

**BJMHR**

British Journal of Medical and Health Research

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## The Effect of Cigarette Smoking on Penile Vasculature and Cardiodynamics among Young Saudi Population

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### ABSTRACT

Erectile and cardiovascular dysfunctions in cigarette smokers are important signs resulting probably due to pelvic autonomic neuropathy with damage to the parasympathetic nervi erigentes. Evidence related to neuropathic etiology comes from studies that show structural changes in autonomic nerve fibers supplying the corpora cavernosa. The objective of this study was to evaluate the effect of cigarette smoking on penile mid shaft circumference and length, penile pulse amplitude, both systolic and diastolic blood pressures, and heart rate in response to erotic stimulation in young Saudi men living in Western region of Saudi Arabia (Makkah). In this free-living population study data was collected from 100 men each (mild, moderate and heavy cigarette smokers) ages between 20 and 35 years with a mean age of  $26.42 \pm 10.69$  years along with 100 age matched healthy non smokers who served as controls. Heavy cigarette smoker group showed a significant decrease ( $p < 0.0005$ ) in mid shaft penile circumference and length and penile pulse amplitude where as both systolic and diastolic blood pressures and heart rate exhibited a significant increase ( $P < 0.025$ ,  $P < 0.0005$  and  $P < 0.005$  respectively). However this difference was found to be non significant in mild smoker group when compared with non smoker controls. We hypothesized that heavy cigarette smoking seems to be associated with sub-fertility in these males with significant alteration in the penile vasculature and cardiodynamics in a dose-dependent manner.

**Keywords:** Cigarette smoking, penile vasculature and cardiodynamics, young Saudi men

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Received 10 November 2021, Accepted 16 December 2021

## INTRODUCTION

Erectile dysfunction (ED) has been found to be increasingly linked to cardiovascular risk factors and comorbidities. Since the physiological mechanism associated with erection is heavily dependent on vascular changes, most of the known cardiovascular risk factors such as hypertension and diabetes seem to be associated with the development of erectile dysfunction. It is now established that cigarette smoking is one of the most prominent factor to cardiovascular dysfunction and an independent risk factor for the development of erectile dysfunction, a more threatening form of vascular disease (1).

Several cross-sectional studies have been established now to show a correlation between cigarette smoking and ED thus exhibiting a variable baseline smoking prevalence (2). Statistically significant confidence intervals in the vast majority of these studies have been found with the odds ratio of smokers with ED ranged between 1.4 and 3.1. In a specific cohort of young men <40 years of age, smoking was a significant risk factor for ED. In these men, the multivariate analysis did not show significance in other vascular risk factors, strongly indicating a role for smoking in the pathogenesis of ED in younger men (3). Further analysis found that smokers who developed vascular disease had three times the risk of developing ED compared to non-smokers without vascular disease (4).

Dose dependent effects of cigarette smoking have been suggested to act as a risk-factor for heart disease as well as ED. Moreover, while reviewing the subgroup analysis from larger sample studies, a significant difference was observed in the odds ratios of patients who developed ED when smoked greater than 10 cigarettes per day (5). Among smokers, a positive but non-significant trend towards increase ED occurred in relation to daily cigarette intake (6).

In a younger, less comorbid population, heavy smokers (>20 cigarettes/day) had doubled the likelihood of severe ED compared to those who smoked less (7). Above literature thus predicts for an odds of developing ED as a result of cumulative dose of cigarette exposure suggesting that heavy smoking causes more severe ED that appears to be not reversible following smoking cessation.

Several other co-existing disorders are also known to be associated with cigarette smoking. These includes atherosclerosis and cardiovascular disease which severely affect erectile function by decreasing penile perfusion pressures resulting in increased time to maximal erection and decreased rigidity during erection (8). Cigarette smoking is associated with arteriogenic ED and is a component of the general process of atherosclerosis (9). Arterio-insufficiency also hinders erectile function by decreasing penile perfusion pressures resulting in increased times to maximal erection and decreased rigidity during erection (10). Current

evidence suggests that there is a direct correlation between smoking and erectile dysfunctions through vascular mechanisms primarily due to depletion of nitric oxide.

