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Association between short-term exposure to high-level particulate matter (PM_1, $PM_{2.5}$, and PM_{10}) of smoke *Peganum harmala* seeds with blood pressure: A quasi-experimental study

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Abstract

Background: Air pollution is considered one of the most important causes of premature deaths. The part of indoor pollution investigated is related to people's culture and behavior. Burning *Peganum harmala* seeds (called Espand) is a religious and cultural practice that is done by many people in Iran, India, and Morocco, which leads to the emission of particulate matters (PMs) into the environment.

Methods: This study aimed to investigate the relationship between the exposures of PMs emitted from burned *P. harmala* seeds with some cardiovascular parameters. For this purpose, the systolic blood pressure (SBP), diastolic blood pressure (DBP), and heart rate (HR) of 37 healthy participants per explanatory factors were compared before and after the exposure to PMs (PM_1, $PM_{2.5}$, and PM_{10}) emitted from burned Espand in a control room.

Results: The results showed a significant decrease and increase in SBP and HR, respectively. The decrease in DBP was insignificant. Younger people (less than 35 years) had a considerable HR increase ($P = 0.028$) compared to older people. Moreover, exposure to PMs increased the DBP of smokers and decreased the blood pressure of non-smokers. Therefore, reducing exposure to PMs emitted from burned Espand is necessary, especially for those with cardiovascular and respiratory problems and children.

Conclusion: The reduction can be made by decreasing the exposure frequency, exposure time, and burned Espand weight. Doing cultural-religious ceremonies outdoors can also considerably reduce exposure to PMs.

Keywords: Blood pressure, Particulate matter, Indoor air, *Peganum*, Air pollution

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Introduction

Air pollution is a risk factor for remarkably increased mortality and morbidity across the world (1-5). Air pollution has adverse effects on the respiratory (6) and cardiovascular systems (7,8). Many researchers have shown a greater and wide-range health effect of particulate matter (PMs) than the gaseous portion, especially on the cardiovascular system (1,9-11). PMs are a complex mixture of very small particles and liquid droplets originating from both natural and human-made (anthropogenic) sources (12,13). Based on the diameter, they include PM_{10} (diameter < 10 μm), $PM_{2.5}$ (diameter < 2.5 μm), PM_1 (diameter < 1 μm), and $PM_{0.1}$ (diameter < 0.1 μm) (14). Fine ($PM_{2.5}$) and ultrafine ($PM_{0.1}$) fractions, penetrate the alveoli and represent greater detrimental effects on health (1). According to the report of the World Health Organization (WHO), 800 000 premature deaths occur annually due to PM air pollution, ranking it the 13th main reason for mortality around the world (12). The inhalable particles (PM_{10}) are responsible for approximately 2.7% of the global burden of diseases (GBD) including acute and chronic pulmonary diseases (15). The risk of

cerebrovascular and cardiovascular diseases (heart failure, ischemic heart disease, and thrombotic/ischemic stroke) (16,17) increases as a result of short- and long-term exposure to PMs (1,12).

Exposure to PM has a significant negative impact on respiratory, cardiovascular, and to a lower extent, cerebrovascular disease (12). The information strongly shows the PMs influence on the cardiovascular system (12). Regarding increasing incidences of cardiovascular diseases (18) and other diseases (19-21), both indoor and outdoor air pollution is listed as a large environmental health risk (15,22). Based on the report of the Environmental Protection Agency (EPA), the concentrations and human detrimental effects of indoor pollutants are greater than outdoor air pollutants (23). Health effects caused by indoor air pollutants can range from coughing and sneezing to outcomes including chronic respiratory infections, asthma, and cancers (24).

PM is the main component of indoor air pollution in homes leading from various natural and human-made sources. It is generally produced in the indoor environment via incomplete combustion of common fuels and open fires (15,24,25). Annually, more than one million deaths occur worldwide due to indoor air pollution through fine PM (15). Indoor PM emission is recognized as an incidence agent of health hazards including acute and chronic respiratory diseases, asthma, lung malfunctioning, and premature births (15). Acute and chronic exposure to PM has correlated with variation in vascular function (rapid increases in systolic blood pressure [SBP], hypertension development, etc) (1).

