

ELECTROLYTE CHANGES IN CIGARETTE SMOKING MALE STUDENTS

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ABSTRACT:

The Cigarette smoke reaches quickly to heart, brain and other parts of our body and may cause effects in less than a second as it is inhaled directly into the alveoli and is diffused into the pulmonary vein. In spite of numerous studies to elucidate the role of electrolytes in smoking, no clear understanding of the influence of cigarette smoking on electrolytes is still known in literature partly because of varying methodological approaches while assessing the clinical and physiological manifestations. Hence, it was planned to carry out the present study involving university male students having habit of cigarette smoking for varying periods. No significant variations for plasma sodium and potassium, but a clear significant decrease in calcium levels were obtained in a group of subjects smoking 3-5 cigarettes per day. Another group of subjects having varying levels of cigarettes smoking activity (cigarettes/ day) showed significant decrease in plasma sodium, potassium and calcium. The present investigation, hence provides basic information about the pathogenetic role of electrolytes in cigarette smoking, and emphasizes for further comprehensive studies essentially required to be conducted with appropriate control measurements.

Keywords: Cigarette smoking; plasma electrolytes; sodium, potassium, calcium.

INTRODUCTION

Cigarette smoking is a kind of lifestyle factor that affects the health of humans. It has been shown to be an important risk factor in a variety of disorders where it is involved in the pathogenetic pathways. The habit of tobacco smoking starts during the period of adolescence or early adulthood as teenagers are attracted more by their peers than by the adults (Harris, 1998). The habit of smoking affects the mood and feelings of the smoker. Hence, for a smoker to be relaxant and remain feeling normal orient to continue smoking during nicotine depletion (Parrott, 1999). The Cigarette smoke reaches quickly to heart, brain and other parts of our body and may cause effects in less than a second as it is inhaled directly into the alveoli and is diffused into the pulmonary vein.

Cigarette smoking is associated with a variety of disorders via effecting various processes, factors, and mechanisms. Electrolyte variations are one set of changes occurring in response to smoking. Change in electrolytes occurs at systemic as well as cellular and molecular level. Electrolyte variations in smoking have been studied by several investigators (Markiewicz *et al.*, 1977; Eliasson *et al.*, 1993; Laine *et al.*, 2002; Erdemir and Erdemir, 2006 ; Avşar *et al.*, 2009; Padmavathi *et al.*, 2010). Erdemir and Erdemir (2006) showed non-significant difference for saliva sodium, potassium and calcium concentrations in smokers and non-smokers. Similar results for salivary electrolytes in smokers were obtained in an earlier (Laine *et al.*, 2002) and later report (Avşar *et al.*, 2009). However, one other previous report showed significantly increased serum levels of sodium and potassium in

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smokers (Eliasson *et al.*, 1993). Decrease in plasma sodium and potassium was obtained in men smoking 4 cigarettes per day (Markiewicz *et al.*, 1977).

In spite of the mentioned studies to elucidate the role of electrolytes in smoking, no clear understanding of the influence of cigarette smoking on electrolytes is still available in literature owing to different reasons mainly related to the varying methodological approaches while dealing the clinical and physiological manifestations. Hence, it was planned to carry out the present study for studying the young university male students having habit of cigarette smoking for varying periods. However, the cellular and molecular studies related to influence of smoking/nicotine on electrolytes via ion channels/receptors/transportation mechanisms cited in below paragraphs, were followed for hypothesizing the underlying intricate mechanisms.

Association of cigarette smoke with lung fluid accumulation and increased risk of acute respiratory distress syndrome has been suggested (Xu *et al.*, 2007) and it was postulated that ENaC alpha-subunit, that has a critical role in lung fluid absorption, is influenced by cigarette smoke. Investigation of the functional nicotinic acetylcholine receptors (nAChRs) in the epithelial cells lining mucocutaneous membranes (Zia *et al.*, 1997) further showed direct toxic effects of nicotine (Nic) on human bronchial epithelial cells (BEC). Nicotine effect has been investigated in the form of slowly inactivating $KV\{\alpha\}$ current in pulmonary neuroepithelial bodies (NEB) (Fu *et al.*, 2007). The NEBs form innervated cell clusters that express voltage-activated potassium currents and they perform the functions as airway O_2 sensors. Furthermore, nicotine is considered in contributing to the immunosuppressive properties of cigarette smoke (Kalra *et al.*, 2000) via depletion of inositol-1,4, 5-trisphosphate-sensitive Ca^{2+} stores.

The enzymes bound to membranes have an important role in neuronal activities via the

maintenance of membrane potential and impulse propagation. Chronic cigarette smoking has shown harmful effects on membrane-bound ATPases in rat brain (Anbarasi *et al.*, 2005). Adult male albino rats exposed to cigarette smoke for 12 weeks showed neuronal membrane damage from the decreased activity of membrane-bound enzymes (Anbarasi *et al.*, 2005). A disturbance in the balance of electrolytes along with accumulation of Na^+ and Ca^{2+} and depletion of K^+ was noticed.

