Effects of Tobacco Consumption on Serum Creatinine & eGFR levels in Smokers

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Abstract:
Background: The recent decades have been a massive global increase in tobacco use. Tobacco use is a major preventable cause of premature death and diseases. Immediate availability and the low price give rise to high consumption of tobacco smoking and causes alteration of renal functions. The study was aimed at to observe the effects of tobacco consumption on renal functions in smokers. **Methods:** This cross sectional analytical study was conducted from July 2016 to June 2017 in the Department of Physiology, Rangpur Medical College, Rangpur. A total number of 60 subjects of both sexes were selected, among them 30 were apparently healthy non-smoker subjects as control group (group A) and 30 were apparently healthy smoker subjects (group B). The subjects were selected from different area of Rangpur city. The effects of cigarette smoking on renal functions were studied by measuring the levels of serum creatinine and eGFR. For statistical analysis independent sample "t" test was performed by computer based software SPSS-17.0 version for windows. **Results:** Serum creatinine levels were significantly higher ($p<0.001$) & eGFR levels were significantly lower ($p<0.001$) in smoker subjects as compared with the healthy control subjects. **Conclusion:** The increased serum creatinine & decreased eGFR levels in smoker subjects were evidence of development of renal function impaired due to tobacco smoking and this might offer a new approach to renal function impairment prevention in population with tobaccco smoking.

Indexing words: Tobacco smoker, Creatinine, eGFR

Introduction:
Tobacco is a product prepared from the plant by curing them[1]. Tobacco contains the alkaloid nicotine, which is an extremely addictive drug[1,2]. In addition to nicotine, tobacco contains thousands of other chemicals such as cresol, pyrene, DDT, carbon monoxide, ammonia, hydrogen cyanide, acetone, methanol, formaldehyde, arsenic, cadmium etc[3,4]. Dried tobacco leaves are mainly used for smoking in cigarettes, cigars, pipe tobacco, and flavored shisha tobacco. They can be also consumed as snuff, chewing tobacco and dipping tobacco[1].There are two kinds of commonly used tobacco products in Bangladesh i.e. smoking and smokeless tobacco products[4].

In Bangladesh 43.3% of adults (41.3 million) use tobacco either in smoking and/or smokeless form. More than five million people die globally each year due to tobacco related illness, the figure expected to increase to 8.3 million by 2030[5,6].

Now a day the adverse effects of smoking on renal function have gained more attention, because it is associated with excessive morbidity and mortality. In addition to its known cardiovascular consequences of cigarette smoking are also considered to be the common particular risk factor for the renal function disorders[7]. Some researchers observed cigarette smoking identified as an important risk factor cause renal dysfunction, not only in subjects with pre-existent primary renal disease, hypertension and diabetes mellitus but also in healthy subjects[8].

Tobacco smoke contains over 4,000 particles and gases, some of which are nephrotoxic. Particles include heavy metals known to cause tubular injury such as cadmium and lead, which may reach serum concentrations above 40% in smokers[9]. Cigarette smokers are exposed to significant amounts of cadmium (Cd) and lead (Pb), which also accumulate in kidney tissue more than in any other organ[10]. Nicotine causes mesangial cell proliferation and this change is observed in kidneys of active smokers[11].

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In smokers alteration of the relevant biochemical parameters may be indicators of onset of renal failure. The kidney functions are affected adversely in smoker non-tobacco chewer group, indicated by the elevation of serum creatinine and decrease of eGFR[13].

According to the official Agricultural Statistics (2010) three varieties of tobacco- Jati, Motihari and Virginia – are grown in different districts of Bangladesh. Rangpur still remains highest with 40,345 acres during 2008-2009[12].

The purpose of this study was to asses the effect of tobacco on some renal parameters of smoker subjects of northern region because the rate of tobacco use is more among the people of this region. As far as our knowledge, this kind of study was not previously done in our country. This study would increase awareness about the adverse effects of unjudicial tobacco use on renal system.

Methods:

The cross-sectional analytical study was conducted in the Department of Physiology, Rangpur Medical College, Rangpur from July 2016 to June 2017. The Rangpur Medical College Ethical Committee and Thesis Protocol Review Committee approved the study protocol. Total number of 60 apparently healthy subjects of both sexes with age 30-45 years was selected for this study by purposive sampling method. They were divided into: Group A – comprises 30 apparently healthy non- smokers and Group B - 30 apparently healthy smokers. The subjects included in each group matched in their age and socio-economic condition. The duration of smoking is more than three years. Height and weight of the subjects were measured. As tobacco chewing may produce similar effects on renal function, so tobacco chewer persons were excluded from both groups. All the subjects were free from history of liver, heart, lung and other chronic systemic diseases, obesity & diabetes mellitus, hypertension. Pregnant and lactating mother was also excluded from the study.