Peganum harmala is a wild, glabrous, and perennial plant belonging to the *Zygophyllaceae* family (26-28). It is spontaneously grown in semi-arid and steppe areas, the eastern Mediterranean region, the Middle East, Central Asia, and North Africa; various parts of the plant are used for folk medicine, disinfection, and to ward off the evil eye (26,28-30). In Iran, its seeds are named "Espand", which is considered a significant medicinal plant, disinfectant agent, and burnt mixed with other ingredients used in religious and cultural practices (26,28,30,31). Burning *P. harmala* seeds makes a cloud of smoke that consists of airborne solids, gases, and liquid particles (29). This smoke can increase the particle concentration in the indoor environment (23). The highest particle concentration was observed at 5 min after burning the seeds. Among particles studied in the indoor air (PM_{10}, $PM_{2.5}$, and PM_{1}), PM_{10} had the highest concentration (23). *P. harmala* smoke was composed of the main compounds including α-pinene (60.4 %), limonene (6.4 %), and styrene (4.2%) (29,31). The major group was monoterpene hydrocarbons (72.9% for smoke) (29). The identification of smoke components using GC/MS analysis showed that the most abundant compound detected in the dichloromethane extraction was harmine (14.1%) (26). The other main compounds were henicosane (12.9%), eicosane (9.3%), nonadecane (8.1%), octadecane (7.6%), and heptadecane (6.2%) (26). It was found that the major active alkaloids of *P. harmala* (harmine, harmaline, Harman, and harmalol) have some cardiovascular outcomes for example Vasorelaxant, angiogenic inhibitory, bradycardia, increased pulse pressure, decreased systemic arterial blood pressure, peak aortic flow, and cardiac contractile force (28). According to a literature search, our knowledge about the impact of acute exposure to indoor PM (PM_{1}, $PM_{2.5}$, and PM_{10}) emitted from the smoke of *P. harmala* seeds on blood pressure is very limited. The review articles that highlighted this issue were not observed. Therefore, this study aimed to assess the association between short-term exposure to PM (PM1, $PM_{2.5}$, and PM_{10}) of the smoke of *Peganum Harmala* seeds with blood pressure parameters (SBP, diastolic blood pressure [DBP], and heart rate [HR]).

Materials and Methods

Study design and participants

This quasi-experimental study (before/after design) was performed from April 24 to May 13, 2021. Thirty-six health workers were invited to Hormozgan University of Medical Sciences, Iran. All participants were healthy and had no previous respiratory, cardiovascular or allergic disease. Before entering the control room (clean room), a questionnaire including height, weight, smoking, and disease was filled out. In the control room, each participant sat on a chair for 5 minutes, and blood pressure was measured (Figure 1). To minimize lateral stress, participants should not have seen or touched their cell phones or talked to the research team. After measuring the blood pressure parameters, each participant was led to the exposure room. Seeds (*P. harmala)* were purchased from city stores. In this study, the use of seeds (*P. harmala)* complies with national guidelines. After 5 minutes of exposure to PM of *P. harmala* seeds, blood pressure parameters were measured and recorded. To prevent the effect of daily blood pressure fluctuation, the blood pressure of all participants was measured from 10 AM to 12 AM.

Exposure to PM of *Peganum harmala* seeds

In the exposure room, 5 gr of *P. harmala* seeds were placed on lit charcoal for 1 minute, and then, extinguished. After 2 minutes, the concentration of PMs (PM_{1}, $PM_{2.5}$, and PM_{10}) was measured in the indoor air by portable Aerocet 531s (Model 531s, Met-One Company). During the exposure period, the doors and windows were closed in the exposure room. The PM concentration was continuously measured. When the PM concentration decreased, the smoke of *P. harmala* was produced.

Measurement of blood pressure parameters

Cardiovascular parameters including SBP, DBP, and

HR were measured and recorded. The parameters were measured by a portable blood pressure monitor (model 451).

Statistical analysis

The categorical and quantitative variables were reported as percentages and mean/standard deviation, respectively. The paired sample t-test was used to compare the before-after exposure for dependent variables including SBP, DBP, and HR. To assess the association of dependent variables with explanatory factors (such as gender, age categories, body mass index [BMI], and cigarette smoking behavior), a series of Mann-Whitney tests were performed. *P* value < 0.05 was considered as a significant level.