Decreased sodium/ potassium-ATPase activity was found in subjects smoking 12 ± 2 cigarettes per day for 7-10 years (Padmavathi *et al.*, 2010). Another report revealed that amiloride (100 microM) completely lost its inhibitory ability in the presence of nicotine (Klimek *et al.*, 2000). Furthermore, amiloride-insensitive sodium channels did not show the effect of nicotine. It was investigated that the Na^+ channel blocker manifested an increased intracellular Ca^{2+} (Klimek *et al.*, 2000) that clearly showed that the nicotine-induced rise in intracellular calcium (Ca^{2+}) stimulated Ca^{2+} -dependent protein kinase (PKC).

A study predicts that cigarette smoke condensate inhibits ENaC alpha-subunit expression at transcriptional level via its promoter (Xu *et al.*, 2007) and this inhibition could be reversed by dexamethasone. This report presents a view of using higher doses of dexamethasone that may activate alpha-subunit expression in smokers' lungs compared to nonsmokers' lungs, and quitting smoking might improve the effectiveness of dexamethasone (Xu *et al.*, 2007). Another report revealed that nicotine at 50 and 100 microM suppressed the slowly inactivating K^+ current in pulmonary neuroepithelial bodies (NEB) (Fu *et al.*, 2007). However, this suppression was not reversed by mecamlamine that is probably a direct effect of nicotine on these K^+ channels. These studies suggest that the exposure to nicotine may directly affect the function of slowly inactivating A-type K^+ channels, involved in smoking-related lung disease.

Nicotine increases $[Ca^{2+}]_i$ (Zhao and Reece, 2005). This information identifies the molecular mechanism of nicotine action in embryonic apoptosis and malformations. Chronic smoking causes T cell anergy by disturbing the antigen receptor-mediated signal transduction that causes depletion of inositol-1,4, 5-trisphosphate-sensitive Ca^{2+} stores (Kalra *et al.*, 2000). It was found that nicotine increases the expression of the alpha 3, alpha 4, alpha 5, and alpha 7 nicotinic receptors that modulate calcium metabolism and regulate adhesion and motility of respiratory epithelial cells (Zia *et al.*, 1997). The long-term exposure to millimolar nicotine gave a steady increase of $[Ca^{2+}]_i$, that may lead to cell damage (Zia *et al.*, 1997).

Electrolyte variations in blood or cellular/molecular processes mentioned above are contradictory while comparing the reports of different investigators. Hence, it was proposed to conduct more controlled study for predicting the precise role of plasma sodium, potassium and calcium levels in smoking and non-smoking male students.

MATERIALS AND METHODS

Two groups of subjects were studied in the present work. These subjects (cigarette smoking and non-smoking) were consulted in Umm Al-Qura University and related institutions in Makkah, Saudi Arabia. All subjects were categorized into Group 1 and group 2.

Group 1 contained 35 smoking and 35 non-smoking male subjects. Age range of these subjects was 17-25 years (mean: 22 years). The smokers in this group were those smoking 3-5 cigarettes/ day with an average of 4.5 cigarettes/ day; and duration of the smoking habit was 1-3 years with average of 2.5 years.

The Group 2 comprised 88 smoking subjects (age range: 18-25 years; mean: 24 years; duration of the smoking habit: 1-4 years

with average of 3 years) accompanied by the normal controls from the group 1.

The Subjects in group 1 were categorized as smokers and non-smokers. However, the subjects in group 2 were categorized as those having habit of smoking 1-5, 6-10, 11-15 and > 15 cigarettes per day as average. The numbers of subjects in these categories were also represented as % of total smoking male subjects, and were compared for various estimations.

The details about the smoking habits, physical/physiological measurements and other information in the form of a standard questionnaire was employed before collecting blood for the estimation of plasma electrolytes (sodium, potassium and calcium) by routine methods in smoking and non-smoking male subjects. Each subject provided the details of his age, blood pressure, BBT, body weight, body height and other physical measurements.

The criteria of the selection of subjects (either smoking or non-smoking) was that no one should have any medical complication such as hypertension, ischemic heart disease, stroke, diabetes or any other disorder. Hence, all male subjects included in the present study are the normal healthy subjects. The data was collected and analyzed statistically using student t test and correlation coefficient 'r' of the regression line where required. The significance values (p) for various comparisons were found and the results were interpreted.

RESULTS AND DISCUSSION

Influence of cigarette smoking on electrolytes was studied in two groups of subjects having the habit of smoking. One group of smoking subjects (Group 1) were those with average activity of smoking in a specified range (3-5 cigarettes per day). Hence, this part of work was considered more interesting. Plasma electrolytes (mmol/L; sodium, potassium and calcium; mean \pm SD)

Table 1
Plasma electrolytes in smoking and non-smoking male students

Plasma electrolytes	Non-smoking (n: 35)	Smoking (n: 35)	Significance Level (p)
Sodium (mmol/L)	142.33±2.41	141.54±2.62	ns
Potassium (mmol/L)	4.62±0.60	4.61±0.53	ns
Calcium (mmol/L)	2.37±0.11	2.29±0.11	p=0.0033

The values are mean ± SD; n: number of subjects; ns: non-significant.

