The effect of pollution on hypertension and on the total risk score in hypertensive patients

ESC European Society of Cardiology

ACCA Acute Cardiovascular Care Association
EACVI European Association of Cardiovascular Imaging
EAPC European Association of Preventive Cardiology
EAPCI European Association of Percutaneous Cardiovascular Interventions
EHRA European Heart Rhythm Association
HFA Heart Failure Association

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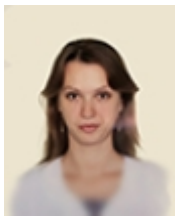
Prof. Susanna Tykhonova

Assoc. Prof Vasyl Shtanko

Dr. Olena Khyzhnyak



Dr. Nataliia Tofan

This brief description highlights some practical aspects for cardiologists regarding the effects of environmental pollution, including the causal role of fine particulate matter (PM) on hypertension development and prognosis, pathophysiological mechanisms, and potential approaches to minimise risks and improve blood pressure (BP) control.

Environmental and Occupational Aspects of Heart Disease

Take-home messages:

Abbreviations

ANS – autonomic nervous system

BP – blood pressure

CI – confidence interval

CV – cardiovascular

CVD – cardiovascular disease

CVR – CV risk

DBP – diastolic BP

DM – diabetes mellitus

NO – nitric oxide

PM – particulate matter

PM2.5 – fine PM with a diameter ≤2.5 μm

POPs – portable air purifiers

PROPs – personal respirators for air purification

SBP – systolic BP

Introduction

The development of hypertension is the result of the interaction between genetic predisposition to elevated blood pressure (BP) and environmental factors. Among them are sedentary lifestyle, weight gain, increased sodium intake, unhealthy diet, and use of pro-hypertensive substances. Environmental factors of greater geographical scale, such as air pollution, that are less subject to individual control are less frequently assessed. Reducing air pollution is a problem that requires involvement of governmental resources and public health systems. However, even in the absence of such initiatives, individual measures could be proposed for patients with hypertension which they could perform to reduce the impact of the polluted environment on their cardiovascular (CV) health. The contribution of cardiologists in solving this problem is in raising awareness of the impact of environmental pollution on the CV system, and discussing with patients the proven ways to reduce such exposure to improve BP control and CV risk (CVR) [1].

Air pollution and the incidence of hypertension

Analysis of hypertension in the world from 1975 to 2015 suggests that mean systolic BP (SBP) in men and women has decreased in the rich industrialised countries of Europe, Central Asia, the Middle East, the Caribbean and Latin America. However, there has been an increase in mean SBP and diastolic BP (DBP) in sub-Saharan Africa, South Asia and Southeast Asia [2]. It is reasonably assumed that this is a consequence of industrial activity and related environmental pollution.

Air pollution is a complex mixture of particulate matter (PM) and gaseous components that can have an independent effect on the body, or through potentially synergistic and antagonistic effects. The statements of the European, American and World Health Organisations (WHO) on air pollution discussed aspects of this problem, such as fractions, sizes, chemical components and types of gaseous air pollutants, and their impact on health. PM is classified according to aerodynamic diameter: <10 μm (PM_{10}), <2.5 μm ($PM_{2.5}$), <0.1 μm ($PM_{0.1}$) and 2.5 to 10 μm ($PM_{2.5–10}$) [3].

Recent epidemiological findings demonstrate particulate pollutants cause significant increases in BP levels in relation to both short- and long-term exposures, with robust evidence for exposures to $PM_{2.5}$. Numerous studies have demonstrated the relationship between $PM_{2.5}$levels, the concentration of pollutants associated with transport emissions

and BP elevation observed within hours to days [4, 5]. A controlled study of 3,700 participants, aged 35–83, from a population cohort in Spain showed that a 10 μg/m^3 increase in NO_2 levels was associated with 1.34 mmHg (95% confidence interval (CI), 0.14–2.55) higher SBP in those who did not receive treatment, after adjusting for traffic noise [6]. In a cohort of 35,303 non-hypertensive adults from Ontario, Canada, between 1996 and 2010, for each 10 μg/m^3 increase in $PM_{2.5}$, the hazard ratio (HR) of incident hypertension was 1.13 (95% CI, 1.05–1.22) [7]. The results of a cohort prospective epidemiological study from urban Delhi, India, with 5,342 participants, demonstrate strong longitudinal associations using repeated measures between ambient $PM_{2.5}$exposure, BP and incident hypertension. Both short- and long-term exposure contributed to higher BP and increased incident hypertension risk [8].

