

# Effect of Passive Smoking on Endothelial Function in Healthy Adults

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## Abstract

**Background :** Active smoking predisposes to atherosclerotic vascular disease but recent evidence that inhalation of environmental tobacco smoke (passive smoking) may also have deleterious cardiovascular effects, has enormous public health implications. Endothelial dysfunction is an important early feature of atherogenic process, which may occur due to passive smoking.

**Objective :** To assess the effect of passive smoking on endothelial function (measured by flow-mediated dilatation, a marker of endothelium-dependent arterial dilatation) and compare it with non-smokers.

**Study Design :** Case control study.

**Setting :** Out-Patient Department of Medicine, Government Medical College, Nagpur.

**Participants :** Seventy-five young, healthy, male adults between 15-30 years age were studied. There were three groups : (a) Non smokers (n= 25) (b) Passive smokers (n= 25) and (c) Active smokers (n= 25). Subjects with diabetes mellitus, hypertension and ischemic heart disease were excluded. Lipid profile was measured in all. Endothelial function was tested non-invasively by using high frequency linear vascular probe on brachial artery. Resting brachial artery lumen, flow at rest and after hyperemia, flow-mediated dilatation and nitroglycerine-induced dilatation were measured.

**Results :** The mean brachial artery lumen dilatation and flow at rest were similar in all the three groups. Flow-mediated dilatation (FMD%, a marker of endothelium-dependent dilatation and endothelial function) was significantly higher in non-smokers than passive smokers ( $8.9 \pm 4.8$  Vs  $5 \pm 2.3$ ,  $p < 0.01$ ) and also as compared with active smokers ( $8.9 \pm 4.8$  Vs  $6.6 \pm 2.2$ ,  $p < 0.05$ ). Nitroglycerine-induced dilatation, (a marker of endothelium-independent dilatation) was similar in all the three groups. Serum lipids (mean cholesterol, LDL, and mean LDL/HDL ratio) were statistically significantly higher in passive and active smokers as compared with non-smokers ( $p < 0.05$ ).

**Conclusion :** Like active smoking, passive smoking was also associated with impaired endothelial function, (a key early event in atherogenesis) and altered lipid profile, in healthy young adults. ©

## INTRODUCTION

A possible relationship between passive smoking and coronary artery disease has been widely debated during the last decade.

Passive smoking which includes exposure to both burning cigarettes and exhaled main-stream smoke has been associated with increased respiratory system diseases in children<sup>1</sup> and excess deaths from lung cancer in adults.<sup>2</sup>

However, the greatest morbidity and mortality related to passive smoking have been attributed to atherosclerotic heart disease in middle and old age, accounts upto 20,000 deaths annually in non-smokers in United States alone.<sup>3-6</sup> Studies in laboratory animals have shown that passive smoking may increase atherosclerosis in cholesterol-fed rabbits<sup>7</sup> and in cockrels<sup>8,9</sup> but few studies have assessed the effects of passive smoking on the arterial wall in humans. Since endothelial dysfunction is an early feature of atherogenesis in vitro<sup>10</sup> in laboratory animals<sup>11,12</sup> and in humans,<sup>13</sup> it may represent an important marker of early vascular damage.

There is paucity of studies in Indian population. Therefore, we assessed the effect of passive smoking on the endothelial functions and compared the results of endothelium-

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dependent arterial dilatation with non-smokers, passive smokers and active smokers.

## MATERIAL AND METHODS

In this case control study, total 75 young healthy male adults between 15-30 years of age were enrolled. The subjects were categorized in three groups. a) Non-smokers as controls; b) Passive smokers; c) Active smokers as cases, with 25 subjects in each group.

Since no female smoker was found, study excluded females from all groups. Thus, it was gender matched study. Subjects having tobacco chewing habits, diabetes mellitus, hypertension, IHD, H/O premature deaths in family and medications for cardiac illness were excluded from study since these conditions also affect endothelial function. Participants were taken from amongst friends, hospital staff and society volunteers giving written consent to participate in the study. Approval from Ethic Committee was obtained.