Combined effects of non-optimal levels of blood pressure (BP) and smoking on cardiovascular events have been reported in epidemiological studies (11-12). A partially synergistic effect between BP and smoking status for the risk of cardiovascular disease (CVD) and stroke (predominately ischemic) has been reported in the literature (13), whereas no such relationship has also been reported. (14). Most of these studies are based on crude classifications of BP and smoking status using small database. An interaction effect between BP and smoking status for each subtype of cardiovascular disease (CVD) has also been reported, however, exact nature of this interaction (synergistic or otherwise) still remains unresolved (13).

Previous reports suggest that chronic smokers have a higher pulse rate and blood pressure compared with nonsmokers, indicating sympathetic hyperactivity (15). It has been shown that cigarette smoking acutely increases plasma catecholamines and cardiac norepinephrine spillover and results in an increase in blood pressure and heart rate and sympathetic outflow (16). However mechanisms by which smoking may affect erectile physiology are not well understood. More recent studies have reported an implication of heart rate variability (HRV) with erectile functions. Individuals with erectile impairments usually show the symptoms of abnormal cardiac autonomic regulation (sympathetic hyperactivity) while smoking cessation improve erectile functions via changes in HRV (17, 18).

Present study has been designed to evaluate the mechanisms involved in penile hemodynamics through which cigarette smoking, as an independent risk factor induces ED. The evaluation of the differential effect of cigarette smoking on the arterial and venous components of penile vasculature and the mediating role of heart rate variability among a sample of younger aged male heavy smokers from Saudi Arabia can be used to localize the pathophysiology of vasculogenic ED in smokers, thus adding to a better understanding of this problem.

## MATERIALS AND METHOD

### Study Design

Present study was conducted in the Makkah Region of Saudi Arabia. Local Ethical and Protocol review committee reviewed and approved the study. Prior to the study all the subjects were provided with a written informed consent.

A total of 500 men in communities within the Makkah region, were spoken. Subjects with the history of chronic urinary tract infection, testicular injury, varicocele, disorders like diabetes, hypertension and coronary heart diseases were excluded from the study. For the experimental

purposes 100 men each (mild, moderate and heavy smokers) ages of 20 and 35 years with a mean age of  $26.42 \pm 10.69$  years along with 100 age matched non smokers healthy participant were included in the study.

Smokers were defined as subjects who were continuously smoking cigarette for at least 5 years. Smokers who smoked less than five ( $<5$ ) sticks of cigarette per day were classified as mild smokers, between 5 and 10 sticks of cigarette per day as moderate smokers and more than ten ( $>10$ ) sticks per day as heavy smokers.

Penile vasculature and cardiovascular responses were assessed using simultaneous monitoring of penile mid shaft circumference and length, penile pulse amplitude, systemic arterial systolic and diastolic blood pressures and heart rate during laboratory based erotic stimulation in all the subject groups according to the method described previously (19). The degree of erection to erotic stimulation distinguished between smoker & non smoker etiologies. For each individual systolic and diastolic blood pressure and heart rate were measured three times with 10–15 min intervals in the sitting position and at the resting state. In most of the cases calibrated mercury sphygmomanometers were used while the use of electronic devices was kept to the minimum. The mean of each blood pressure and heart rate value was calculated by dividing the total values on the number of measurements.

### Statistical analysis

Comparisons between mild, moderate and heavy smokers were performed by Student *t* tests using SPSS program 17.0 (SPSS Institute, Inc.; Chicago, IL, USA) software. All results were tabulated as mean  $\pm$  standard deviation. In all the instances probability ( $p < 0.05$ ) was regarded as statistically significant.

