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IMPACT OF AIR POLLUTION ON DEPRESSION AND SUICIDE

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Abstract

Air pollution is one of the greatest public health threats worldwide. All substances appearing in excessive quantities in the atmosphere, such as particulate matter, nitrogen oxides or sulphur oxides may be its ingredients. Depending on their size and nature, these compounds may cause greater risk of suffering from respiratory or cardiovascular diseases for exposed people as well as exacerbation and increased mortality due to these illnesses. Smaller particles may penetrate the brain's blood barrier and thus affect the central nervous system. In many studies, they have been shown to have negative effects on brain structure, like diminishing white matter or neuronal degeneration, leading to the earlier onset of Alzheimer or Parkinson disease. Nevertheless, there are reports of association of air pollution with mood disorders, depression, and even suicide. There are many risk factors for these conditions, most important of which are the social situation or chronic diseases. However, it has also been confirmed that the environment may affect mental health. This article will present experimental, clinical and epidemiological studies on exposure to air pollution and its impact on depressive disorders and suicide. Our goal is to determine the relationship between air pollution and incidence of depression and suicides. Int J Occup Med Environ Health 2018;31(6):711–721

Key words:
Depression, Suicide, Mental health, Air pollution, Air quality, Mood disorders

INTRODUCTION

Poor air quality is now one of the most important environmental problems in the world. Substances occurring in excessive concentrations in the air and causing air pollution include: carbon (CO, CO_2), nitrogen (NO_x) and sulfur oxides (SO_2, SO_3), fluorine (F), ozone (O_3), hydrocarbons, phenols or particular matter (PM). Depending on the average aerodynamic particle size, PM_{10}, $PM_{2.5}$ and ultrafine particulate matter (UFPM) of < 0.1 μm are distinguished.

Polluted air affects health, increases morbidity and mortality due to cardiovascular and respiratory diseases [1]. According to the European Environment Agency (EEA) report, in Europe, 467 000 people die prematurely due to air pollution. In Poland for instance, only one component of air pollution, particulate matter, with a mean aerodynamic particle below 2.5 m ($PM_{2.5}$) causes more than 48 000 premature deaths per year [2]. This is most often associated with respiratory and cardiovascular diseases [3]. Nevertheless, more and more evidence is emerging that these harmful compounds may reach every organ, even beyond the cerebral blood barrier. What happens with them when they reach brain is a subject of a numerous of investigations that may explain their impact on mental health. It is known, mostly from epidemiological data, that there is an association between poor quality of

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air and psychiatric conditions, including neurodegenerative diseases, depression and suicide attempts. Of course, there is a variety of risk factors, nevertheless air pollution may be one of them.

Suicide, as the most serious consequence of mental diseases, may result from many variables such as alcohol abuse, difficult life situations or social isolation. However, the most important risk factor is mental disorder. It is estimated that around 60–80% of all suicide victims suffer from depression, while 15% of patients with severe depression eventually commit suicide [4]. The influence of environmental factors such as meteorological variables (air temperature, humidity, atmospheric pressure) [5] is also proven, but little is known about the possible effects of air pollution on mental health.

In our article we will briefly explain how air pollution impacts on nervous system, then we will present experimental, clinical and epidemiological studies related to an exposure to air pollution and its impact on depression and suicide. The aim of this article, in addition to determining the impact of air pollution on depression and suicide, is to provide sufficient evidence to support intervention strategies aimed to protect human health against further adverse effects caused by bad air quality.

MATERIAL AND METHODS

The study was conducted in the electronic databases MEDLINE and Scopus. The relevant articles were searched by keywords and medical topics (medical subject headings, MeSH): air pollution, air pollutants, suicide, suicide, depression, mood disorders, affective disorders. We followed Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Peer-reviewed and academically published observational or experimental articles in English were included. We excluded papers concerning indoor air pollution and tobacco smoking. The 558 publications were collected, 406 of which did not meet our criteria or were duplicated. The 39 articles were excluded during full text screen. We qualified 12 articles concerning depression, 9 – suicides.

AIR POLLUTION'S EFFECT ON NERVOUS SYSTEM

There are many mechanisms by means of which air pollutants may cause pathologies of the nervous system. Experimental studies have confirmed that one of the main components of air pollution, $PM_{2.5}$, as well as compounds adsorbed on its surface, causes cell cycle arrest and apoptosis of neurons. This action, together with the oxidative stress and gene damage induced by these particles, may lead to degenerative changes in the brain [6].

