndrome. Sick-building syndrome (SBS) is the name for a phenomenon in which non-specific health symptoms occur while in a building (usually while working or living). These may include, for example, non-specific headaches, eye, nose or throat irritation symptoms, coughing, nausea, dizziness or skin complaints. These symptoms disappear entirely or mostly after leaving the building and cannot be attributed to a specific disease or cause. Additionally, they are not symptoms of a disease caused by a specific air pollutant. SBS can affect several or all occupants of a building, and is suspected to be caused by poor indoor or whole building air quality (IAQ) [17]. Formaldehyde, being an irritant, can be one of the main causes of SBS development [18–21]. In addition to worsening the quality of life for residents and workers, SBS leads, among other things, to increased health care costs, longer absenteeism from work, and reduced worker efficiency. Monitoring concentrations of harmful substances in workplaces and awareness of SBS can be a key factor in reducing the phenomenon [22].

Occupational exposure to formaldehyde. Many occupational groups are exposed to high concentrations of formaldehyde in the workplace. These include healthcare workers (employees of pathomorphology facilities, medical and research laboratories, doctors, nurses, veterinarians) [23–26], firefighters [27], employees of manufacturing plants, wood processing, construction (construction carpenter) [28], beauty industry [29], hair salons, dairy plants, fish hatcheries [30], employees of facilities using or producing formaldehyde derivatives [31], food industry workers [32], and many others.

In 2006, a broader analysis of formaldehyde concentration measurements at various workplaces in different industries was published. It turns out that the highest continuous exposure (formaldehyde levels of 2500–6100 μg/m^3) was shown in measurements during the varnishing of wood floors and furniture, as well as in the clothing and textile finishing industries, fur processing, and during selected work in foundries and cardboard factories. High short-term occupational exposure – formaldehyde levels of 3,700 μg/m^3 and higher – was found in occupations such as pathology, embalming, and in paper processing workers. It was proven that better ventilation of rooms in the workplace and the use of resins which release less formaldehyde, resulted in much lower exposure of workers to formaldehyde [15, 33].

Formaldehyde as a potential carcinogen. According to 2019 WHO data, in 112 out of 183 countries, cancer was the most common or second most common cause of death in people before the age of 70, and is a growing problem worldwide [34], with formaldehyde being one of many chemicals suspected of being carcinogens [35]. Jeongsik Park et al. [36] examined the effects of formaldehyde exposure on the immune response of the spleen. The study was conducted on mice subjected to two concentrations of formaldehyde: 1.38 mg/m^3 (a concentration often found in the work environment) and 5.36 mg/m^3 for four hours per day for five days per week, for two consecutive weeks. The mRNA expression, cytokine production and distribution of helper and regulatory T cells, were examined. Formaldehyde exposure was shown to inhibit the splenic immune response. Reduced activity of effector T cells, reduced cytokine secretion from T cells and reduced mRNA expression were found as a result of FA exposure. In the group with exposure to a concentration of 5.36 mg/m^3 of formaldehyde, histopathological examination showed a slight increase in inflammatory cell infiltration in the lungs of the mice. The results of the study may indicate a link between formaldehyde exposure and the risk of developing or progressing cancer.

The results of several studies suggest a possible link between formaldehyde exposure and the risk of developing nasopharyngeal cancer. The results of a meta-analysis by Awan et al. [37] published in 2018, confirm this association (OR 2.7; 95% CI 1.2–6.0), highlighting that the increase in nasopharyngeal cancer risk increases with the length of formaldehyde exposure. Binazzi et al. [38] through an analysis of 28 studies (11 cohorts, 17 case-control) confirmed the association between formaldehyde exposure and the risk of developing sinonasal cancer. However, they indicate the need for further studies focused on specific occupational groups. Kyeongmin Kwak et al. [39] in their meta-analysis looked for an association between occupational exposure to formaldehyde and the risk of developing lung cancer. The results of the meta-analysis showed that the risk of lung cancer was not significantly increased, even in the higher exposure groups, with an overall pooled risk estimate of 1.04 (95% CI, 0.97–1.12). Despite this, the most recent and highest-quality studies analyzed indicated an increased risk of the disease; therefore a link between the two cannot be ruled out. Much evidence suggests a possible link between formaldehyde exposure and an increased risk of non-Hodgkin lymphoma (NHL). Simona Catalani et al. [40] in 2019 published the results of a meta-analysis examining this link. They found that an analysis of studies published after 1986 found no association between the two factors, and that the risk of developing the disease did not increase.