## RESULTS AND DISCUSSION

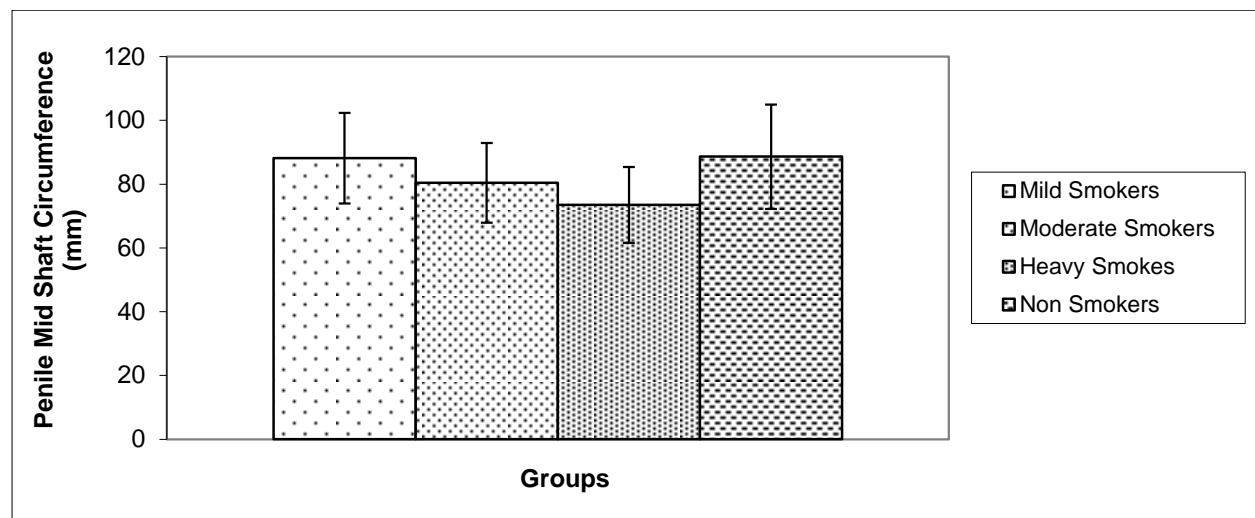
Data for the measurement of penile mid shaft circumference and penile length in response to film and fantasy in smoker groups (100 each) in comparison with 100 age matched nonsmokers are presented in figures- 1 and 2 respectively.

A consistent decrease in the level of penile circumference and length in the smoker groups was observed, being significant in moderate smokers ( $p < 0.005$ ), and highly significant in heavy smoker group ( $p < 0.0005$ ). However this difference was found to be non significant in mild smoker group when compared with non smoker controls.

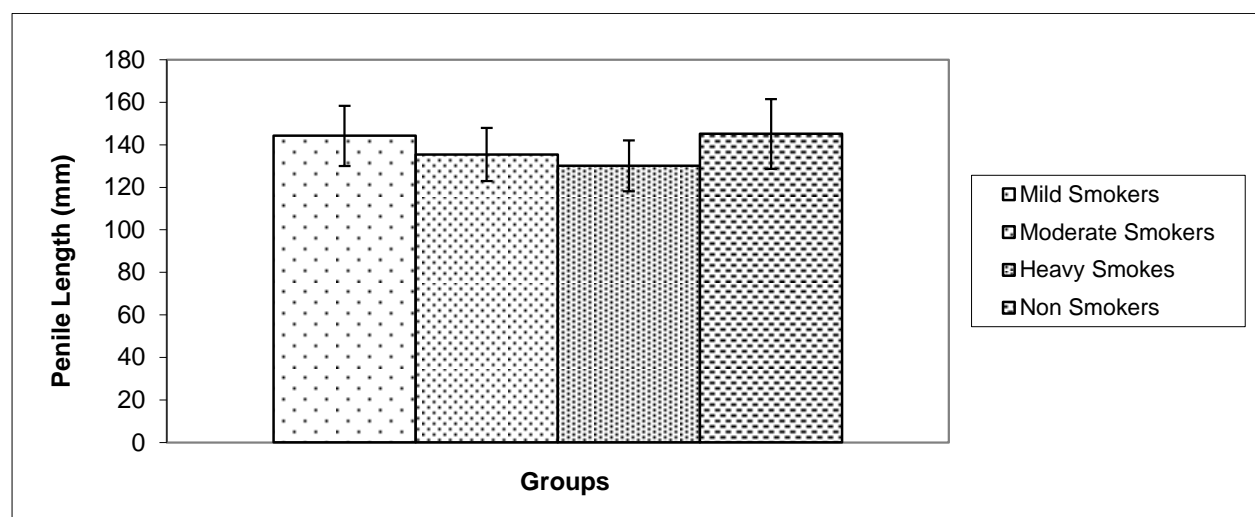
The estimated values of penile pulse amplitude of the smoker groups and their age matched non smoker controls are presented in figure-3. Exactly in a similar manner a consistently decreased level of penile pulse amplitude was noted in almost all the smoker groups. The values of the penile pulse amplitude were found to be significant ( $p < 0.005$ ) and highly significant ( $p < 0.0005$ ) in moderate and heavy smokers respectively than their respective

controls. However this difference was found to be non significant in mild smoker group when compared with non smoker controls.