Moreover, substances occurring in smog may also cause systemic infection. In response to the exposed organism, an increased number of immune cells produces cytokines that pass through the blood-brain barrier via active transport. In response, there is an increased migration of monocytes to the central nervous system [7]. This phenomenon was confirmed in the brain tissue analysis of people who lived in highly polluted areas. Increased CD-68, CD-163 and HLA-DR cells (indicating infectious monocytes or increased microglial activity in the patient), elevated inflammatory markers (interleukin-1β, IL-1), endothelial cell activation, prefrontal brain damage, increase in Aβ42 protein (Alzheimer's protein) and damage to the blood – brain barrier were detected [8]. Hippocampus is most susceptible to inflammatory damage due to multiple receptors for proinflammatory cytokines such as interleukin (IL) 1 p, IL-6 and tumor necrosis factor α (TNFα) [9]. In research on the etiology of affective and cognitive disorders, attention is increasingly focused on the generalized inflammatory state [10].

In addition, it has been confirmed that ozone and particulate matter interfere with cerebral blood vessels by modulating the expression of genes involved in key vasoreactive pathways in the brain [11]. This is consistent with increased prevalence of cerebral stroke in populations exposed to increased air pollution [12].

Also, neurodegenerative diseases may be associated with poor air quality. It has been shown, that air pollution induces a decrease in white matter volume in older adults [13] and may be a risk factor for Alzheimer disease. It represents 60–80% of dementia [14], and one of its causes is deposition of amyloid plaques in the brain. In studies of animals exposed to contaminated environment, symptoms of increased oxidative stress, premature appearance of amyloid plaques and a significant increase in the number of DNA lesions in the olfactory bulb, frontal cortex and hippocampus were observed [15]. Other publications also show that heavy metal particles (nickel and vanadium) get through the nose and the olfactory tract reaches the frontal cortex. This may indicate that the early symptoms of Parkinson's and Alzheimer's disease due to damage to the olfactory tract may be caused by air pollution [16].

Additionally, air pollution's compounds may have a specific impact on a cell cycle. It is shown, that simultaneous exposure to $PM_{2.5}$, SO_2 and NO_2 results in impaired apoptosis gene expression (p53, bax and bcl-2), which may lead to neuropathic changes, memory disorders and spatial orientation [17].

Overall, the complexity of the interaction of air pollution on the nervous system may be due to the multitude of inhaled compounds coexisting. However, to better understand the effect of smog, clinical and epidemiological aspects should also be considered.

AIR POLLUTION AND DEPRESSION

Depressive disorders are one of the most common problem affecting approximately 350 million people worldwide, which accounts for about 5–6% of the population [18]. It may lead, among others, to a significantly reduced quality of life [19], an increased risk of morbidity and mortality from cardiovascular diseases [20] and even a rise in suicides. There are many environmental factors that may cause its higher risk, including ambient air pollution. Although, it has been confirmed that also polluted air within households may cause depressive mood in vulnerable individuals [21,22].

Scientists proposed many possible mechanisms to explain this phenomenon. Experimentally it has been shown that particulate matter may be transported through the bloodstream [23] and directly through the olfactory pathway [24] to the brain. This has been confirmed by finding particles in olfactory neurons, intracellular erythrocytes in the frontal lobe [15]. It is possible due to its small size, which allows some particles to penetrate through lungs and blood-brain barrier to reach neurons [25]. Consequently, those compounds may stimulate innate immunity. It has been confirmed that particular matter induces proinflammatory cytokines (IL1-β, TNFα and INFγ) in olfactory neurons [26]. Studies have shown that exposure to $PM_{2.5}$ in mice causes, in addition to neuropathic inflammation, changed morphology of hippocampal neurons which may lead to altered affective behaviors and impairment of cognitive abilities [27].

Particulate matter

Numerous studies have documented that exposure to particular matter may be associated with more frequent incidences of depression (Table 1). This association was specified in the Kim study, where it was found that the risk of a depressive episode rises with increasing concentration of $PM_{2.5}$ by 10 $\mu g/m^3$, especially in people who suffer from concomitant chronic diseases [28]. Another study has shown, that the increase in PM_{10} as well as NO_2 and O_3 may lead to the onset of depressive symptoms among the elderly, which is most strongly associated with emotional symptoms [29]. Pathogenesis is probably related to particular matter induced oxidative stress and generalized inflammation. Experimental studies suggest that both pathomechanisms have been associated with vascular lesions and neurodegenerative disorders [30]. As a result, these processes may cause or exacerbate the symptoms of depression [31].

