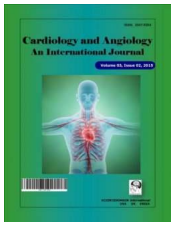

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Haemodynamic Responses to Tobacco Smoke Inhalation in Male Adolescents in Lusaka, Zambia

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Authors' contributions

This work was carried out in collaboration between both authors. The study was a collaborative effort from the Cardiovascular Sciences Laboratory at University of Zambia School of Medicine. Author CT designed the experimental protocol, conducted the experiments, data analysis and drafted the manuscript. Author MGF supervised the study protocol, data collection, management and the finalization of the manuscript. Both authors read and approved the final manuscript.

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ABSTRACT

Background: Tobacco smoke is said to cause changes in the levels of catecholamines in the blood, this leads to an increase in blood pressure and heart rate. This is due to nicotine which has also been noted to cause a decrease in vasodilatory activities leading to an increase in both the blood pressure and heart rate.
Aim: To determine the acute effects of tobacco smoke on haemodynamics in black male adolescents in Lusaka, Zambia.
Study Design: This was an observational study done at the University of Zambia School of Medicine Cardiovascular Research Laboratory in the month of December, 2014.
Methodology: Twenty-two (22) black, male-adolescent (age range 19-25 years), active-smokers, consented to participate in the study. The Diasys Ambulatory Blood Pressure Monitoring system (Novacor, France) was used to obtain the Systolic and Diastolic blood pressures (SBP and DBP) and the heart rate. These were obtained 15 minutes before smoking at 5 minute intervals and averaged to obtain the baseline, during the 15 minutes of smoking and on immediate cessation of smoking and thereafter every 15 minutes up to an hour after smoking.

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Results: There was a significant rise in SBP (mmHg) during smoking (127.9±13.80 mmHg) from baseline values (113.5±13.15 mmHg) (P < .001). It took 30 minutes for the SBP to return to baseline after cessation of smoking. DBP (mmHg) also increased from baseline (79.5±8.79 mmHg) to 85.6±10.92 mmHg during smoking (P <.01). It returned to baseline values immediately after cessation of smoking. The heart rate (bpm) was also noted to significantly increase during smoking (95.2±16.72 bpm) from the values noted before smoking (74.3±13.75 bpm) (P < .05). The mean value for heart rate returned to baseline value by the 15th minute of recovery.
Conclusion: The present study demonstrates that smoking may be the cause for the acute increases in SBP, DBP and heart rate in smokers. The smoking caused significant increases in all the haemodynamic indices considered in this study within 15 minutes. Both SBP and DBP increases are indices for stroke and coronary heart disease respectively. The effect of increased SBP was noted to last for 30 minutes while DBP returned to baseline immediately after smoking. A significant increase in heart rate was also noted in the study.

Keywords: Systolic Blood Pressure (SBP); Diastolic Blood Pressure (DBP); Heart Rate (HR); adolescents.

1. INTRODUCTION

Tobacco smoking, the commonest mode of tobacco use in Zambia, is predominantly a male vice with a prevalence of 19.8% among men aged 15-49 years compared to 2.1% of women [1]. The use of tobacco among adolescents is said to be on the increase. The ZDHS, 2014 [1] reported a prevalence of 16.1% among males aged 15 – 24 years who may be classified as late adolescents [2] and are said to be an emerging priority population for the tobacco industry.

While much has been documented about the impact of chronic tobacco use on morbidity and mortality, much less has been reported on the acute effects of tobacco on health. In this study we sort to determine the acute influences of tobacco smoke on haemodynamic responses in male adolescents.

Changes in heart rate and blood pressure have been reported following exposure to tobacco smoke [3]. These influences are said to be largely a result of nicotine uptake. Indeed, the two substances absorbed in appreciable amounts from tobacco smoke are carbon monoxide and nicotine.