In contrast, an inverse relationship was found when systolic and diastolic blood pressures and heart rate values were measured in the same groups. Both moderate and heavy smoker groups showed a less significant increase ( $p < 0.025$ ) in the values of systolic blood pressure (Figure 4) whereas the values of diastolic blood pressure were found to be significant ( $p < 0.005$ ) and highly significant ( $p < 0.0005$ ) in moderate and heavy smokers respectively than mild smoker group and their respective controls (Figure 5). Both moderate and heavy smokers showed a significant increase in the values of heart rate ( $P < 0.005$ ) respectively when compared with mild smokers and the respective control group.

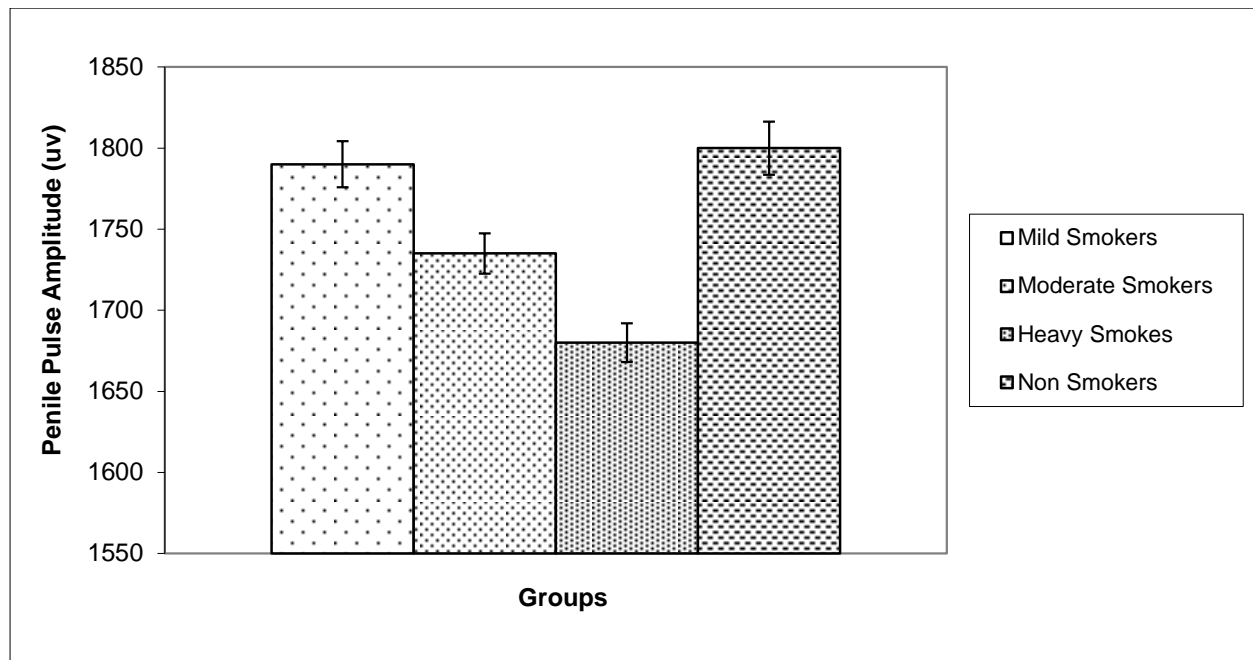


**Figure 1: Changes in penile mid shaft circumference (mm) in mild, moderate and heavy cigarette smokers compared with the age matched non smokers group in Saudi young men. Values are Mean  $\pm$  SD, (n = 100). Note: n = Total number of subjects examined.**



