KRÓL, Dominika, SAK, Justyna, MAZURKIEWICZ, Wojciech, NOWIŃSKI, Michał and FUS-MAZURKIEWICZ, Laura. The effect of air pollution on the risk of inflammatory bowel disease, colorectal cancer and appendicitis. Journal of Education, Health and Sport. 2024;60:76-89. eISSN 2391-8306. https://dx.doi.org/10.12775/JEHS.2024.60.005
https://apcz.umk.pl/JEHS/article/view/48168
https://zenodo.org/records/10663344

The journal has had 40 points in Minister of Science and Higher Education of Poland parametric evaluation. Annex to the announcement of the Minister of Education and Science of 05.01.2024 No. 32318. Has a Journal's Unique Identifier: 201159. Scientific disciplines assigned: Physical culture sciences (Field of medical and health sciences); Health Sciences (Field of medical and health sciences).
Punkty Ministerialne 40 punktów. Załącznik do komunikatu Ministra Nauki i Szkolnictwa Wyższego z dnia 05.01.2024 Lp. 32318. Posiada Unikatowy Identyfikator Czasopisma: 201159. Przypisane dyscypliny naukowe: Nauki o kulturze fizycznej (Dziedzina nauk medycznych i nauk o zdrowiu); Nauki o zdrowiu (Dziedzina nauk medycznych i nauk o zdrowiu).© The Authors 2024;

The authors declare that there is no conflict of interests regarding the publication of this paper.
Received: 17.01.2023. Revised: 08.02.2024. Accepted: 15.02.2024. Published: 15.02.2024.

The effect of air pollution on the risk of inflammatory bowel disease, colorectal cancer and appendicitis

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Keywords
air pollution, inflammatory bowel disease, colorectal cancer, appendicitis

Abstract
Introduction and objective
Intense industrial development is contributing to increased emissions of air pollutants. Numerous studies indicate a link between air pollution and a higher risk of pulmonary and cardiovascular diseases. Our goal is to analyze available scientific studies to demonstrate the relationship between air pollution and the risk of developing and complicating inflammatory bowel disease, colorectal cancer and appendicitis.
Brief description of the state of knowledge
Air pollution is a global health challenge. Particles such as PM, nitrogen oxides, sulfur oxides or ozone have a significant impact on health. Studies suggest a link between pollution and intestinal diseases (IBD, CRC, appendicitis). Air pollutants can affect the gut by causing inflammation, oxidative stress and disruption of the gut

microbiota. Exposure to PM2.5 can increase the risk of IBD, CRC, and PM10 can increase the risk of UC. There is a correlation between pollution and the rate of hospitalization for IBD. In addition, exposure to PM2.5 increases the risk of colorectal cancer mortality. Short-term exposure to air pollution is associated with more hospitalizations for appendicitis.
Summary
Air pollution is a real health risk. Reducing air pollution could potentially reduce the risk of developing these intestinal diseases and their complications. Despite the potential links, further research is required to better understand the mechanisms of action of pollutants on intestinal health. Urgent and coordinated global and local action is needed to reduce air pollution emissions and protect the health of the public.

Abbreviations

PM2.5 - particulate matter with aerodynamic diameter < 2.5 μm; PM 10 - particulate matter with aerodynamic diameter < 10 μm; NO2 - nitrogen oxide, SO2 - sulfur oxide; O3 - ozone; IBD - inflammatory bowel disease; CRC - colorectal cancer; UC - ulcerative colitis

Introduction

Modern society faces a global health challenge from air pollution. Comprising particulate matter (PM), volatile organic compounds and a range of gaseous substances such as nitrogen oxide (NO2), sulfur dioxide (SO2), ozone (O3) and carbon monoxide (CO), it is a significant factor affecting human health [1]. Intense industrial development and associated chemical emissions have the potential for negative health effects [2]. Focusing attention on previous studies, increased concentrations of air pollutants have been correlated with a higher risk of hospitalization, as well as with a decline in lung function, which may have implications for the development of asthma or chronic obstructive pulmonary disease. They have also been associated with increased rates of cardiovascular disease, including mortality from myocardial infarction and stroke [3,4]. Increased cancer mortality has been linked to exposure to particulate matter [5]. However, there is a growing body of evidence suggesting a possible link between air pollution exposure and gastrointestinal health, particularly the colon. This paper focuses on an analysis of studies suggesting a link between exposure to air pollution and the occurrence of

intestinal diseases, such as inflammatory bowel disease (IBD), colorectal cancer (CRC) and appendicitis. The purpose of this study is to review the available scientific reports and analyze them to demonstrate the relationship between air pollution and the risk of development and complications in patients with the listed disease entities. Studies published in reputable sources such as PubMed, Google Scholar and other available publications were reviewed to better understand this potential relationship. Discussing this issue is crucial to understanding the effects of air pollution on public health, as well as to identifying areas for further research and preventive interventions.