Table 2
Influence of daily cigarette smoking on plasma electrolytes in male students

Cigarette smoking (Cigarettes/day)	Subjects		Plasma electrolytes		
	n	%	Sodium (mmol/L)	Potassium (mmol/L)	Calcium (mmol/L)
1-5	14	15.91	142.04±2.58	4.53±0.70	2.38±0.09
6-10	25	28.41	141.20±2.56	4.63±0.69	2.38±0.09
10-15	22	25.00	140.11±3.12*	3.98±0.75*b	2.34±0.12
>15	27	30.68	138.23±3.12*a	3.71±0.74*c	2.21±0.13*d

The values are mean± SD; n: number of subjects; ns: non-significant; * p=0.0038, *a p<0.0001, *b p=0.0008, *c p<0.0001, *d p<0.0001

respectively in this part of study were 142.33±2.41, 4.62±0.60 and 2.37±0.11 for non-smoking control male subjects and 141.54±2.62, 4.61±0.53 and 2.29±0.11 in smoking male subjects.

These results are presented in Table 1. Statistical comparisons showed no significant variations for plasma sodium and potassium, but a clear significant decrease in calcium levels in smoking subjects (p=0.0033). Though the change in plasma sodium and potassium was not found significant, however, a non-significant decrease was noticed in cigarette smokers (Table 1).

The second group of cigarette smokers comprised sub-groups on the basis of their cigarette smoking activity (1-5 (15.91% subjects), 6-10 (28.41% subjects), 10-15 (25 % subjects) and >15 (30.68 % subjects) cigarettes per day). The results (mean ± SD) are shown in Table 2. The mean ± SD values for plasma sodium (142.04±2.58 for subjects smoking 1-5 cigarettes per day; 141.20±2.56 for subjects

smoking 6-10 cigarettes per day; 140.11±3.12 for subjects smoking 10-15 cigarettes per day; and 138.23±3.12 for subjects smoking >15 cigarettes per day) showed significant change in subjects smoking 10-15 cigarettes per day (p=0.0038) and highly significant variation in subjects smoking > 15 cigarettes per day (p<0.0001). It was quite interesting to note that a negative linear relationship (though non-significant) was obtained while plotting cigarettes/day against sodium levels.

The mean ± SD values for plasma potassium (4.53±0.70 for subjects smoking 1-5 cigarettes per day; 4.63±0.69 for subjects smoking 6-10 cigarettes per day; 3.98±0.75 for subjects smoking 10-15 cigarettes per day; and 3.71±0.74 for subjects smoking >15 cigarettes per day) showed significant variation in subjects smoking 10-15 cigarettes per day (p=0.0008) and highly significant variation in those smoking >15 cigarettes per day (p<0.0001). A negative linear relationship (though non-significant) was obtained while

plotting cigarettes/day against potassium levels.

The mean \pm SD values for plasma calcium (2.38 \pm 0.09 for subjects smoking 1-5 cigarettes per day; 2.38 \pm 0.09 for subjects smoking 6-10 cigarettes per day; 2.34 \pm 0.12 for subjects smoking 10-15 cigarettes per day; and 2.21 \pm 0.13 for subjects smoking >15 cigarettes per day) showed significant variation in subjects smoking >15 cigarettes per day ($p < 0.0001$). A negative linear relationship (though non-significant) was obtained while plotting cigarettes/day against potassium levels.

The results obtained for electrolyte fluctuations in cigarette smoking in the present report resemble to the investigations of Markiewicz *et al.* (1977) whereas differ from other reports (Eliasson *et al.*, 1993; Laine *et al.*, 2002; Erdemir and Erdemir, 2006; Avşar *et al.*, 2009). Dissimilarity of present findings from the mentioned reports might had been due to their investigations in saliva in certain specific additional conditions except Eliasson *et al.* (1993) who used serum for assessing the variations, though that report does not comprise the study of precise changes in cigarette smokers, and has assumed that some of the abnormalities noted in smokers did not seem to be mediated by nicotine. Whereas influence of nicotine on reducing the body weight and indirectly on decreasing the electrolytes is evident.

The report of Markiewicz *et al.* (1977), however, provides the information partly as has been obtained in the present study. But the present investigation can further be verified by carrying out studies on the effect of nicotine and other active components in tobacco on electrolyte metabolism. The literature documents quite a few reports describing the influence of smoking on plasma/serum electrolytes. Hence, for the precise understanding, further comprehensive studies are essentially required to be conducted with appropriate control measurements.

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