Nicotine is an alkaloid found in the tobacco leaves. Nicotine is carried on the tar droplets which are inhaled and it gets absorbed across surfaces such as skin and mucous membranes of both mouth and nose. Its absorption across the biological membranes depends on pH. Nicotine is a weak base with a pKa of 8.0 [4]. In its ionized state, such as in acidic environments, nicotine does not rapidly cross membranes thus the need for cigarette manufacturers to put some additives to the tobacco. Nicotine is said to be best absorbed from the small airways and alveoli due to the basic nature (pH 7.5) of alveoli fluid [5].

The average cigarette contains 6 - 11 mg nicotine though it delivers only about 1 - 3 mg of the nicotine systemically to the smoker [6]. Upon absorption, it is said to reach a blood maximum concentration in 5 - 8 minutes [7,8] where it induces increased secretion of epinephrine and norepinephrine consequently increasing heart rate, cardiac output and blood pressure [9,5,10-13]. This mechanism is primarily through the stimulation of the sympathetic nervous system and the adrenal medulla [14].

An additional factor to changes in blood pressure has been shown to result from an increase in peripheral resistance secondarily due to a decrease in vasodilatory function [15-17]. This impaired endothelium-dependent vasodilation has been noted to occur in macro vascular beds such as brachial arteries and in microvascular beds [18,15,16,19]. Nicotine is said to down-regulate the expression of endothelial nitric oxide synthase (NOS), an enzyme involved in the generation of Nitric Oxide (NO), which mediates vasodilation [20]. It has also been noted to up-regulate asymmetric dimethyl arginine, which would further impair the release of NO [21]. Therefore, an alteration in NO biosynthesis could have both primary and secondary effects on the initiation of increased peripheral resistance.

This study aimed at determining the acute effect of smoking on the haemodynamic indices in black male adolescents. It outlines the acute

effects of smoking on haemodynamic parameters such as systolic and diastolic blood pressure and heart rate. Appreciation of these changes may help determine the magnitude of the effects that smoking has on the dynamics of blood flow and the potential to initiate and/or augment cardiovascular pathology.

2. MATERIALS AND METHODS

This observational study involved healthy young men who were active tobacco smokers. These were recruited by advertisements placed on the student notice boards within the University of Zambia (Ridgeway campus) and also by the use of the chain–referral (snowball) sampling. The sample population included all tobacco smoking, male adolescents between ages 18 and 25 years who were daily smokers (someone who has smoked daily during the past month). Excluded were adolescents with known disease such as hypertension, diabetes mellitus, high levels of cholesterol, and respiratory diseases such as bronchitis or asthma.

The participants were required to abstain from smoking, taking alcohol and coffee beverages for at least 12 hours prior to the study protocol. Written consent was obtained from each one of the participants and they were assured that denial of participation was not consequential on their academic progression and they were free to withdraw from the study at any time. All measurements taken were non-invasive and were taken in a research unit specifically designed for participant's privacy and comfort. All participants recruited were smokers and none of them were subjected to abnormal levels of smoking (more than what the participant usually smokes). Any abnormalities in the results were highlighted and the participants were advised to consult a clinician as appropriate. All data was stored on a trusted, password protected computer. Identification of participants was by unique research laboratory numbers and was stored as such. The research ethics clearance was obtained from the University of Zambia Biomedical Research Ethics Committee (UNZABREC).

2.1 Baseline Information

All consenting participants were invited to the Cardiovascular Laboratory at the University of Zambia, School of Medicine. They were interviewed to note socio-demographic data and health information such as age, marital status, current medications, existing pathological conditions, age at which participants started smoking, duration of smoking to date, amount of cigarettes smoked in a day, type of tobacco smoked, alcohol consumption and time of last meal and beverage consumption.

2.2 Anthropometric Measurements

Height and weight were measured using a Micro T3 PW-BMI Digital Physician Scale with a height measure. Height was measured in meters (m) while weight was measure in kilograms (Kg). Static blood pressure was measured by OMRON HEM-757 (Omron, Kyoto, Japan) digital blood pressure measuring machine in both sitting and lying down positions (in mmHg).