Cases and controls were defined.

### Passive smokers<sup>14,15</sup>

Passive smokers are those exposed to both side-stream smoke from burning cigarettes and exhaled main-stream smoke.

In the present study passive smokers were the non-smokers with self-reported H/O exposure to environmental tobacco smoke at home or work place or both for atleast 1 hr/day for consecutive 3 yrs or more. They were sub-grouped according to the duration of environmental tobacco smoke exposure which was assessed by questionnaire as

a) *Light* : Exposed to ETS (environmental tobacco smoke) for 1-3 hrs / day / 3yrs.

b) *Moderate* : Exposed to ETS for 4-6 hrs / day / 3 yrs.

c) *Heavy* : Exposed to ETS for > 6hrs / day / 3yrs.

### Active smokers<sup>14</sup>

They are defined as subjects who had smoked atleast 20 cigarettes / day for atleast 1 year (1 pack-yr). They are divided into three subgroups.

A1) Those who smoked 20-30 cigarettes /day; A2) 31-40 cigarettes /day; A3) > 40 cigarettes /day.

### Non-smokers<sup>14</sup>

Non smokers are those who had never been regularly exposed to tobacco smoke at home or work place and had never smoked.

All the subjects were examined thoroughly. Serum lipid profile was done in all subjects.

Endothelial function was assessed on right brachial artery 5 cm. above the elbow with high resolution echo Doppler with 7.5 mHz high frequency linear vascular probe.<sup>14</sup>

Endothelial dysfunction in brachial artery appears to be well correlated with coronary endothelial physiology and coronary atherosclerosis.<sup>16</sup> Hence brachial artery was chosen for assessment of endothelial function. The brachial artery lumen diameter was measured at rest, during reactive

hyperemia and after glyceryl trinitrate (GTN) 400 microgms spray. Percentage increase in lumen diameter during post-ischemic hyperemia as compared to basal lumen diameter was labelled as flow-mediated dilatation (FMD%), a marker of endothelium-dependent dilatation. Percentage increase in lumen diameter after administration of GTN spray (400 microgms) as compared to basal lumen diameter was labelled as GTN% as a marker of endothelium-independent dilatation.

Statistical analysis was done. Unpaired "t" test was used to assess the significance of difference between the means of two independent groups. Paired "t" test was applied for comparing the difference in means of subgroups.

## RESULTS

The mean brachial artery lumen dilatation and flow at rest was similar in all the three groups. Flow-mediated dilatation (FMD%, a marker of endothelial-dependent dilatation and endothelial function) was significantly higher in non-smokers than passive smokers ( $8.9 \pm 4.8$  Vs  $5 \pm 2.3$ ,  $p < 0.01$ ) and also as compared with active smokers ( $8.9 \pm 4.8$  Vs  $6.6 \pm 2.2$ ,  $p < 0.05$ ) (Table 1). GTN-induced dilatation a marker of endothelium-independent dilatation was similar in all the three groups (Table 2).

The serum lipids (mean cholesterol, LDL, mean LDL/HDL ratio) were statistically significantly higher in passive and active smokers as compared with non-smokers ( $p < 0.05$ ) (Table 3).

In subgroup analysis, FMD% did not show dose-dependent relationship with endothelial dysfunction in passive as well as active smokers.

## DISCUSSION

An active cigarette smoking has long been known to predispose people to atherosclerotic diseases but it has recently become evident that exposure to environmental tobacco smoke may also have deleterious cardiovascular effects with enormous public health implications.<sup>3</sup>

The present study shows the endothelial dysfunction, an important early feature of the atherogenic process, which may occur in systemic arteries of healthy teenagers and young adults as a result of passive smoking.

