

Endothelial Function Assessment in Smokers and Passive Smokers

Gaiane Simonia, Mariam Kutateladze, Irina Andronikashvili, Karlo Matitaishvili, Maka Mirziashvili

Department of Internal Medicine, Tbilisi State Medical University, Georgia

ABSTRACT

Smoking impairs endothelial function in passive smokers as well as in active smokers. The aim of our study was evaluation of endothelial function using noninvasive ultrasonography methods flow-mediated dilatation (FMD) and peak blood flow (PBF) in nonsmoker passive smoker and smoker population. We investigated 32 normotensive, normocholesterolemic male subjects without clinical evidence of diabetes mellitus and CAD, mean age (34±9), of them -12 age-matched nonsmoker subjects, 6 passive smokers, and 14 active smokers. Our investigation revealed high positive correlation between FMD and PBF, especially in nonsmokers and passive smokers. FMD and PBF were significantly lower in smokers, than in nonsmokers. Endothelial function was significantly impaired in passive smokers compared to nonsmokers and did not significantly differ from endothelial function of smokers. Both FMD and PBF have shown similar degrees of impairment in passive smokers and smokers. Therefore, we suppose that both methods may be used for non-invasive assessment of endothelial dysfunction in clinical studies.

KEYWORDS: *endothelial dysfunction, flow-mediated dilatation, peak blood flow, passive smoking*

Smoking is one of the most important risk factors for cardiovascular events. Several mechanisms might account for the smoking-induced alterations in endothelial function. Cigarette smoke contains a large number of oxidants, that cause oxidative stress of endothelial cells [8,9]. Smoking is associated with a direct toxic effect on human endothelial cells [3,6], reduces endothelial prostacyclin production [11] and increases leukocyte adhesion to endothelial cells [1]. Alternatively, smoking increases endothelial angiotensin II production, which reduces nitric oxide activity that might contribute to endothelial dysfunction in smokers [4]. Increased platelet aggregation [3] and serum fibrinogen [7], as well as decreased serum plasminogen levels [12] known to occur in smokers, might also impair endothelial function in smokers. It has been shown, that environmental tobacco smoke causes arterial damage in passive smokers that might be related to enhanced degradation of nitric oxide secondary to the formation of oxygen-derived free radicals [10].

Brachial artery ultrasonography is a reliable non-invasive marker of endothelial function, which allows repetitive dynamic assessment of both arterial diameter and velocity [2]. Flow mediated dilation (FMD) of the brachial artery in response to occlusion is proven to be one of effective measurements of endothelial dysfunction [2]. The extent of increase in peak blood flow (PBF) in response to transient arterial ischemia has been reported as a measure of resistance vessel endothelial function and has shown better repeatability and reproducibility [5].

The aim of our study was evaluation of endothelial function using two aforementioned noninvasive methods in nonsmoker passive smoker and smoker population.

METHODS

We investigated 32 normotensive, normocholesterolemic male subjects without clinical evidence of diabetes mellitus and CAD, mean age (34±9), of them -12 age-matched subjects with no exposure to active or passive smoking (I group), 6 nonsmoking passive smokers (exposure to environmental tobacco smoke for > 1 hour per day for > 2 years) (II group), 14 active smokers (>1 packs per day for > 2 years) (III group). The diameter of the brachial

artery was measured from 2D ultrasound images. The brachial artery was scanned in longitudinal section. Three cardiac cycles were analyzed for each scan, and measurements were averaged. After the baseline measurements, a pneumatic tourniquet was inflated below the elbow to at least 50 mmHg above the systolic pressure; forearm cuff occlusion was maintained for 4.5 minutes and the diameter of the artery was measured at 1 minute after cuff deflation. Endothelium-dependent peripheral FMD was expressed as the percent change of brachial artery diameter 1 minute after forearm occlusion release, with baseline resting diameter used as a reference. PBF (in milliliters per minute) in the early postischemic period was calculated as the blood flow velocity-time integral multiplied by the diastolic vessel cross-sectional area.