Table 1. General characteristics of studies concerning relationship between depression and air pollution

Author	Study design	Exposure assessment	Main outcome
Perera et al. (2006) [45]	prospective cohort study	polycyclic aromatic hydrocarbons (PAH)	high prenatal exposure positively associated with anxious/depressed symptoms and attention problems
Fonken et al. (2011) [27]	experimental study	particulate matter	long-term exposure to particulate air pollution levels alter affective responses and impair cognition
Lim et al. (2012) [30]	cross-sectional study	PM_{10}, nitrogen dioxide, ozone	increases in PM_{10}, NO_2, and O_3 levels may increase depressive symptoms among the elderly
Davis al. (2013) [44]	experimental study	nPM	increased depression-like responses after prenatal exposure to nPM
Cho et al. (2014) [22]	time-stratified case-crossover study	sulphur dioxide, PM_{10}, nitrogen dioxide, carbon monoxide	SO_2, PM_{10}, NO_2, and CO significantly increase the risk of ED visits for depressive episode, especially among individuals with cardiovascular disease, diabetes mellitus, or asthma
Wang et al. (2014) [47]	prospective cohort study	$PM_{2.5}$, sulfates, black carbon, ultrafine particles	no evidence of a positive association between depressive symptoms and mean pollutant levels in the preceding 2 weeks
Mokoena et al. (2015) [41]	experimental study	ozone	ozone inhalation induces memory impairment, anxiety and depression-like effects
Zijlema et al. (2016) [42]	cross-sectional cohort study	PM_{10}, nitrogen dioxide	heterogeneous results of associations of the air pollutants and depressed mood
Szyszkowicz et al. (2016) [35]	case-crossover study	$PM_{2.5}$, nitrogen dioxide, sulphur dioxide	positive association between exposure to air pollution and visits for depression
Kioumourtzoglou et al. (2017) [34]	prospective cohort study	ozone, $PM_{2.5}$, PM_{10}	association between both long-term ozone and $PM_{2.5}$ exposure and depression onset, specifically stronger with antidepressant use
Lin et al. (2017) [43]	cross-sectional study	sulphur dioxide, sarticulate matter	dose-dependent association between air pollution and emotional stress during pregnancy
Tallon et al. (2017) [28]	observational, longitudinal, population-based study	$PM_{2.5}$	positive associations between recent long-term ambient $PM_{2.5}$ levels and erectile dysfunction, depression and stress

$PM_{2.5}$ – particulate matter, particles with a diameter of 2.5 μm or less; PM_{10} – particulate matter, particles with a diameter of 10 μm or less; NO_2 – nitrogen dioxide; O_3 – ozone; SO_2 – sulphur dioxide; CO – carbon monoxide; nPM – nanoparticulate matter; ED – emergency department.

Ozone

The influence of ozone exposure on the incidence of depression [32,33] has also been confirmed. Kioumourtzoglou et al. [34] in prospective cohort studies among a large group of women have demonstrated an association between prolonged exposure to this allotropic variant of oxygen and $PM_{2.5}$ and depression. It was particularly strong in people taking antidepressants [34]. Another article has shown a positive association of short-term exposure to ozone and depressive episodes. In the case of women, exposure to ozone was associated with an increased risk of medical visits due to this condition from 1 to 7 days after exposure, while in men between 1 and 8 days [35]. Also, the study of Tallon et al. [32] proved relationship between exposure to increased concentrations of $PM_{2.5}$, NO_2, and O_3, depressive episodes and erectile dysfunction among older men. However, statistical significance has not been demonstrated [32].

To understand an impact of ozone on mental health, it is crucial to explain ways it may distort processes in human body. It has been shown, that ozone may affect the immune system, irritate mucous membranes, alter neurotransmitters concentrations such as serotonin, which play a major role in impulse responses, and thereby increase the risk of suicide [36]. Moreover, exposure to ozone may lead to brain lipid peroxidation, neuronal death in the substantia nigra [37] and thereby to motor disorders [38] and memory impairment [39]. In animal studies, it has been observed that ozone exposure results in the production of cytokines in the brain such as IL-6 and TNFα, as well as vascular endothelial growth factor, which, however, may be considered a beneficial compensatory response. Moreover, Thomson found that exposure to ozone induced a twofold increase in serum cortisol levels, which is elevated in depressive states without affecting adrenaline levels [40].