Previous evidence of an association between endothelial

**Table 1 : Comparison of FMD% between controls, passive and active smokers**

Variable	Controls	Passive smokers	P value	Active smokers	Pvalue
FMD %	$8.9 \pm 4.8$	$5 \pm 2.3$	$< 0.01$	$6.6 \pm 2.2$	$< 0.05$

**Table 2 : Comparison of GTN % between passive and active smokers**

Variable	Controls	Passive smokers	P value	Active smokers	P value
GTN %	$18.08 \pm 6.78$	$16.90 \pm 7.05$	$0.549$	$17.88 \pm 4.72$	$0.904$

**Table 3 : Comparison of lipid profile in study subjects**

Variable n=25	Controls n = 25	Passive smokers n =25	P Value	Active smokers	P value
Total cholesterol	151.6 ± 13 .05	169 ± 27.6	0.005	172.2 ± 24.04	0 .0002
Total triglyceride	116.6 ± 14 .20	125.76 ± 19.2	0 .0532	128.44 ± 26.2	0 .0609
HDL cholesterol	55.24 ± 6.7	51.48 ± 6	0.0394	51.5 ± 7	0.0597
LDL cholesterol	92.76 ± 15.5	106.96 ± 20.4	0.0079	116.56 ± 16.5	0.0001
LDL / HDL ratio	1.59 ± 0.38	2.09 ± 0.5	0.0001	2.31 ± 0.6	0.0003

dysfunction and passive smoking came from Celermajer,<sup>14</sup> Raitaker *et al*<sup>15</sup> and Celermajer *et al*<sup>17</sup> who have reported significantly lower FMD% in passive and active smokers.

Dilatation mediated by brachial artery blood flow is endothelium-dependent and is mediated by the release of nitric oxide. Thus suggesting that the activity of endothelial nitric oxide might be impaired in young passive and active smokers.

Literature says that environmental tobacco consists of approximately 85% side-stream smoke (from burning ends of cigarettes) and 15% exhaled main-stream smoke.<sup>5</sup> Since cigarettes burn at higher temperature during inhalation, combustion is more complete and some toxic components of tobacco smoke are broken down or filtered out before inhalation. Consequently many toxic constituents such as carbon monoxide and benzopyrene are found in higher concentration in side-stream than in inhaled smoke.<sup>4</sup> More than 4000 chemicals are contained in environmental tobacco smoke.<sup>5</sup> One or more of these compounds may be injurious to the arterial wall in laboratory animals.

Passive smoking may also have adverse effect on lipid profile.<sup>18,19</sup> In the present study, total cholesterol, LDL, and LDL/HDL ratio in passive and active smokers were found significantly more than in controls. While total triglyceride and HDL cholesterol levels did not show statistically significant difference in all the three groups.

Maskowitz *et al*<sup>19</sup> and Craig WY<sup>20</sup> showed significant association between passive smoking and dyslipidemia while Celermajer *et al*<sup>14</sup> in their study have reported endothelial dysfunction in passive smokers but the study did not find any association between passive smoking and lipid levels.

All the passive smokers in the present study were exposed to environmental tobacco smoke for atleast 1 hour daily. Subgroup analysis in passive smokers failed to show any significant correlation between dose severity of tobacco exposure and endothelial dysfunction. But it might be due to less sample size in each group.

However the intensity of exposure to environmental tobacco smoke depends on the large number of variables, such as the number of hours of exposure per day, the proximity of the active smokers, the number of active smokers at the home or work place and size and ventilation of the room where passive smoking occurs. Assessment of all these factors were beyond the scope of the present study.

Thus this noninvasive method for in vivo assessment of

endothelium-dependent and independent arterial dilatation in young adult has been found to be accurate and reproducible.

Because the present study was conducted on healthy young adults without known atherogenic risk factors such as DM and hypertension, we were able to investigate the effect of passive and active smoking themselves on endothelial physiology. Larger sample size may be needed to support the results of the present study.

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### *Announcement*

**Second Madras Diabetes Research Foundation (MDRF) - American Diabetes Association (ADA), Postgraduate Course on Diabetes, at Chennai, India, September 2004.** The second MDRF-ADA Postgraduate Course on Diabetes will be held from 24th to 26th September 2004 at Chennai, India. The meeting will be hosted by the Madras Diabetes Research Foundation, Chennai.

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### *Announcement*

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