RESULTS

Our investigation revealed high positive correlation between FMD and PBF, especially in nonsmokers and passive smokers ($r=0,74$ and $r=0,69$ respectively). In smokers correlation coefficient was lower ($r=0,37$) than in I and II groups, but the difference was not significant using comparison method of correlation coefficients.

FMD was significantly lower in smokers ($2,7\% \pm 2,1\%$), than in nonsmokers ($7,4\% \pm 3,2\%$) ($p=0,0002$). Endothelial function was impaired in passive smokers ($FMD=3,8\% \pm 2,7\%$) compared to nonsmokers ($p=0,03$) and did not significantly differ from endothelial function of smokers ($p=0,33$) (Fig 1).

There was no significant difference in PBF between smokers and passive smokers group (702 ± 234 ml/min and 767 ± 226 ml/min respectively, $p=0,57$), although endothelial dysfunction was clearly detected in both groups compared with nonsmoking group (1121 ± 366 ml/min), ($p=0,0017$ and $p=0,047$ for both comparisons respectively) (Fig 1).

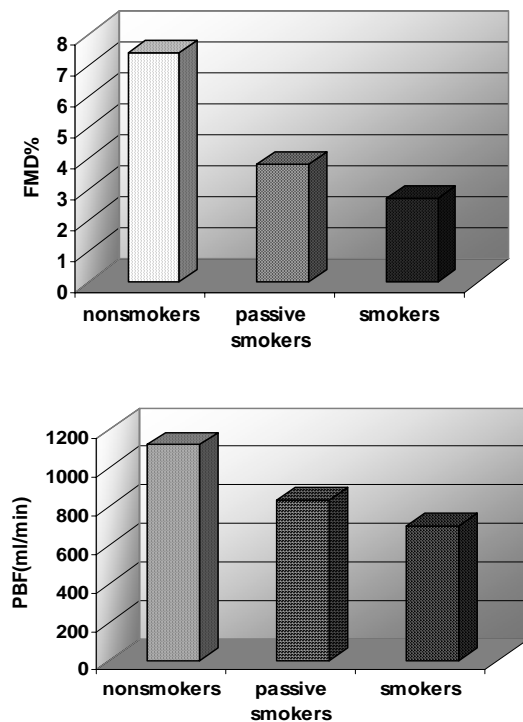


Fig.1 Influence of passive and active smoking on FMD and PBF

DISCUSSION

FMD is considered to be sensitive marker for endothelial dysfunction, as it has been shown to be mediated mainly by nitric oxide. Increase of blood flow velocity during reactive hyperemia induces increase of wall shear stress with subsequent local hyperproduction endothelial nitric oxide. PBF is not considered to be a specific marker of endothelial function, because PBF is fully determined by the extent of arteriolar dilation in ischemic area and just partially depends upon endothelium and nitric oxide.

However, extent of vasodilatation during shear stress is principally determined by peripheral arteriolar dilation and FMD is phenomenon secondary to PBF. Our results of positive correlation between FMD and PBF fully correspond to this suggestion.

Our results come in agreement to previous studies that endothelial dysfunction is significantly impaired in passive smokers as well as in smokers. It should be noticed that extent of endothelial dysfunction did not differ significantly in both groups, that might has to be taken into consideration while conducting preventive measures in aforementioned population groups.

Both FMD and PBF have shown similar degrees of impairment in passive smokers and smokers. Therefore, we suppose that PBF is not a less specific quantifier of endothelial function than FMD, and both methods may be used for non-invasive assessment of endothelial dysfunction in clinical studies.