2.3 Haemodynamics Data Collections

The main equipment used for the data collection was the Diasys Ambulatory Blood Pressure Monitoring System (Novacor, France). The participant's chest was cleaned with alcohol solution to ensure good attachment of the ECG electrodes and, if necessary, shaved to help the electrodes stick. Three electrodes were placed on the chest for the detection of the QRS signal. The electrodes were then connected to the Diasys II. The brachial artery was located about 2 cm above the crease of the elbow and the cuff was applied taking care to correctly position the microphone for the detection of the Korotkoff sounds. Upon confirming optimal signals from the Diasys, the cuff was secured to stay in place during the period of the recording. The recording was set to read at 5 minute intervals.

The participant was then left to rest on the couch and the recording was started. After 15 minutes of recording, the participant was requested to smoke two cigarettes (1.4 mg nicotine content each) in fifteen minutes, during which period the measurements continued being recorded at 5-minute intervals. The participant stopped smoking at 15 minutes and the measurements continued thereafter for an hour at 15-minute intervals.

The means and ranges for the data were obtained using STATISTIX statistical package for Windows Version 10, 2013. The mean haemodynamics readings obtained from the Diasys for all individuals at 15-minute intervals during and after smoking were compared with their respective baseline readings to note for any significant differences using ANOVA of repeated

measures. The differences in mean haemodynamic readings over time were used to determine how long it takes for the values to return to baseline after smoking. All analyses were done at 0.05 error. All statistical analyses were performed using the STATISTIX statistical package for Windows Version 10, 2013.

3. RESULTS

3.1 Anthropometric and Baseline Data

Twenty-two (22) male participants were recruited for the study. The participants were all active-smokers aged between 19 and 25 years old. The anthropometric data of the study population is shown in Table 1 and the characteristics of smoking in the group are illustrated in Table 2.

As noted in Table 2, among the 22 smokers, the mean number of cigarettes smoked per day was 6.9±5.05 cigarettes. The group was characterised by smokers who had a total duration of smoking ranging from 12 months to 192 months. The youngest age at which the participants initiated the habit of smoking was 7 years and the latest age was noted as 19 years.

3.2 Systolic Blood Pressure Response

The baseline means SBP was 113.5±13.15 mmHg. There was a significant rise in SBP (mmHg) during smoking to 127.9±13.80 mmHg) (P <.001) as shown in Fig. 1. The increased values were statistically significantly higher than the baseline values (Bonferroni pairwise comparison test) until 30 minutes after smoking cessation.

Table 1. Anthropometric and baseline data for smokers

Variable	Mean	SD	Minimum	Maximum
Age (years)	20.6	2.08	19	25
Height (m)	1.7	0.05	1.6	1.81
Weight (kilograms)	61.5	11.00	49.0	92.2
BMI (kg/m^2)	18.2	2.81	14.2	25.5
SBP* (mmHg)	113.5	13.15	88.5	156.0
DBP** (mmHg)	79.5	8.79	60.0	116.0
Heart Rate (bpm)	74.3	13.75	50.0	133.5

**SBP – Systolic blood pressure; **DBP – Diastolic blood pressure*

Table 2. Smoking parameters in study population

Variable	Mean	SD	Minimum	Maximum
No. of cigarettes smoked per day	6.9	5.0	1	20
Duration of smoking (months)	71.4	45.0	12	192
Starting age of smoking (years)	14.7	3.0	7	19