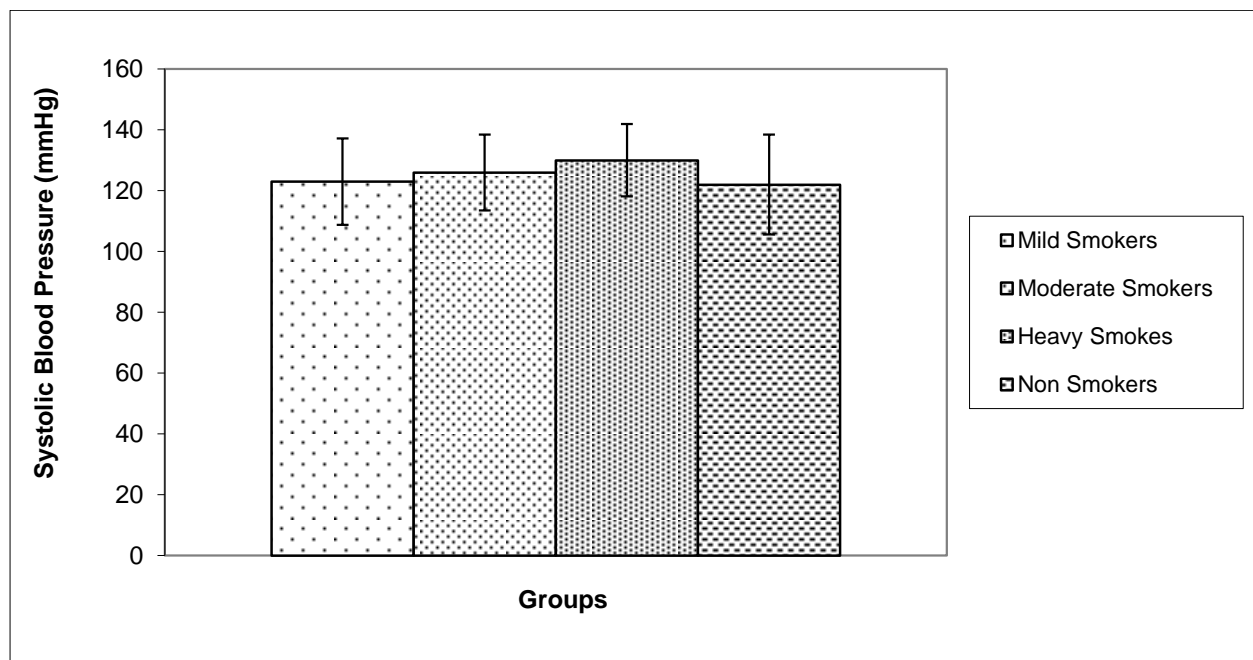
**Figure 2: Changes in penile length (mm) in mild, moderate and heavy cigarette smokers compared with the age matched non smokers group in Saudi young men.**

Values are Mean  $\pm$  SD, (n = 100). Note: n = Total number of subjects examined.



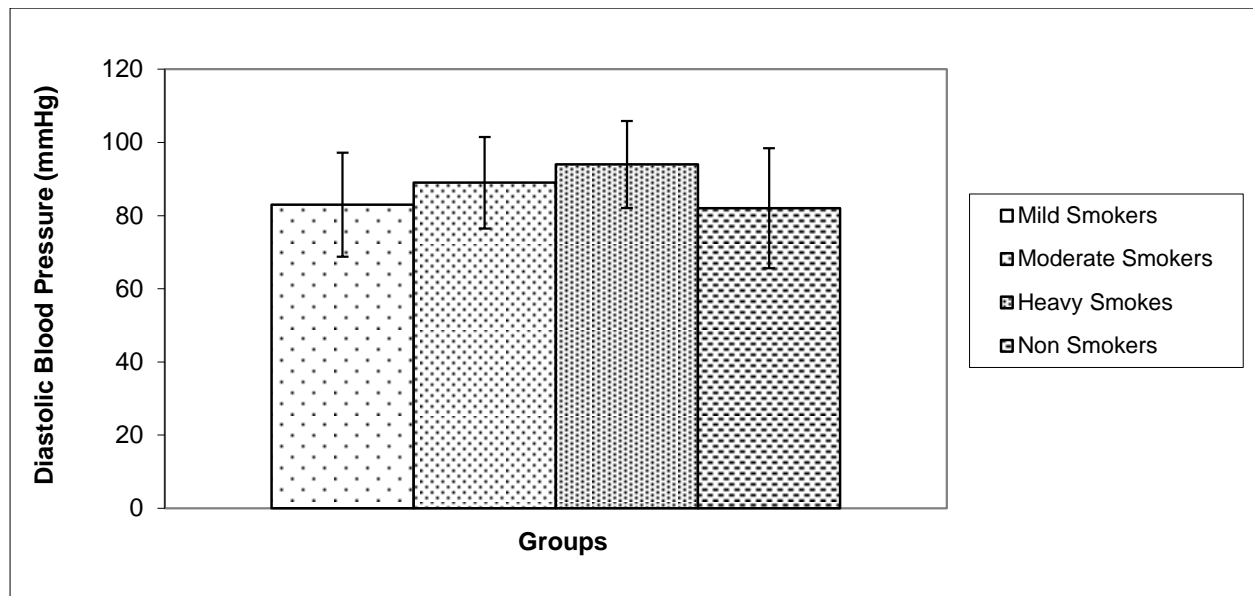
**Figure 3: Changes in penile pulse amplitude ( $\mu\text{v}$ ) in mild, moderate and heavy cigarette smokers compared with the age matched non smokers group in Saudi young men.**