Results

The present study examined the association between short-term exposure to high-level PMs (PM_1, $PM_{2.5}$, and PM_{10}) of the smoke of *P. harmala* seeds with cardiovascular parameters (SBP, DBP, and HR) based on explanatory factors (gender, age, BMI, and smoking behavior) (Table 1). According to the results, the SBP and DBP of all participants decreased significantly and insignificantly, respectively. HR significantly increased after exposure to the smoke of *P. harmala* seeds. The findings revealed a significant decrease in SBP and an insignificant reduction of DBP in all subjects after short-term exposure to the smoke of *P. harmala* seeds (Table 2). As shown in Table 3, exposure to *P. harmala* significantly increased the HR among adults aged less than 35 years old than older individuals

Discussion

Blood pressure and exposure to Peganum harmala seeds' smoke

Environmental pollution in indoor and outdoor air (32),

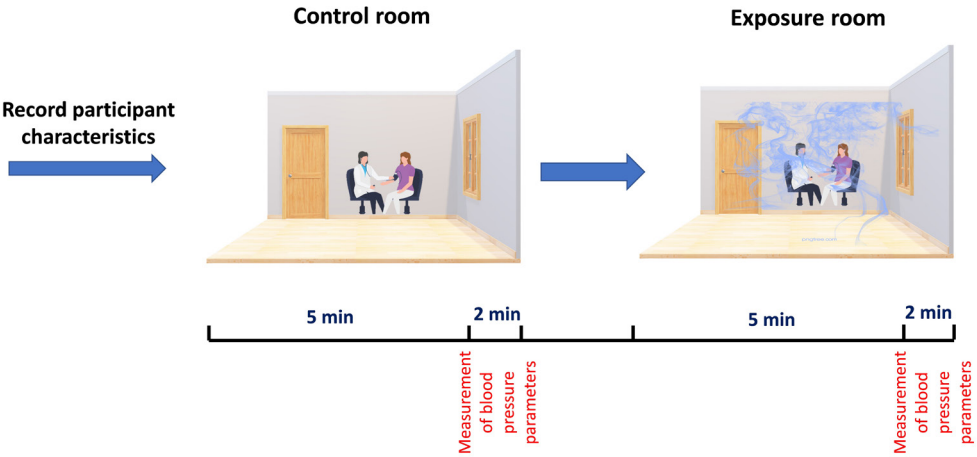

Figure 1. Flow chart of before-after study design

Table 1. Summary statistics of explanatory and environmental variables

Variable	Group	N	Percent	Mean±SD
Gender	Female	21	58.3	
	Male	15	41.7	
Age (y)	<35 years	19	52.8	34.47±8.97
	≥35 years	17	47.2	
Weight (kg)		36		64.94±12.59
Height (m)		36		1.68±0.10
BMI	Normal (18.5–24.9)	27	75.0	
	Overweight/Obese (25.0–29.9)	9	25.0	
Smoking behavior	Non-smoker	33	91.7	
	Smoker	3	8.3	
PM_1 (μg/m³)	Control			30.62±9.24
$PM_{2.5}$ (μg/m³)	Control			72.70±19.68
PM_{10} (μg/m³)	Control			203.13±55.89
PM_1 (μg/m³)	Exposure			178.53±29.79
$PM_{2.5}$ (μg/m³)	Exposure			2304.11±238.00
PM_{10} (μg/m³)	Exposure			8229.84±10267.46

water resources (33), food such as mycotoxins (34) in yogurt (35) and maize (36), etc. have harmful effects on human health. *P. harmala* is one of the popular medicinal plants that has been widely used to treat hypertension in Asia, Africa, and Europe for many years (37,38). The smoke of *P. harmala* seeds to reduce blood pressure (BP) can be attributed to its chemical ingredients, especially beta-carboline alkaloids. Various studies reported that *P. harmala* alkaloids especially harmine, harmaline, harmalol, Harman, and harmol had several cardiovascular effects such as decreased systemic arterial blood pressure (39), decreased total peripheral vascular resistance (40), increased effect on NO (nitric oxide) release from the vascular endothelial cells (41), vasorelaxant (41,42) and angiogenic inhibitory (43) effect, bradycardia (41), inducing transient hypotension and long-lasting bradycardia (40,41), increased peak aortic flow, increased cardiac contractile force, and increased pulse pressure (39,44). Seeds and roots of *P. harmala* contain high levels of various beta-carboline alkaloids such as harmaline, harmine, harmalol, harmol, and tetrahydroharmine; while a small level of alkaloids is found in the leaves and stems (45,46). Therefore, it is expected that there are some amounts of these alkaloids in the emitted PMs of *P. harmala* seed, and exposure to it leads to a decrease in BP (47).