After selection of subjects, the objectives and the procedure of the study were explained in detail to them and their informed written consent were taken. A standard questionnaire was filled after taking history and through clinical examinations. At the first day all study procedures were maintained and advised the subjects to be in overnight (8-10 hrs) fasting state. They were asked to attend next day at 8.00 A.M. at the Department of Physiology, Rangpur Medical College, Rangpur. Fasting venous blood sample was collected following standard procedure. Serum creatinine was estimated at the Department of Biochemistry, Rangpur Medical College, Rangpur.

eGFR (estimated glomerular filtration rate) was calculated by Cockcroft-Gault formula by using serum creatinine level, age, sex and body weight of the patients[14].

For statistical analysis independent sample "t" test was performed by computer based software SPSS-17.0 version for windows.

Results:

Table 1 shows that the mean serum creatinine levels was significantly higher ($p<0.01$) and eGFR levels was significantly lower ($p<0.01$) in smoker non- tobacco chewer subjects than those of healthy control subjects.

Table 1: Mean ± SD of serum Creatinine and eGFR levels in two groups (n=60)

Variables	Group A (non-smokers) Mean ± SD Range (L- H)	Group B (Smokers) Mean ± SD Range (L- H)	p value
Serum Creatinine mg/dl	0.8967 ± 0.13515 (0.70–1.10)	1.4000 ± 0.15536 (1.10–1.70)	0.000***
eGFR ml/min/1.73m^2 of body surface area	96.4440 ± 19.40323 (66.30–139.68)	68.0887 ± 8.78026 (53.94–87.50)	0.000***

A= Apparently healthy subjects of non-smokers (Control)
B= Apparently healthy subjects of smokers (Experimental)
n= Number `of subjects
$p<0.05$ was considered as significant
Normal range of serum creatinine level is 0.6 – 1.3 mg/dl[15]
Normal range of eGFR level is ≥ 90 ml/min per m^2 body surface area[16]

Discussion:

In this cross sectional study, serum creatinine levels were significantly higher ($p<0.01$) and eGFR levels were significantly lower ($p<0.01$) in smoker non tobacco chewer subjects than those of healthy control subjects which is comparable to others.[7,17]

Literature review suggested several mechanisms for these changes of serum creatinine and eGFR levels in smoker non-tobacco chewer subjects. Higher levels of serum creatinine and lower levels of eGFR in smoker non-tobacco chewer subjects might be due to tobacco contains nicotine and also some toxic components which are nephrotoxic cause alteration of the kidney functions. The effects of heavy metals in tobacco like Cadmium (Cd) and Lead (Pb) cause glomerular dysfunction lead to renal damage. Tobacco smoking induces renal damage through enhancing the synthesis of free radicals lead to alter the glomerular functions and increase the serum creatinine and decrease eGFR levels. In addition, smoking causes generation of high amounts of carboxyhemoglobin and decrease oxygen delivery to tissue lead to hypoxia causes ischemia in renal glomeruli and basement membrane which causes impairment of renal functions. Nicotine increases mesangial cell proliferation through activation of nicotinic receptors. Tobacco smokes responsible for impairment of renal function which indicated by increase serum creatinine and decrease eGFR levels.[7]

Smoking increases the risk of atherosclerosis in the arteries of lower extremity and increased stiffness of central vessels causes increased energy transmission to low resistance arterioles in the kidneys, which is a key factor in the pathogenesis of glomerular and tubular damage.[17]

From the results of the present study, higher serum creatinine and lower eGFR levels in smoker non tobacco chewer subjects might be due to tobacco smoking for a prolong period of time which induced sustained rise of blood nicotine, carboxyhemoglobin levels and also free radicals cause impaired renal functions in tobacco smokers.

Conclusion

In this present study, it has been concluded that higher serum creatinine and lower eGFR levels in smoker non-tobacco chewer subjects might be due to renal functions impairment in tobacco smoking for a prolong period of time which induced sustained rise of blood nicotine level. But exact mechanism of high levels of serum creatinine and lower levels of eGFR in this group of people could not be demonstrated from this type of study. So, estimation of serum nicotine level, in same study population with large sample size which may help us to avoid bias. Reduction in tobacco smokes improves renal function impairment & reduces mortality and morbidity in smokers.

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