REFERENCES:

1. Adams MR, Jessup W, Celermajer DS. Cigarette smoking is associated with increased human monocyte adhesion to endothelial cells: reversibility with oral L-arginine but not vitamin C. *J Am Coll Cardiol.* 1997;29:491-497.
2. Celermajer DS, Sorensen KE, Gooch VM, et al. Non-invasive detection of endothelial dysfunction in children and adults at risk of atherosclerosis. *Lancet* 1992;340:1111-5.
3. Davis JW, Shelton L, Eigenberg DA, Hignite CE, Watanabe IS. Effects of tobacco and non-tobacco cigarette smoking on endothelium and platelets. *Clin Pharmacol Ther.* 1985;37:529-533
4. Gibbons GH. Endothelial function as a determinant of vascular function and structure: a new therapeutic target. *Am J Cardiol.* 1997;79:3-8
5. Jan Malik, MD, PhD, Dan Wichterle, MD, Tomas Haas, PhD, Vojtech Melenovsky, MD, PhD, Jan Simek, MD, and Tomas Stulc, MD Repeatability of Noninvasive Surrogates of Endothelial Function, *Am J Cardiol* 2004;94:693-696
6. Kugiyama K, Yasue H, Ohgushi M, Motoyama T, Kawano H, Inobe Y, Hirashima O, Sugiyama S. Deficiency in nitric oxide bioactivity in epicardial coronary arteries of cigarette smokers. *J Am Coll Cardiol.* 1996;28:1161-1167
7. Meade TW, Vickers MV, Thompson SG, Stirling Y, Haines AP, Miller GJ. Epidemiological characteristics of platelet aggregability. *BMJ.* 1986;290:428-432.
8. Morrow JD, Frei B, Longmire AW, Gaziano JM, Lynch SM, Shyr Y, Strauss WE, Oates JA, Roberts LJ. Increase in circulating products of lipid peroxidation (F2-isoprostanes) in smokers. *N Engl J Med.* 1995;332:1198-1203.
9. Murohara T, Kugiyama K, Ohgushi M, Sugiyama S, Yasue H. Cigarette smoke extract contracts isolated porcine coronary arteries by superoxide anion-mediated degradation. *Am J Physiol.* 1994;266:H874-H880.
10. Raitakari OT, Adams MR, McCredie RJ, Griffiths KA, Celermajer DS. Arterial endothelial dysfunction related to passive smoking is potentially reversible in healthy young adults, *Annals of Internal Medicine*, 1999, Vol. 130, Number 7, 580-586
11. Reinders JH, Brinkman HJ, van Mourik JA, de Groot PG. Cigarette smoke impairs endothelial cell prostacyclin production. *Arteriosclerosis.* 1986;6:15-23.
12. Wilhelmsen L, Svardsudd K, Korsan-Bengtson K, Larsson B, Welin L, Tibblin G. Fibrinogen as a risk factor for stroke and myocardial infarction. *N Engl J Med.* 1984;311:501-505

Оценка эндотелиальной функции у пассивных и активных курильщиков

*Гаяне Симония, Мириам Кутателадзе, Ирина Андроникашвили, Карло Матиташвили,
Мака Мирзиашвили*

Кафедра внутренней медицины #1 Тбилисского государственного медицинского университета, Грузия

Р Е З Ю М Е

Курение вызывает нарушение эндотелиальной функции не только у активных, но и у пассивных курильщиков. Целью исследования являлось изучение эндотелиальной функции неинвазивными методами с помощью ультразвукографии - обусловленная кровотоком дилатация (ОКД) и пиковый кровоток (ПК) в некурящей и курящей популяциях. Обследовано 32 лиц мужчин с нормальными показателями артериального давления и содержания холестерина в крови: из них 14 - активные курильщики, 6 - пассивные, 12 некурящие. Среди обследованных отсутствовали клинические признаки сердечно-сосудистых заболеваний и сахарного диабета. Установлена отчетливая положительная корреляция между ОКД и ПК, особенно у некурящих и пассивных курильщиков. ОКД и ПК оказались значительно ниже у курящих в сравнении с некурящими. Эндотелиальная функция была значительно нарушена у пассивных курильщиков по сравнению с некурящими и недостоверно отличалась от эндотелиальной функций курильщиков. Как ОКД, так и ПК были в равной мере нарушены как у активных, так и у пассивных курильщиков. Полагаем, что оба метода могут быть использованы как неинвазивные для оценки эндотелиальной функции в клинической практике.

Ключевые слова: эндотелиальная функция, обусловленная кровотоком дилатация, пиковый кровоток, пассивное курение