Some studies provide evidence toward a positive association between both short-term and long-term exposure to some air pollutants and BP among children and adolescents. In a meta-analysis of 14 articles, short-term exposure to PM_{10} and long-term exposure to NO_2, PM_{10} and $PM_{2.5}$were significantly associated with elevated BP values. A 10 μg/m^3 PM_{10} increase was significantly associated with a 0.276 mmHg (95% CI, 0.033−0.501) SBP elevation. Long-term exposure to NO_2, $PM_{2.5}$, and PM_{10} was associated with SBP elevation and long-term exposure to $PM_{2.5}$and PM_{10} was associated with DBP increase [9].

Interaction with traditional risk factors

There is a bidirectional relationship between air pollution and CV risk factors. It is reasonable to assume that environmental factors may increase the overall burden of CV diseases worldwide through interactions with traditional risk factors. For example, regions with the highest rates of hypertension and diabetes mellitus (DM) (e.g., India and Asia) also suffer from the highest $PM_{2.5}$levels and noise exposure [1]. The Environmental Protection Agency proposes to identify the most susceptible groups (e.g., elderly adults) as those at higher risk for adverse health effects than the general population facing the same level of exposure [10]. Obese people and diabetic patients might be at higher risk of CV events from exposure to $PM_{2.5}$[1, 4, 11].

Both high BP and elevated $PM_{2.5}$concentrations in polluted air are associated with an increased risk of stroke. Elevated concentrations of pollutants increase hospital admissions and/or emergency visits for hypertensive disorders. Epidemiological studies show the most pronounced negative impact of pollution among vulnerable populations such as pregnant women and patients with high CVR [11].

The study including 136,094 participants with an average 7-year follow-up period, found that a 10 μg/m^3 increase in long-term exposure to $PM_{2.5}$was associated with a 36% increased risk of CV events among healthy participants without a history of CV disease (CVD) who lived in Seoul, Korea. Air pollutants, including $PM_{2.5}$, $PM_{2.5–10}$, carbon monoxide (CO), sulfur oxide (SO2), and nitrogen oxide (NO_2), have been shown to be

positively associated with CVR after adjustment for traditional CV risk factors [12]. The attributable risk from air pollution was as large as that of conventional CV risk factors such as hypertension and DM.

Air pollution and hypertension prognosis

A meta-analysis of 6.2 million events in 28 countries demonstrated a significant association between stroke hospitalisation and/or mortality and exposure to elevated concentrations of $PM_{2.5}$ and PM10 (per 10 μg/m^3 increment) and gaseous air pollutants during the previous 7 days [13].

In a multicentre cohort study and meta-analysis of 11 European cohorts, a 5 μg/m^3 increase in annual $PM_{2.5}$ exposure was associated with a 19% increased risk of incident stroke (95% CI: 0.88–1.62). The results were robust to adjustment for other CVR factors and noise co-exposure. The association was more apparent among those ≥60 years of age (HR 1.40, 95% CI: 1.05-1.87) and among never-smokers (HR 1.74, 95% CI: 1.06-2.88) [14].

The main pathophysiological mechanisms

In recent decades, numerous studies have been conducted to elucidate the pathophysiological mechanisms of BP elevation and increased CVR due to pollution. These potential mechanisms are: (a) disorders of the autonomic nervous system (ANS) and/or sympathoadrenal overactivity; (b) release of pro-inflammatory mediators, modified lipids or phospholipids and activation of leukocyte populations; (c) endothelial dysfunction caused by oxidative stress; and (d) activation of prothrombotic pathways [15].