State of knowledge

Impact of air pollution on the pathomechanism of colorectal diseases

The effect of air pollutants on the gut is an issue that has not been fully understood. These substances, usually inhaled into the lungs, have the ability to penetrate the bloodstream and reach the intestines. In addition, PM particles, which are removed from the lungs by the ciliary-mucosal apparatus, can be ingested, resulting in their entry into the intestines. Pre-entry into the gastrointestinal tract can result from the ingestion of food and water that may be contaminated [3]. The negative effects on the gut are thought to be due to inflammation, oxidative stress, and changes in the intestinal microflora as a result of harmful airborne substances, especially PM2.5. These pollutants can increase inflammation through increased production of pro-inflammatory cytokines such as IL-6, IL-8, and tumor necrosis factor. The result can be damage to intestinal cells and increased permeability of the intestinal barrier [1,5,6]. Exposure to air pollution can also affect the gut microbiota, leading to a reduction in the diversity of microorganisms in the gut. Urbanization, antibiotics, poor diet and living in urban areas are all factors that can reduce the diversity of the gut microbiota [7]. Exposure to PM10 can lead to a disruption in the production of fatty acids and butyrate, which plays an important protective role for colon epithelial cells, which in turn affects microbiotic balance and gut health [6]. In addition, oxidative stress caused by air pollution can promote the development of intestinal cell mutations and increase the risk of developing cancer [5]. It is suggested that the possible negative effects on the body and intestinal health correlate with each other, increasing the possibility of developing diseases and their complications. However, there is a

need for further research into the exact mechanism of action of air pollutants on intestinal health to reduce the risk of their effects on metabolic function and the intestinal microbiota.

Inflammatory bowel diseases

Inflammatory bowel disease (IBD) is a term that primarily includes Crohn's disease (CD) and ulcerative colitis (UC). These are chronic inflammatory conditions of the intestines, resulting from an impaired immune system response to an abnormal intestinal microbiome, with a concomitant genetic predisposition. However, genetics explains only part of the risk of the disease, while environmental factors play a significant and important role in the development of the disease and its natural course [8]. An interesting theory suggests that westernization of lifestyle may initiate chronic inflammatory bowel disease or exacerbate existing conditions in genetically susceptible individuals [9]. The increasing incidence in developing countries, where low prevalence has previously been reported, suggests that IBD is related to both the adaptation of Western lifestyles and the process of industrialization [10].

A study by Kaplan and colleagues found that the risk of developing inflammatory bowel disease (IBD) increases in people under the age of 23 who live in areas with higher concentrations of sulfur dioxide (SO2) and nitric oxide (NO2). The study's conclusions indicated a higher prevalence of ulcerative colitis in areas exposed to SO2, while Crohn's disease was more prevalent in areas exposed to NO2 [11].

Fine particles such as PM2.5 may be more associated with IBD risk than larger particles (PM10), with differences due to factors such as gender and smoking. According to a study by Giovanni Adami and team (2022), exposure to PM2.5 increased the risk of developing IBD. Coarse-grained particles (PM10), on the other hand, showed no such association. These results suggest that finer particles may have a more significant effect on the development of IBD than larger particles [12]. Another study by Rong Li and colleagues (2022), examining long-term exposure to PM2.5, PM10, NO2 and NOx, observed similar results in the context of ulcerative colitis (UC) risk. A significant increase in risk occurred with exposure to the aforementioned substances in non-smokers. An interesting aspect of the results was the suggestion of a protective effect of cigarette smoking on the development of UC, which corresponds with previous studies on the effect of nicotine on reducing the risk

of gastrointestinal diseases. It is worth noting that the risk of developing Crohn's disease has not been clearly linked to the substances studied, but observations indicate that exposure to NO2 significantly increased this risk in men [13].