Formaldehyde and leukemia. Epidemiological studies indicate a possible link between formaldehyde exposure and the risk of developing leukemia. Zhang et al. [41] in their study analyzed the effects of formaldehyde on haematopoiesis in 94 Chinese workers. Forty-three workers were exposed to formaldehyde, while the remaining 51 workers were a control sample. The results of complete blood counts were evaluated and colonies of peripheral stem/progenitor cells cultured. Among the study group, peripheral blood cell

counts were significantly reduced, and chromosome changes characteristic of leukemia were found to be significantly elevated in bone marrow progenitor cells. These results may indicate the adverse effects of formaldehyde on the blood system and the increased risk of leukemia induction by this compound. However, the study was conducted on a small population group, without dividing the subjects by exposure, and should be expanded and repeated. Epigenetic aging biomarkers, on the other hand, are changes in leukocyte DNA that increase morbidity and mortality. A study analyzing the effect of occupational formaldehyde exposure and lack of exposure (31 exposed, 39 controls) showed that there was no evidence of an effect of formaldehyde on epigenetic age acceleration [42]. In contrast, Mundt et al. [43] in their analysis observed no association between formaldehyde exposure during resin factory work and the incidence of aneuploidy (which serves as an indicator of myeloid leukemia risk). Allegra et al. came to similar conclusions [44] after analyzing the results of 81 primary studies. They found no confirmation of the effect of formaldehyde exposure on the risk of developing acute myeloid leukemia. More thorough research conducted on larger study and control groups are needed to unequivocally confirm or reject the thesis that formaldehyde may have an effect on the development of leukemia.

Bronchial asthma and nervous tissue diseases from long-term formaldehyde exposure. Asthma is a serious disease of the airways, associated with their inflammation and narrowing, and can affect both adults and children. According to the WHO [45], it is the most common chronic disease in children. In 2019, asthma affected 262 million people worldwide and caused 455,000 deaths. A large meta-analysis by Juleen Lam et al. [46] found a significant effect of formaldehyde exposure and the frequency of asthma diagnosis and severity of symptoms among both children and adults. In children, a 10 $\mu g/m^3$ increase in formaldehyde exposure was associated with a higher rate of asthma diagnosis (OR = 1.20, 95% CI: [1.02, 1.41]). A positive association with childhood asthma exacerbation was also confirmed (OR = 1.08, 95% CI: [0.92, 1.28]).

Jiufei Duan et al. [47] analyzed the effect of exposure of asthmatic subjects to formaldehyde and diisononyl phthalate on the development of neuroinflammation in the brain, and investigated the mechanism of this effect. The results of the study suggest that diisononyl phthalate and formaldehyde may be factors that induce an increase in oxidative stress and activate NF-κB, leading to an increase in pro-inflammatory factors (IL-1β, IL-17 and NGF) in brain tissue. Consequently, this can exacerbate neuroinflammation in the brain. The implication is that formaldehyde has a pro-inflammatory effect, not only on the respiratory tract, but also may have a more systemic effect and affect nerve tissue. Another study by Noemie Letellier et al. [48] analyzed the effects of formaldehyde exposure on the brain. They used data from the large French CONSTANCES cohort, and analyzed the effects of occupational exposure to formaldehyde on the development of cognitive impairment among workers aged 45 and older. The study involved 75,322 workers exposed to high concentrations of formaldehyde for long periods of time. The results confirmed the effect of high-dose formaldehyde during long-term exposure on cognitive impairment, with a dose-effect relationship for exposure continuance.

SUMMARY

Human exposure to formaldehyde is widespread due to the large distribution of this toxic substance in the environment, and enters the human body mainly through inhalation. Definitely higher concentrations of formaldehyde in the air are recorded indoors than outdoors. Many workers, because of the place and type of work they perform, are exposed to significant concentrations of formaldehyde. Adequate worker education on exposure prevention, compliance with withdrawal period for products containing formaldehyde, replacement of materials with those containing lower concentrations of formaldehyde, air purification systems and less use of formaldehyde in products, can reduce the adverse effects of exposure.

There is evidence of a link between exposure to formaldehyde and an increased risk of cancer, particularly nasopharyngeal cancer and leukemia. Although a number of studies also indicate an increased risk of developing asthma and nervous tissue diseases as a result of formaldehyde exposure, there is a lack of new studies conducted on larger groups; therefore further analyses in this regard are crucial.

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