Values are Mean  $\pm$  SD, (n = 100). Note: n = Total number of subjects examined.



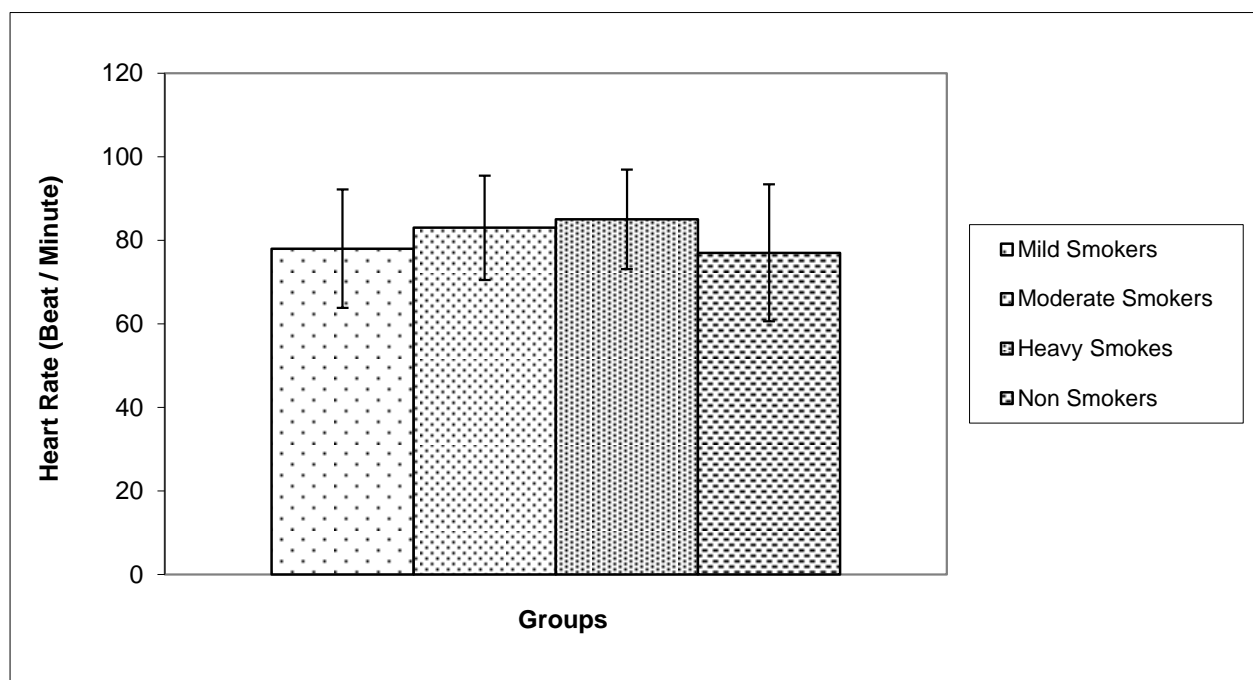
**Figure 4: Changes in systolic blood pressure (mmHg) in mild, moderate and heavy cigarette smokers compared with the age matched nonsmokers group in Saudi young men.**

Values are Mean  $\pm$  SD, (n = 100). Note: n = Total number of subjects examined.