Not all studies have confirmed a clear link between specific air components and the onset of inflammatory bowel disease (IBD). A study conducted by the European Prospective Investigation on Cancer and Nutrition team sought to identify a link between exposure to air pollution and IBD. It was discovered that air pollution increases the incidence of IBD, but it was not possible to correlate this with individual components, but rather as a co-occurrence of different elements in the air. Additionally, it has been observed that traffic can increase the risk of IBD [14]. Similarly, another retrospective study found no clear relationship between specific air components and the development of inflammatory bowel disease. In contrast, it was noted that exposure to an oxidant (Ox) in childhood was associated with the risk of IBD in children under the age of 18. These findings may suggest that individual concentrations of particular air components may be less important in the development of IBD, and their potential to induce oxidative stress may be more important [15].

There is a hypothesis that maternal exposure to air pollutants could potentially increase the risk of IBD in the child, however, there are not enough studies to conclusively confirm this. Previous observations indicate that maternal exposure to an oxidant (Ox), especially during the second trimester of pregnancy, was associated with an increased risk of IBD in the child [15]. In analyzing the impact of air pollution on the course of inflammatory bowel disease (IBD), accumulated data show a number of associations between air quality parameters and various health aspects in IBD patients.

A study by Ananthakrishnan and colleagues suggests that an increase in emissions correlates with an increased incidence of hospitalization for IBD [19]. Nejad and colleagues noted in their study that CO may influence the increase in hospitalizations due to UC. However, they also observed that it is possible that O3 has a protective effect when it comes to Crohn's disease exacerbation [17]. Short-term exposure to elevated concentrations of air pollutants is associated with more frequent outpatient visits. Such conclusions are drawn from a study from China that analyzed the relationship between increased outpatient visits for inflammatory bowel disease and

short-term increases in PM10, PM2.5, NO2, SO2, and CO concentrations [18], and increased PM2.5 concentrations and increased outpatient visits for UC, particularly in young people [19]. The increase in outpatient visits may have been associated with more frequent exacerbations of previously diagnosed IBD.

It is worth noting the work of Chen et al. which shows that increasing concentrations of PM2.5, PM10, NO2, NOx are associated with a higher risk of death in IBD patients due to various causes. At the same time, current studies do not show a direct link between increased concentrations of air pollutants and the development of gastrointestinal cancer. However, associations between PM2.5 concentrations and the risk of enterotomy appear to be important, indicating potential side effects associated with exposure to these substances [20].

However, it is important to keep in mind that conflicting study results may be due to differences in methodology, study population and external factors. More research is needed to better understand these associations and their implications for disease prevention and management in patients with IBD. Nonetheless, the results suggest that reducing air pollution may benefit healthy individuals by reducing the risk of developing IBD and in patients diagnosed with IBD by potentially reducing disease exacerbations and preventing complications.

Colorectal cancer

Air pollution, particularly exposure to PM2.5 in both the short and long term, has been linked to a significant increase in the risk of colorectal cancer. A study by Jenwitheesuka and team found a direct link between exposure to PM2.5, soot and organic carbon and an increased risk of colon cancer. Other components of air pollution, such as sulfates, did not show a significant association with increased risk of the disease [21]. Many other studies confirm this correlation. For example, analyses by Chu and team and other scientific reports indicate a significant association between PM2.5 exposure and increased risk of colorectal cancer [22-25]. In addition, there is evidence to suggest that exposure to PM2.5 may increase the risk of precancerous colorectal conditions by 14%, and areas with higher PM2.5 pollution are correlated with a higher risk of developing this cancer [26]. Also of interest are findings suggesting that five specific genetic loci interact with PM2.5 exposure to increase the risk of developing colorectal cancer. These genetic variants may

influence cancer risk through the VEGF receptor signaling pathway, which is associated with vascular function and inflammatory responses [22]. The discovery of these loci may help develop new diagnostic and therapeutic approaches.

The present study analyzed the impact of air pollution on colorectal cancer complications. It is hypothesized that exposure to PM2.5 exacerbates clinicopathological manifestations in symptomatic colorectal cancer, causing a 21% increase in progression from preclinical to clinical status [26]. Also, observational results on the effect of air pollution on colorectal cancer mortality are significant. Studies show that PM 2.5 concentrations ≥12 μg/m³ are associated with a 20-30% increase in mortality risk, and an increase of 10 μg/m³ PM2.5 increases the likelihood of mortality risk by 9% [27,28]. Furthermore, there is evidence of an increased risk of death from CRC associated with PM2.5 exposure that co-occurs with other air pollutants such as NO2 and O3 [29,30]. In addition, each 6.5 ppb increase in NO2 concentration has been shown to be associated with a 6% increase in colorectal cancer mortality [29]. In conclusion, there is a consistent correlation between PM2.5 exposure and the risk of CRC and associated deaths. Reducing exposure to air pollution may have the potential to reduce the incidence of this cancer and its negative consequences, including mortality.