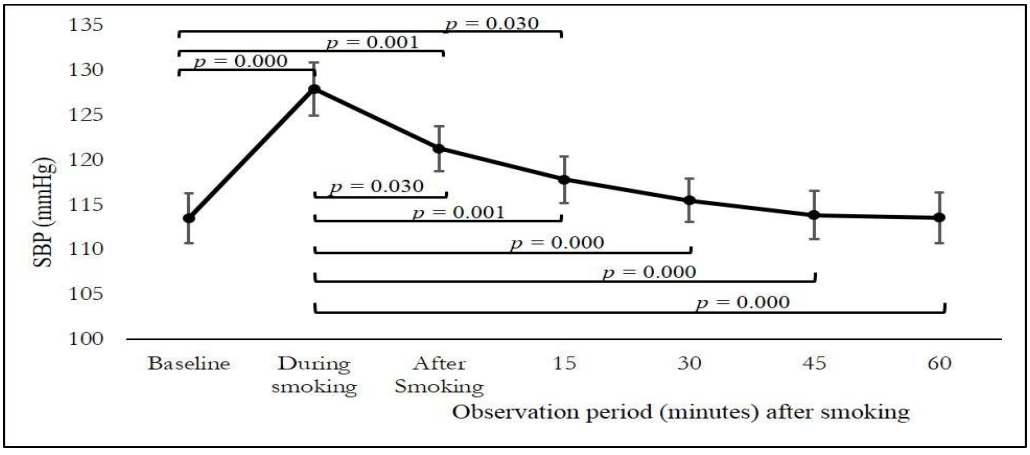

Fig. 1. Mean Systolic Blood Pressure (SBP) (mmHg) before during and after smoking with statistical significance of mean differences (P<.05) shown. Bars represent the standard deviation

3.3 Diastolic Blood Pressure Responses

DBP (mmHg) increased significantly from baseline (79.5±8.79 mmHg) to 85.6±10.92 mmHg during smoking (*P* =.01) as shown in Fig. 2. Immediately after smoking, the means obtained were noted to be of no significant difference with those obtained at baseline when tested with the Bonferroni comparison test indicating a quick return to baseline.

3.4 Heart Rate Responses

Heart rate (HR) was also noted to significantly increase during smoking (95.2± 16.72 bpm) from the values noted before smoking (74.3±13.75 bpm) (*P*<.05). There was a considerable drop in HR immediately after the participants stopped smoking to 81.6±14.98 bpm but the mean value for heart rate returned to baseline by the 15th minute of recovery.

4. DISCUSSION

4.1 Anthropometric and Baseline Data

The twenty-two (22) participants who were recruited to participate in this study were all active-smokers. The average age at which the participants started smoking was 14 years, with some reporting that they started smoking at 7 years of age. They were all normotensive, with a mean blood pressure of 118/81 mmHg and none of the participants were overweight or obese.

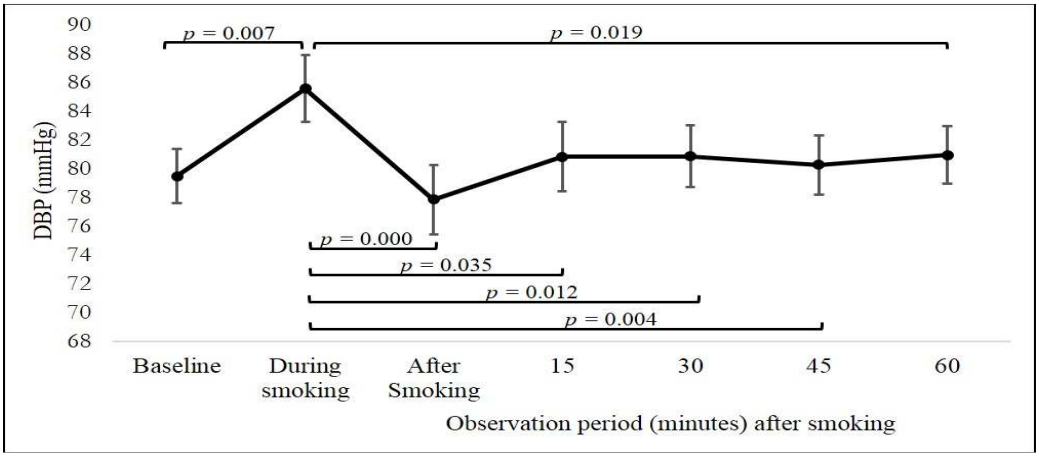

Fig. 2. Mean Diastolic Blood Pressure (DBP) (mmHg) before, during and after smoking with statistical significance of mean differences (*P*<.05) shown. Bars represent the standard deviation