Direct and indirect effects of pollution on systemic vasculature

An indirect effect of particulate matter exposure, mediated through systemic proinflammatory and oxidative responses, may lead to increased sympathetic tone and potentially cause arterial remodelling. Experimental and clinical data show that PM-induced oxidative stress and reduced NO bioavailability are likely to be key factors in systemic vascular dysfunction [16], and can result in an increased total peripheral resistance and a fixation of elevated BP [17].

A direct effect of particulate matter exposure is vasoconstriction, which is a result of $PM_{2.5}$-induced ANS imbalance [18].

Additionally, exposure to PM may reduce daytime sodium excretion and weaken nocturnal BP reduction, which over time may be one of the reasons for steady elevated BP [19].

Acute and chronic responses after exposure to pollution

Acute responses may occur within seconds, minutes or hours after PM inhalation, and are probably associated with imbalance in the ANS and/or sympathetic overactivity, endothelial dysfunction, and the release of procoagulant proteins [15, 17].

To date, the time required to potentiate the impact of environmental pollution on hypertension onset remains unclear [8].

The PURE study, involving 21 countries, reported positive associations of 3-year exposure and 4% increased odds of hypertension globally. $PM_{2.5}$concentration >62 μg/m^3 was associated with 36% increased odds of hypertension compared to $PM_{2.5}$<14 μg/m^3 [20]. In a prospective cohort study in India, strong effects of long-term exposure to $PM_{2.5}$on the risk of hypertension were observed irrespective of the exposure window. Odds of hypertension increased by 53%, 59%, and 16% in the 1-, 1.5-, and 2-year periods, respectively. Significantly higher risks of incident hypertension were observed in higher quartiles of exposure, and among individuals with waist-hip ratios >0.95 [8].

When discussing the chronic impact of air pollution on the structural and functional state of the CV system, the important role of epigenetics in determining phenotypic changes should be mentioned. Epigenetic changes determine the individual diversity, severity and prognosis of the disease. Genetically identical twins who grew up in different environments have different life expectancies or risks of developing DM and hypertension. Environment modifies the epigenome, and thus provides a link to translate environmental influences on changes in gene expression and pathological preconditions. Epigenetic modifications of the renin-angiotensin system genes, which are responsible for regulating BP and many structural changes in the CV system, can lead to hyperactivity of the system, sympathetic overactivity and/or ANS dysfunction, resulting in hypertension and accompanying pathological metabolic changes [21].

Clinical approaches to hypertension prevention with reduced exposure to pollution

The American Heart Association scientific statement provides strong arguments for providing the public with practical personalised approaches to reducing the potential negative health effects of PM. The interventions are offered not only for people living in heavily polluted areas, but also for those at high CVR or from vulnerable groups, and those who travel to areas with high pollution. The statement focuses on the most proven measures and viable approaches to reduce the impact of PM pollution, and provides expert consensus on measures to reduce the impact of pollution on a personal level, while acknowledging the current uncertainty and limited evidence base for many interventions [1].

Basic principles of approaches to reduce exposure to pollution should be: (a) practical, safe and inexpensive; (b) appropriate to the patient's risk (susceptible populations); (c) applied to all who need it.

It is important to assess the risk for the patient's health and the degree of environmental pollution to select the optimal intervention. The urgency and intensity of the recommended intervention should be weighed, taking into account the potential benefit-risk balance for an individual [1, 4]. Education on pollution-mediated impact on CV adverse events should be provided to all patients, regardless of risk, especially in environments with high PM levels [4].

Individual strategies

Individual strategies to mitigate the effects of environmental pollution consist of (a) reducing personal impact, (b) behavioural habits modification, and (c) pharmacological approaches.

Portable air purifiers (POPs) are inexpensive and can be used in all homes where there is electricity. Since 2008, a few studies have been conducted using POPs on CV surrogate effects. The study participants were mostly healthy patients in the age range from schoolchildren to the elderly, and the reduction in $PM_{2.5}$ concentration indoors ranged from 18% to 82%. The studies have shown a general trend toward decreased SBP and DBP, but in some of them BP levels have not changed [1]. By experts' opinion, the use of POPs could be considered in high CVR patients [1, 22].