Appendicitis

Appendicitis is one of the most common cases that require immediate abdominal surgical intervention. The primary treatment in this situation is appendectomy, or surgical removal of the appendix [31]. Previous studies suggest that air pollution can significantly affect the risk of appendicitis. Studies, such as the work of Kaplan and colleagues, show that short-term exposure to substances such as SO2, NO2, O3, CO and PM10 may be associated with a higher risk of appendicitis [32]. The Xin Yi Yi study also confirmed significant associations of short-term exposure to PM10, SO2 and NO2 with more frequent hospitalizations for appendicitis, further suggesting that gaseous pollutants may have a greater impact than PM10 [33]. Analyses of studies indicate a higher incidence of appendicitis in men. This may be related to outdoor work, such as roadwork, which increases exposure to the effects of air pollution [32,33]. In addition, studies suggest a differential risk based on age. Ji Yu and colleagues noted a higher risk of appendicitis in those aged 21-39 years [33], while

Kaplan and team found an increased risk in young adults after ozone exposure and in older adults after nitrogen dioxide exposure [3]. Another study by Kaplan suggests that age and gender do not appear to affect the association between O3 and appendicitis in the groups studied [34].

Some associations between appendicitis risk and weather conditions have also been observed, although these results are inconclusive [32, 33]. For example, on warmer days (>23°C), increased admissions for appendicitis were associated with PM2.5, NO2, CO and O3, while on colder days (<23°C), increased hospitalizations were associated with PM10, NO2 and O3 [35]. Complicated appendicitis includes perforation of the appendix, the presence of a periappendiceal abscess and peritonitis as a consequence of appendiceal infection [36]. It is hypothesized that short-term exposure to elevated concentrations of ozone [34] and PM10 [37] may increase the risk of developing perforated appendicitis. Exposure to PM10 is also possible with a higher incidence of complicated appendicitis [38]. Nevertheless, the relationship between air pollution exposure and the risk of appendicitis is still poorly studied. Nevertheless, there is a suggestion that reducing air pollution levels may reduce the number of emergency surgical interventions associated with acute appendicitis, as well as the occurrence of its complications.

Summary

An analysis of previous research on the effects of air pollutants on colorectal health indicates a likely link between these factors and disease development. Studies suggest that air pollutants may be a risk factor for inflammatory bowel disease, colorectal cancer and appendicitis. Importantly, they not only increase the risk of disease, but also exacerbate potential complications, including significantly increasing the risk of death associated with these conditions. An apparent trend indicates that residents of highly urbanized areas are particularly vulnerable to the adverse effects of air pollution on colorectal health. Intense urban development often correlates with higher pollutant emissions, compounding the risk of the ailments mentioned above and their complications. Implementing strategies that include both global measures and local actions to reduce air pollutant emissions is a key element in protecting colorectal health and reducing the risk of the aforementioned complications. The implementation of a comprehensive approach, based on public education and public

policy changes, has the potential to effectively reduce the impact of air pollution on increasing the incidence of the aforementioned diseases and the associated serious risks to human health. However, further research in this area is needed to better understand the mechanisms of the negative impact of air pollution on these conditions, which could open the way for the development of new diagnostic and intervention methods.

Funding statement: No external funding was received to perform this review

Conflict of interest: The authors declare no conflict of interest

Authors contribution: Conceptualization: Dominika Król, Laura Fus-Mazurkiewicz, Michał Nowiński; methodology: Justyna Sak, Dominika Król; formal analysis: Wojciech Mazurkiewicz, Michał Nowiński, Dominika Król; investigation: Justyna Sak, Michał Nowiński, Wojciech Mazurkiewicz, Dominika Król, Laura Fus-Mazurkiewicz; writing - rough preparation: Justyna Sak, Michał Nowiński, Wojciech Mazurkiewicz, Dominika Król, Laura Fus-Mazurkiewicz: Writing -review and editing: Justyna Sak, Michał Nowiński, Wojciech Mazurkiewicz, Dominika Król, Laura Fus-Mazurkiewicz; visualization: Dominika Król.

All authors have read and agreed with the final, published version of the manuscript.

Board statement: Not applicable - this review included analysis of the available literature.

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