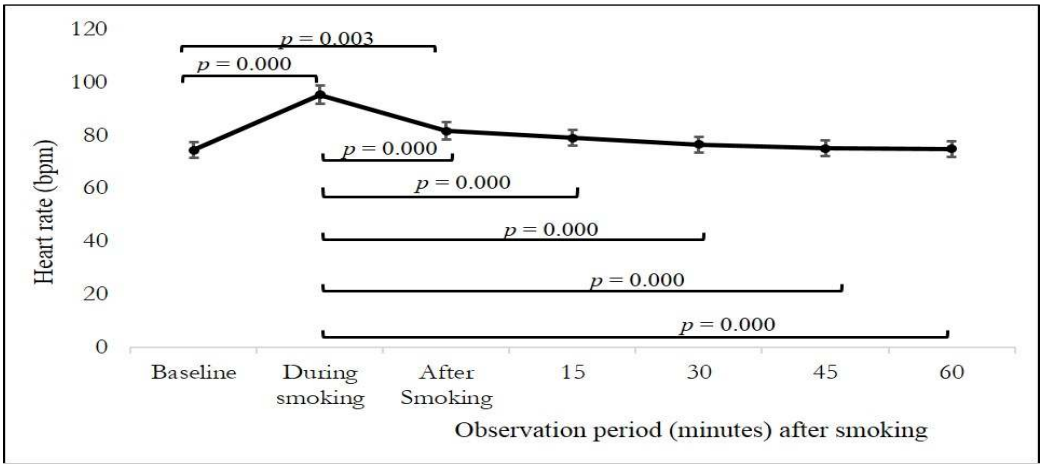

Fig. 3. Mean Heart Rate (HR) (bpm) before, during and after smoking with statistical significance of mean differences (*P*<.05) shown. Bars represent the standard deviation

Table 3. Summary of mean haemodynamic values over the period of observation

Variable	Baseline	During smoking	0 MAS	15 MAS	30 MAS	45 MAS	60MAS
SBP (mmHg)	113.5±13.15	127.0±13.80	121.2±11.68	117.8±12.00	115.5±11.30	113.8±12.65	113.55±13.13
DBP (mmHg)	79.5±8.79	85.6±10.92	77.8±11.31	80.8±11.28	80.9±10. 14	80.3±9.62	81.0±9.37
HR (bpm)	74.3±13.75	95.2±16.72	81.6±14.98	78.8±13.88	76.4±14 .20	74.9±13.78	74.7±14.27

***MAS – Minutes after smoking*

4.2 Baseline Values for Blood Pressure and Heart Rate

Notable changes in baseline heart rate, systolic and diastolic blood pressures have been reported in candidates who smoke tobacco.

The baseline SBP noted in this study was 113.5±13.15 mmHg. It was lower than the SBP noted by Mushabati et al. [22], who reported an SBP of 123±9.7 mmHg. The difference could be due to the fact that Mushabati's population comprised older subjects (42±8.7 years) compared to the current study. With age, the larger elastic arteries increase in collagen content, elastin fracture, and calcification and reduction in the elastin content. There are also changes in endothelial function, wall media thickness to lumen ratio, and arterial stiffness with ageing. These lead to an increase in peripheral resistance thus influencing SBP [23].

The baseline DBP (79.5±8.79 mmHg) in this study was similar to the values noted in Lemogoum's study (79±4 mmHg) and that observed by Mushabati et al. [22] in a normotensive Zambian population (79±7.1 mmHg). However, lower DBP values have been observed in healthy non-smokers by Vandanah [24], who observed a mean value of 70 mmHg. The higher DBP noted in smokers may be mostly attributed to the nicotine mediated activation of the sympathetic nervous system with local and systemic release of catecholamines and, possibly, the release of vasopressin [25,14,26]. These cause vasoconstriction that increase peripheral resistance.