Personal respirators for air purification (PROPs) are individual protective devices covering the nose and mouth, and are used to reduce the inhalation of PM2.5 and other particles. PROPs N95 or N99 remove >95% or 99% of inhaled 0.3 μm size particles. A key factor in protective ability is fit and frequency of use. In the study of healthy volunteers in Beijing, China, the use of N95 respirators resulted in SBP decrease by 7 mmHg during a 2-hour walk on a prescribed route [1, 23]. Current evidence from small controlled experimental observations using standard N95 respirators for several hours or days may improve surrogate markers of CVR in areas with high $PM_{2.5}$levels, but this evidence is not supported in controlled randomised trials [1].

Surgical masks are not recommended as a protection method against pollutants, including $PM_{2.5}$. However, if PROPs are not available, a surgical mask might be considered, making sure that it fits snugly against the face, covers nose and mouth, and that it is changed frequently in high $PM_{2.5}$environments [1].

Behavioural habits modification is a strategy to avoid areas and times of greatest pollution, using changes in usual routes. But there is no current evidence that this strategy can change health status [1, 4].

An important practical issue is the need to reduce outdoor physical activity, or to limit certain physical exercises and their intensity during periods of higher pollution in order to reduce the negative health consequences [1, 4]. Some studies have evaluated the relationship between the benefits of exercise and their intensity and adverse effects of $PM_{2.5}$pollution. General results demonstrated the advantage of aerobic exercise during regular physical activity over the risk of exposure to air pollution in various concentrations [1, 4]. However, patients with CVD should be encouraged to exercise at a distance of

more than 400 m from major roads to reduce the impact of pollution, despite the lack of evidence from well-controlled studies. It is recommended to avoid walking and cycling on high-traffic streets, especially during peak hours, to exercise in parks, and to limit the time spent outdoors during heavy pollution periods [4].

According to the Green Position, it is advisable to follow eco-friendly habits in daily life: (a) 30 minutes of walking (1–2 km), considering that the WHO suggests at least 30 minutes of physical activity per day; (b) 30 minutes biking may be sufficient to buy groceries or to get to work; (c) it is better to walk or ride a bike, or use a scooter for that "last mile" on the way to the office and back. Nowadays, the majority of countries are implementing projects and programs to improve the efficiency of environmentally friendly vehicles and the organisation of eco-friendly walking routes.

There are no recommendations for additional medications to reduce pollution-mediated adverse effects, including elevated BP. However, the use of medication for primary and secondary CV prevention is supported, if indicated for other reasons. Patients at high CVR should strictly follow recommendations for doses and regimens of prescribed drugs, including antihypertensives [1]. Adherence to medicament and non-medicament recommendations (healthy diet, salt restriction) in patients at high CVR should be constantly monitored. Hypertensive patients should be explained the rules of home BP monitoring and the importance of achievement and support of goal BP.

Conclusion

Given that millions of people around the world are exposed to higher concentrations of PM, patients with already diagnosed CVD or at high CVR should be made aware about the potential negative health effects of air pollution.

Mechanisms of BP elevation induced by air pollution (oxidative stress, vascular dysfunction, ANS imbalance, and metabolic disorders) have been identified, and not only potentiate early development and worsen prognosis of hypertension, but also contribute to the progression of susceptibility to CV adverse events.

Thus, air pollution can be considered a significant but potentially modifiable CV risk factor.

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Notes to editor

Authors:

Susanna Tykhonova, MD, PhD; Vasyl Shtanko, MD, PhD; Olena Khyzhnyak, MD, PhD; Nataliia Tofan, MD, PhD

Internal Medicine Department #2, Odessa National Medical University of Ministry of Health of Ukraine, Odessa, Ukraine

Address for correspondence:

Professor Susanna Tykhonova, Center Of Reconstructive and Recovery Medicine (University Clinic) of Odessa National Medical University, Tynista Street, 8, Odessa, 65009 Ukraine

E-mail: s.tykhonova@gmail.com

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