**Figure 5: Changes in diastolic blood pressure (mmHg) in mild, moderate and heavy cigarette smokers compared with the age matched non smokers group in Saudi young men.**

**Values are Mean  $\pm$  SD, (n = 100). Note: n = Total number of subjects examined.**



**Figure 6: Changes in heart rate (beat / minute) in mild, moderate and heavy cigarette smokers compared with the age matched non smokers group in Saudi young men.**

**Values are Mean  $\pm$  SD, (n = 100). Note: n = Total number of subjects examined.**

## DISCUSSION

Laboratory assessment of erectile response to erotic stimuli has been used for many years to assess sexual preferences as the out come of modification of deviant sexual behavior (19). In the recent years, there has been increasing recognition that many cases of erectile dysfunctions are due, at least in part, to physical factors. Evidence indicates that erection may



involve the activation of several separate mechanisms (20). In addition to parasympathetically mediated arterial vasodilatation, there may also be active reduction of venous drainage (21) and the active closure of intra cavernosal arterio-venous shunts (22). Studies have suggested that tobacco- induced ED is mainly a result of vasculogenic etiology and is an independent risk factor in the development of atherosclerotic lesions in the internal pudendal and common penile arteries of young impotent men (23). Indirect evidences further suggest that smoking affects penile erection by impairment of endothelium-dependent smooth muscle relaxation (24). Our results indicated that during the period of erotic stimulation penile mid shaft circumference, penile length, and penile pulse amplitude exhibited a highly significant decrease ( $P<0.0005$ ) in heavy smoker group, however this difference was found to be less significant in moderate smoker group ( $P<0.005$ ) and non-significant in mild smoker group when compared with their respective nonsmoker control group. These results are in agreement with previous findings where penile rigidity during nocturnal erections was inversely correlated with the number of cigarettes smoked per day (25).

Numerous previous studies have indicated that ED in smokers is mainly due to underlying vascular pathology and an independent risk factor in the development of atherosclerotic lesions in the internal pudendal and common penile arteries of young impotent men (23). We found an increase in the values of systolic and diastolic blood pressures and heart rate in both heavy and moderate smoker groups where as this difference was found to be non significant in mild smoker group when compared with their respective control subjects.

Although several studies have been published in the recent years on this topic, however, there is no firm consensus on the relationship between smoking and blood pressure and heart rate and this issue still remains controversial due to multiple confounding factors (26), since the precise effect of smoking habits on blood pressure and heart rate is unclear. Some investigators demonstrated that there were no association between smoking habits and blood pressure values (27). However, other investigators confirmed that smokers had either lower (28) or higher (29) blood pressure values than non-smokers. Furthermore, some studies confirmed the presence of a significant dose–effect correlation between the number of cigarettes smoked per day and the alteration of blood pressure (28). Furthermore in epidemiologic investigation, smokers have higher blood pressure and heart rate than non-smokers (26). These results are in agreement with our findings as well as other investigations (29). This increase may be attributed to the activation of nicotinic receptors of the sympathetic ganglia leading to increase in norepinephrine release and elevation of blood pressure. The dose–effect correlation of smoking on heart rate was positive and significant in our studies. This may be interpreted as an effect of the nicotine of cigarettes which enhances local and systemic catecholamine release, and may also stimulate vasopressin release by



acting as an adrenergic agonist. Our results are thus in conformity with the previous findings (30). In agreement with our results, a prompt increase in heart rate and blood pressure has been observed during the first 5 minutes after smoking (31). The mechanism of acute smoking-induced changes in heart rate variability is probably complex; however, most of the acute effects of smoking on neuro-cardiovascular regulation have been mainly attributed to nicotine, which is the main constituent of cigarette. Nicotine is known to exert both acute and chronic cardiovascular effects, mainly through sympathetic activation as a consequence of enhanced release of catecholamine. Indeed, nicotine is implicated in a wide spectrum of cardiac rhythm disorders, including transient sinus arrest and/or bradycardia, sinus tachycardia, atrial fibrillation, sinoatrial block, atrio-ventricular block, and ventricular tachyarrhythmias, therefore, nicotine may in part be associated with the changes in heart rate variability as observed after smoking a cigarette (32).

## CONCLUSION

On the basis of our findings, we concluded that cigarette smoking has a significant adverse reproductive outcome in younger aged Saudi men probably due to impaired penile veno-occlusive mechanisms. These changes seem to be associated with cardiac adverse events attributed to smoking. These findings might serve to guide further studies investigating the pathophysiological basis of penile hemodynamics in smoking males.

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