BP reduction can also be explained by the presence of carbon monoxide (CO) in the smoke of *P. harmala* seeds. Some studies indicated that CO has a complex dual effect on BP. They reported that high levels of CO (≥1 μmol/L) lead to an increase in BP through impaired vascular relaxation and prevent vascular endothelial cells from releasing NO while low concentrations of CO (0.001 to 0.1 μmol/L) lead to a decrease in BP by stimulating NO release and vasodilation (through activating sGC to increase cGMP levels) (48-52). The study conducted by Quinn et al indicated that high levels of CO increased both SBP and DBP, but it was more effective in increasing DBP than SBP (51). Furthermore, it has been proven that CO inhalation causes an increase in blood and tissue levels of CO (50). Owing to DBP being more affected by CO and PM, it is predictable that CO inhibits more from decreasing DBP than SBP. Thus, the interaction between CO and the alkaloids of *P. harmala* led to a decrease in DBP in all participants, although it was insignificant. Lee et al. investigated the association between BP and in-vehicle exposure to CO and reported that CO affected DBP significantly and SBP insignificantly, which is consistent with the results of the present study (53).

Table 2. Comparison of SBP, DBP, and HR before and after the exposure

Variable	Time	N	Mean (mm Hg)	SD (mm Hg)	*P* value[a]
SBP	Before	36	108.32	9.50	0.001
	After	36	102.63	13.36	
DBP	Before	36	70.722	8.82	0.251
	After	36	69.85	8.38	
HR	Before	36	73.63	9.36	0.001
	After	36	77.31	10.84	

SBP: Systolic blood pressure; DBP: Diastolic blood pressure; HR: Heart rate.
[a] Paired sample t-test.

Heart rate and exposure to the smoke of Peganum harmala seeds

Several studies mentioned that exposure to *P. harmala* can decrease HR and even lead to bradycardia in acute exposure to high levels of beta-carboline alkaloids of *P. harmala* (54), which is inconsistent with the results of the present study. On the other hand, some studies have reported that high levels of PM and CO content in smoke can increase HR or can cause tachycardia (55-57). Thus, the increase in the HR after exposure to the smoke of *P. harmala* can be explained by the fact that the CO content of the smoke leads to hypoxia, which is caused by increased creation of carboxyhemoglobin instead of oxyhemoglobin, so the increased cardiac output is needed to compensate for hypoxia. Moreover, Ataee et al conducted a rare case report on acute poisoning with *P. harmala* and reported that exposure to *P. harmala* led to tachycardia (increase in the HR), which is consistent with

Table 3. Association of SBP, DBP, and HR with explanatory factors

Explanatory Variable		SBP (after-before)		DBP (after-before)		HR (after-before)	
		Mean difference	*P* value	Mean difference	*P* value	Mean difference	*P* value
Gender	Female	-7.76	0.108	-1.07	0.762	4.74	0.225
	Male	-2.80		-0.60		2.20	
Age	<35 years	-7.47	0.148	-1.50	0.281	5.97	0.028*
	≥35 years	-3.71		-0.18		1.12	
BMI	Normal	-5.78	0.694	-0.76	0.984	3.33	0.345
	Overweight/Obese	-4.88		-1.38		5.06	
Smoking behavior	No	-6.26	0.058	4.83	0.025*	-0.33	0.129
	Yes	0.50		-1.39		4.05	

SBP: Systolic blood pressure; DBP: Diastolic blood pressure; HR: Heart rate.
* Significant at level 0.05 based on the Mann-Whitney test.

the results of the present study (58).

Cardiovascular parameters and explanatory factors

Age and heart rate

With increasing age, HR decreases and BP increases due to stiffness and gradual narrowing of large blood vessels in cardiothoracic circulation, declining glomerular filtration rate, decreasing renal flow rate, and elevating blood osmolality (59-64). Therefore, younger individuals generally have higher baseline HR and lower baseline BP. Owing to *P. harmala's* increasing effect on HR, its effect was greater among younger individuals.