In the current study, the baseline heart rate was 74.3±13.75 bpm. This was similar to the baseline heart rate noted in black adolescent smokers by Lemogoum [27], who recorded a mean value of 70±10 bpm. In a study by Papathanasiou et al. [28] in male adolescents, the resting heart rate was higher in the smokers (72.8±6.1 bpm) compared to non-smokers (66.3±6.1 bpm). In healthy non-smokers, heart rate values observed by Farha et al. [29] were also lower (64 bpm) than those observed in this study. Smoking is associated with autonomic dysfunctions and with selective alterations in cardiac autonomic control. More specifically, smoking, acting at peripheral sympathetic sites, increases circulating levels of catecholamines, augments sympathetic outflow, and causes a long-term reduction in vagal drive [30]. This sympathetic predominance, seen even in young heavy smokers, is also associated with impaired baroreflex function, leading to a marked increase in baseline heart rate.

4.3 Acute Effects of Smoking on the Systolic Blood Pressure

The SBP increased by an average 13% during smoking. The increase noted in this study was higher than SBP increase reported in white smokers by Rhee et al. [31]. He observed an increase in SBP of 4.1% from 121.2±1.8 mmHg to 126.2±1.6 mmHg (P<.05) after 5 minutes of smoking. This difference in increment between the two studies could be due to the difference in race in the two populations. Nicotine metabolism via N-glucuronidation and cotinine pathway, which is known to be mediated primarily by cytochrome P-450 2A6 [32], is said to be slower in blacks compared to whites [33]. As a result, black smokers have a higher plasma cotinine concentration at all levels of cigarette smoking [34] and have lower cotinine clearance [33]. The black smokers are therefore prone to a higher increase in blood pressure compared to their white counterparts. Smokers have been observed to have higher SBP compared to non-smokers after smoking the same amount of nicotine [24]. He observed that SBP in smokers increased to near hypertensive values (140 mmHg) after smoking and that of non-smokers only increased to normotensive values (120 mmHg) after smoking.

The acute increase in SBP in smokers is said to be due to greater contractility of the heart caused

by increased sympathetic discharge during smoking. Enhanced contractility causes an increase in the stroke volume, causing greater cardiac output. This increased cardiac output causes an increase in blood being pushed into the arterial tree, thus elevating the systolic pressure. The increase in heart rate also increases the cardiac output, elevating the SBP. The increase in SBP as observed in this study, according to Lewington [35], can be associated with more than 40% greater risk of stroke and more than 30% greater risk of death from coronary heart disease in adult populations. The author further postulated that the observed increase in SBP could be associated with more than 10% and 7% greater risk of mortality from stroke and ischaemic heart disease, respectively.

SBP values in this study were noted to return to baseline 30 minutes after cessation of smoking. The average time for SBP to revert to baseline, as noted by Lemogoum et al. [27], was 5 minutes after smoking cigarettes containing a total of 1.2 mg of nicotine. The slightly longer period of recovery in this study could be due to a higher amount of nicotine taken (2.8 mg in 15 minutes). According to Hukkanen et al. [7], it takes 5 to 8 minutes for the inhaled smoke to be absorbed and reach blood maximum concentration. Extending the time of smoking would therefore give increased time for absorption of the 2.8 mg of nicotine and hence increased recovery time. Indeed Benowitz et al. [36] stated that smoking represents a multiple dosing situation with considerable accumulation while smoking. The longer period of recovery of SBP in this population places these adolescents at an increased risk of cerebro-vascular injury, considering increased SBP is an index for stroke [35].

4.4 Acute Effects of Smoking on the Diastolic Blood Pressure

The mean DBP increased by an average 8% during smoking. Lemogoum et al. [27] reported a 5% increase in DBP in adolescent smokers from a baseline of 79±5 mmHg to 83±9 mmHg (P<.05) 5 minutes after smoking. The higher values observed in this study could be due to the fact that our study population comprised only males while Lemogoum et al.'s population comprised both males and females. The latter generally have a lower mean DBP compared to males, hence lowering the average DBP values observed. Kim et al. [37] observed a 5.9% increase in DBP in white smokers from a baseline of 68.2 mmHg to 72.7 mmHg (P< .05) after 5 minutes of smoking. It has been noted that whites have lower DBP values compared to blacks of African descent [38]. This places the black smokers at a higher risk of the harmful effects of smoking.