Other data indicates that chronic ozone inhalation results in cortical and hippocampal changes that involve reduced oxygen suppression and catalase activity, as well as lowered central monoamine levels similar to those observed in depression. What is more, it was found that effects of melatonin, desipramine and escitalopram are significantly impaired in the presence of ozone [41].

Nitrogen dioxide

Furthermore, numerous publications suggest, that exposure to NO_2 and NO_x increase the likelihood of depression [27,29,35]. On the other hand, a cohort study conducted in several European countries showed inconsistent results, indicating a positive correlation between long-term exposure to NO_2 in subjects in the Netherlands and negative in Norway [42].

Sulphur dioxide

Another compound of air pollution, sulphur dioxide, among others, may have a detrimental impact on mood [23,35]. Interestingly, in an article by Lin et al. it was found that women living in areas with higher levels of NO_2, PM_{10} and SO_2 in addition to increased levels of stress during pregnancy have a higher risk of depressive episodes [43].

Impact on children

It is important to mention about air pollution's possible effect on affective disorders in children. Experimental studies have demonstrated the influence of ultrafine particulate matter (UFPM < 100 nm) on prenatal development of the central nervous system and the resulting increased risk of depression [44]. Furthermore, other dangerous compounds, polycyclic aromatic hydrocarbons, have been found to cause anxiety and depression in children aged 7–8 years [45]. Air pollution also affects cognitive disorders and abnormalities in the architecture of the white matter in later childhood [46].

Nevertheless, there are reports that contradict air pollution influence on the prevalence of depression. Wang did not find evidence of the relationship between depressive symptoms in persons over 65 years of age and long-term or short-term exposure to pollution levels [24].

SUICIDES AND SUICIDE ATTEMPTS

Suicide, which may be a consequence of untreated affective disorders, accounts for nearly one million deaths per year worldwide, with a frequency of 10.1/100 000 inhabitants [47]. In Poland, this indicator is nearly twice as high (18.5/100 000 inhabitants; 32.7 for males, 4.9 for females). The etiology of this phenomenon is extremely complex, but mental disorders are the most important risk factor. It is estimated that 7–15% of patients with depressive disorders commits suicide [48]. In the case of bipolar disorder, the percentage is 15%.

Suicide is the result of a complicated interaction of many variables, including psychological features (i.e., personality traits, emotional responses), biological (genetic predispositions, drugs, co-occurring diseases) and environmen-

Table 2. General characteristics of studies concerning relationship between suicides and air pollution

Author	Study design	Exposure assessment	Main outcome
Biermann et al. (2008) [36]	population study	ozone	ozone might even be a causative agent in the multifactorial genesis of a suicide
Szyszkowicz et al. (2010) [50]	case-crossover study	carbon monoxide, nitrogen dioxide, sulphur dioxide, PM_{10}	positive association between air pollution and emergency department visits for suicide attempts
Yang et al. (2011) [56]	case-crossover study	sulfur dioxide, ozone	positive associations between suicide and air pollution, weather and unemployment data
Kim et al. (2015) [51]	nationwide study	ozone, particular matter, nitrogen dioxide, carbon monoxide, sulfur dioxide	ozone and atmospheric particulate matter increased concentrations related to suicide rate, no significant associations for nitrogen dioxide, carbon monoxide and sulfur dioxide
Bakian et al. (2015) [57]	case-crossover study	nitrogen dioxide, particulate matter, sulfur dioxide	positive associations between air pollution and suicide across study locations with vastly different meteorological, geographical, and cultural characteristics
Lin et al. (2016) [52]	case-crossover study	PM_{10}, sulphur dioxide, nitrogen dioxide	suicide risk positively associated with ambient air pollution level
Ng et al. (2016) [54]	time-stratified case-crossover study	$PM_{2.5}$, nitrogen dioxide, sulphur dioxide	$PM_{2.5}$, NO_2 and SO_2 linked to suicide mortality in certain population subgroups
Stickley et al. (2017) [53]	time-stratified case-crossover study	airborne pollen	airborne pollen linked to suicide mortality among females
Casas et al. (2017) [55]	time-stratified case-crossover study	PM_{10}, ozone	PM_{10} or O_3 may trigger suicide, particularly during warm periods; PM_{10} especially among children and elderly population

Abbreviations as in Table 1.

tal factors (support, demography). However, there are also reports that air pollution may play a significant role in suicides (Table 2).