Gender and blood pressure

Although some studies revealed that DBP and SBP were usually higher in females than males in Iran, various studies reported that the prevalence of hypertension and the amount of BP are higher in men than women until after menopause (63,65-69). It can be due to lifestyle intervention (70). In the present study, BP and HR (before exposure to *P. harmala* smoke) were lower and higher in female and male participants, respectively. This is consistent with the results of the study conducted by Sun et al on 14657 men and 16,977 women aged 12 to 85 years, indicating that both SBP and DBP of females were lower than those of males for the same age group before women's menopause (61). In the present study, the lower BP in females can be because the average age and BMI were lower in females than in males. Various studies reported a positive association between age (59-61) and BMI (63,69,71) with BP. The findings also indicated that exposure to the smoke of *P. harmala* seed led to a greater decline in DBP and SBP and a higher increase in HR in females than males. However, these effects were insignificant. The results also showed that the increase in PM_{10} concentration in the respiratory area of men was more than that of women after exposure to the smoke of *P. harmala* seed. Due to the increased effect of PM on BP (72,73), the high concentrations of PM_{10} have declined the reducing effect of the alkaloids of *P. harmala* seed on blood pressure. More interference of extremely high levels of PM_{10} in the respiratory area of men than that of women can also be the reason for the insignificant effect of gender on reducing BP and increasing HR. Furthermore, there may be some confounding factors such as lifestyle intervention, which is different between participants, and make an insignificant association between gender and BP.

Smoking and blood pressure

There is no consensus regarding the interaction between cigarette smoking and BP (74,75). Some studies reported no relationship between smoking habits and blood pressure (75,76). A meta-analysis conducted by Linneberg et al indicated that there was no causal association between smoking in current smokers and SBP or DBP (77). Various studies illustrated that smoking led to an immediate increase in BP and HR (72). The most common reason mentioned in literature included inducing the activities of the sympathetic nervous system as a result of high nicotine (78,79), the secretion of epinephrine, norepinephrine, and vasopressin hormones (80,81), endothelial dysfunction, and vascular inflammation due to the accumulation of free radicals and active oxygen during smoking, prevention of NO release through endothelial vasodilation impairment (82), and stimulating release of thromboxane A_2, which has a strong vasoconstrictive effect (83). Furthermore, the CO content of cigarette smoke creates carboxyhemoglobin instead of oxyhemoglobin and stimulates cholesterol degeneration, which disrupts endothelial function (84). Alomari et al. conducted a study on cardiovascular changes immediately after water pipe smoking and found that smoking immediately increased DBP (85). However, there is still controversy over the long-term effect of smoking on BP (74,75). Okubo et al. in a cohort study in Japan concluded that the change in blood pressure of current smokers was lower than in nonsmokers (86) while Janzon et al conducted a cohort study in Sweden women and reported that the change in blood pressure of current smokers was higher than in nonsmokers (87) which is consistent with our results. The present study revealed that exposure to the smoke of *P. harmala* led to a significantly higher reduction in DBP and insignificantly higher elevation of HR in smokers than in nonsmokers. The same results were observed in a cross-sectional study by Li et al who reported that the DBP was significantly lower in current smokers versus nonsmokers and SBP was insignificantly lower in smokers (74). In agreement with our findings, the study conducted by Alomari et al. on adolescent males revealed that SBP and DBP were lower in smokers than nonsmokers.

Conclusion

In the present study, the effect of PMs (PM_1, $PM_{2.5}$, and PM_{10}) emitted from burned *P. harmala* seeds on SBP, DBP, and HR was investigated. In this regard, the cardiovascular parameters of 37 healthy participants based on explanatory factors of gender, age, BMI, and smoking behavior were compared before and after exposure to PMs. According to the results, the exposure had considerable effects on the investigated parameters, described as follows:

- SBP and HR significantly decreased and increased, respectively.
- The HR for people who were less than 35 years old significantly increased.
- The DBP significantly increased and decreased for smokers and non-smokers, respectively.

Therefore, it is necessary to reduce exposure, especially for people who have cardiovascular and respiratory problems. Decreasing the exposure and duration, burned Espand weight, and doing cultural-religious ceremonies

in outdoor areas are the practices that considerably reduce the exposure.

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Competing interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Ethics issues

All methods were conducted according to relevant guidelines and regulations and all participants have read and declared their consent in accordance with relevant guidelines. Written informed consent was obtained before data collection from the participants. This study was approved by the Ethics Committee of the Tobacco and Health Research Center, Hormozgan University of Medical Sciences, Bandar Abbas, Iran (Ethical code: IR.HUMS.REC.1400.102).

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