The increase in DBP in smokers is due to greater peripheral resistance being caused by an increase in sympathetic stimulation. Nicotine and other products in cigarettes cause blood vessels to constrict. This, in turn, increases the total peripheral resistance, which traps more blood as stressed volume in the arteries, increasing the pressure. This over time causes Injury to blood vessel walls speeding up stiffening of the arteries further leading to an increase in the peripheral resistance and this elevates the diastolic pressure. This increase in DBP is speculated to increase the chance of death from coronary heart disease in adult life by 30% [35].

DBP in this study returned to baseline immediately after stopping to smoke. This was a shorter period when compared to Rhee [31], who noted more than 15 minutes as the time required for DBP to return to baseline after smoking. However, the population in Rhee's study had older smokers with an average age of 39 years. Rhee's population was also characterised by individuals who has been smoking for a longer time compared to the current study population. This could explain why the current study had a shorter time to revert to baseline. This entails that with increased duration of smoking, time to revert to normal blood pressure also increases. This could explain the increased arterial stiffness due to chronic smoking.

4.5 Acute Effects of Smoking on the Heart Rate

There was a significant increase in heart rate by an average 28% during smoking. This was a comparatively higher increase in heart rate when compared to Rhee et al.'s [31], who observed a 22% increase in heart rate from 60.6±1.6 bpm to 73.4±2.0 bpm (P<.05) and Farha et al. [29], who also reported a 15% rise in heart rate in smokers from a baseline of 69.7 bpm to 76 bpm after smoking (P<.05). Both Rhee and Farha had observed these changes in white populations and Farha's population comprised both males and females.

The increase in heart rate is said to be due to the nicotine that stimulates release of endogenous

adrenergic neurotransmitters [39]. Within minutes of cigarette smoking, nicotine receptors in the adrenal medulla are stimulated, triggering the release of epinephrine and norepinephrine leading to an increase in plasma levels of the adreno-medullary hormones [40,41]. Grassi [25], in 1994 showed that the sympathetic activation induced by smoking depends on an increased release or a reduced clearance of catecholamine at the neuro-effector junctions. The heart rate in this study reverted to baseline in 15 minutes. This is similar to what was reported by Rhee et al. [31] and Kim et al. [37], who also noted a 15 minute recovery period in their populations.

5. CONCLUSION

The study has demonstrated that smoking may cause acute increases in SBP, DBP and HR in individuals exposed to the tobacco smoke. These repeated influences may actually affect baseline measurements thus predisposing these individuals to higher risk for cardiovascular morbidity in later life. The smoking caused significant increases in all the haemodynamic indices considered in this study within 15 minutes. The effect of increased SBP lasted for 30 minutes while the DBP returned to baseline almost immediately after cessation of smoking. A significant increase in heart rate was also noted in the study which remained elevated for another 15 minutes after cessation of smoking. There is also a suggestion that this HR response is rather exaggerated in black adolescents as compared to their white counterparts. This study contributes significantly to the scanty literature existing of cardiovascular responses to tobacco smoke in black adolescents and is the first study to use central blood pressures as measured using the Diasys II in Zambia.

This study is limited by the relatively small size of population studied. Confounders such as blood nicotine concentration that are subject to puff volume, depth of inhalation, rate of puffing and type of tobacco may call for a larger sample sized study. This would increase the power of analysis and give more insight into the acute physiologic and non-physiologic hemodynamic responses to tobacco smoke inhalation.

This study exposes the harmful effects of acute tobacco smoke inhalation on the adolescent cardiovascular system and provides evidence for the need to protect this age group from the harmful effects of environmental tobacco smoke. There must be deliberate measures taken by health practitioners to make adolescents aware of these risks and thus make them stop smoking and/or keep away from tobacco smoke polluted environments. Policymakers ought to formulate and enforce legislation for smoke free environments. As the methods used in this study are simple and reproducible, parameters used in this study may be a useful tool to assess the effect of smoking and also for screening the risk of CVD in adolescents as part of routine clinical procedures.

ETHICAL APPROVAL

All authors hereby declare that the protocol was approved by University of Zambia Biomedical Research Ethics Committee (UNZABREC).

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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