Particular matter

It has been shown that the number of suicide attempts is increasing during the period of the highest concentrations of particulate matter in the atmosphere [49]. Still, the mechanism of this phenomenon is still tentative. In investigations where authors were looking for a relationship between timing of exposure and suicides, it has been revealed, that PM_{10} particles (with average aerodynamic ≤ 10 μm) have the highest influence 0–2 days before suicide and $PM_{2.5}$ particles 1 day before suicide. Additionally, other study concerning co-morbidity found that people with cardiovascular diseases are more susceptible to PM_{10} [50]. In a study conducted in Guangzhou, China, it has been shown that particulate matter contributes to more frequent suicide, but at different seasons of the year and to other social groups. There was an increased risk, especially in brutal ways, during the winter, while less drastic during the summer. Authors of this publication also explicit a risk groups by revealing, that this relationship was stronger for men and for those with higher

education [51]. On the other hand, in the paper from Tokyo, particular matter was associated with a 50% higher risk of suicide among women compared to days where there was practically no increased level of particular matter [52]. Among the same population, it was also found that $PM_{2.5}$ and SO_2 increase the proportion of suicide among widows and widowers [53].

Finally, the latest article from Belgium on more than 20 000 cases of suicides has also confirmed that short-term increases in PM_{10} and O_3, even below European levels, may increase the risk of suicide. In addition, PM_{10} may have a strong impact on the deaths of children and older people [54].

Sulfur dioxide

Sulfur dioxide may be also associated with an increased risk of suicide. The study conducted in Taiwan indicated sulfur dioxide and ozone as factors that increased the probability of this event [55].

Ozone

Numerous of studies show, that ozone is one of the main contributing factors for suicides. Biologically, it can affect the distribution of serotonin, which plays a major role in impulsivity, aggression, depression, and thus may affect suicide. In addition, the highest concentration of this substance coincides with the peak of suicide death in summer. Alternatively, it may be caused by the influence of higher ambient temperatures leading to more violent behavior, which may result in suicide [36].

Nevertheless, epidemiological data shows a relationship between ozone and number of suicides. Yang et al. [55] found that both sulfur dioxide and ozone increased the risk of this way of death among people who were exposed to it for a long time. This study showed significant correlations between suicide and air pollution, while also taking into account data on weather and unemployment [55]. These reports have been corroborated in the analysis of South Korea's data, where a 4-week period of high ozone concentration was correlated with a rise in suicides. Authors precise, that adjusted suicide rate was increased by approximately 7.8% during months of the highest contamination of ozone [50].

Nitrogen dioxide

Nitrogen dioxide was also investigated for its effects on suicide. In study based on nearly 30 000 cases, high levels of NO_2 have been associated with a higher risk of suicide in people under the age of 30 [53]. A similar relationship was confirmed by Szyszkowicz, who published evidence of the link between admissions to emergency departments due to suicide attempts and increased PM_{10}, CO and NO_2 concentrations [49].

Bakian's article has shown that the risk of suicide increases in people between 36–64 years who are exposed to high levels of nitrogen dioxide and $PM_{2.5}$, and this is particularly visible two days after an exposure. In addition, in case of high levels of $PM_{2.5}$ during spring and autumn, the risk increases on the second day, while for nitrogen dioxide after 3 days. Finally, after 3 days of exposure to both pollutants, the risk of violent suicide rises [56].

DISCUSSION

Air pollution may affect the central nervous system in many ways, among others through a neuropathic inflammation, an oxidative stress or a damage to blood vessels. Its components pass through the blood-brain barrier, where not only the particles themselves, but also various toxic compounds adsorbed on their surface may cause pathological changes. Taking into account the complexity of the body's response to air pollution, central nervous system pathology is probably caused by the synergistic interaction of many pathways and mechanisms.

Numerous articles suggest the relationship between air pollution and higher prevalence of depressive disorders and suicides. As we have learned, their etiology is extremely complex, as does the health effects of many sub-

stances present in the air. While epidemiology indicates an increased risk of depression and suicides in exposed to contaminated air individuals, further research is still required to fully explain these findings. Epidemiological data may show a particular dependence, but more clinical and experimental studies are needed for better understanding the impact of air pollution on mental health.

Limitations in the current study include the fact, that it was not conducted by two independent researchers and the lack of many long-term exposure studies for air pollution. Articles were also limited in diversity, according to air pollutants. Additionally, inconsistent results of included studies should require further metaanalysis to settle final conclusions. Future directions should include exploring depression morbidity and suicide statistics and compare areas with high average concentrations of pollutants to those with low pollution.

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