IMPACT OF TOBACCO USE ON NEUROCOGNITIVE FUNCTION IN ADULT MALES VISITING RURAL HEALTH AND TRAINING CENTRE AT VILLAGE PALI, FARIDABAD

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Abstract:

Background and Objectives: Use of tobacco has complex effects on human health. In India the use of smokeless tobacco is as rampant as the use of smoked tobacco. The present study was designed to assess differences in the neurocognitive status between users of smoked tobacco / smokeless tobacco and tobacco non-users and to explore whether cognitive changes vary with the degree of physical dependence on tobacco use. **Methods:** The study sample comprised of 160 males in the age group of 30-50yrs and grouped them as smoked tobacco users, smokeless tobacco users and tobacco non- users. FTND and FTND-ST scales were used for assessing the intensity of physical addiction to nicotine related to tobacco use. ACE-R was used for cognitive assessment. The data was entered in Microsoft Office Excel and was analysed using Epi info version 7 software. **Results**: In the present study mean ACE-R score, the measure of cognitive performance was highest among tobacco non-users and lowest in users of smoked tobacco. There was statistically significant negative correlation between Fagerstrom score the measure of nicotine dependence and ACE-R score. **Interpretation and Conclusion:** We conclude, there may be a link between tobacco use and cognitive impairment. Smokeless tobacco also affects cognition adversely.

Key words: Neurocognition, Physical dependence, tobacco use

Abbreviations: FTND**,** Fagerstrom Test for Nicotine Dependence; FTND-ST, Fagerstrom Test for Nicotine Dependence – Smokeless Tobacco; ACE-R, Adden Brooke's Cognitive Examination – Revised Version.

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INTRODUCTION: Smoking is the leading cause of preventable deaths in the world. Tobacco use causes more than 5 million deaths per year worldwide. WHO report predicts that the annual death toll due to tobacco consumption could rise to over 8 million in the next two decades[1]. Nicotine the principal component in tobacco smoke is highly addictive and meets all established criteria for a drug that produces addiction – specifically, dependence and withdrawal. Besides nicotine's addictive properties, other factors to consider include its easy availability, the small number of legal and social consequences of tobacco use and the sophisticated marketing and advertising methods of tobacco companies. Smoking related diseases include cancer, heart disease, and lung diseases such as emphysema and bronchitis. A large number of studies have documented the adverse effects of smoking on respiratory and cardiac function. However, only few studies have explored the impact of smoking on cognition. Literature search on the effect of smoking on cognition has revealed conflicting results. Some researchers have reported nicotine as a cognitive enhancer[2,3] whereas a meta- analysis has revealed faster cognitive decline among smokers[4]. In India the use of smokeless tobacco is as rampant as the use of smoked tobacco. Literature search did not find any systematic reviews or studies which examined the impact of use of smokeless tobacco on cognitive function. Since adequate cognitive functioning plays a vital role in leading an independent life and at present, no treatment is available to cure or alter the progressive course of cognitive impairment, it is essential to identify modifiable risk factors for reducing the occurrence of the disease, delaying its onset or reducing its burden. The objectives of the present study were to assess differences in the neurocognitive status between users of smoked tobacco / smokeless tobacco and tobacco non-users and to explore whether cognitive changes vary with the degree of physical dependence on tobacco use.

Materials and Methods: The observational cross sectional study sample comprised of 160 males in the age group of 30-50yrs from the community residing at village Pali which is a field practice area under Rural Health and Training Centre (RHTC) of ESIC Medical College, Faridabad. Informed consent was obtained from all the subjects and prior approval of Institutional Ethics Committee was taken. The sample size was calculated using Epi info version 7 software. Taking prevalence of adult tobacco users in India according to Global Adult Tobacco Survey-2 (GATS-2, 2016-17) as 28.6%, at 10% absolute error and 95% confidence interval and design effect of 2, the minimum sample size was 156. We recruited 160 adults and divided them into three groups as smoked tobacco users, smokeless tobacco users and tobacco non-users (not exposed to even second-hand smoke). Subjects using tobacco for more than 5yrs were included in the study. Known hypertensives, diabetics and individuals with diagnosed mental illness or vascular disease were excluded from the study. To avoid the bias resulting from age related cognitive decline, males ≥50yrs of age were excluded from the study.

The Fagerstrom Test for Nicotine Dependence (FTND) and Fagerstrom Test for Nicotine Dependence – Smokeless Tobacco (FTND-ST) were used for assessing the intensity of physical addiction to nicotine related to smoked tobacco / smokeless tobacco[5,6]. The instrument contains six items that evaluate the quantity of nicotine consumption, the compulsion to use, and dependence. In scoring the FTND, yes/no items are scored from 0-1 and multiple- choice items are scored from 0-3. The items are summed to yield a score of 0-10. The higher the total Fagerstrom score, the more intense is the subject's physical dependence on nicotine.

Adden Brooke's Cognitive Examination – Revised Version (ACE-R) was used for cognitive assessment[7]. It takes 12-20 minutes to administer and score. It contains 5 sub-scores, each one representing one cognitive domain: attention/orientation (18 points), memory (26 points), fluency (14 points), language (26 points) and visuospatial (16 points). ACE-R maximum score is 100, composed by the addition of all the domains. Higher scores indicate a better cognitive function. A score of ≤82 is considered for the diagnosis of dementia. As ACE-R is a literacy based assessment, only literate participants (matriculate or more) were recruited into the study. In Indian set up, literate females using smoked / smokeless tobacco are difficult to find, therefore female subjects were excluded from the study.

The data was entered in Microsoft Office Excel and was analysed using Epi info version 7 software. The continuous variables (scores) are presented as mean. Student's t- test and ANOVA were applied to test the statistical significance of difference in means between different groups of tobacco users and non users. Correlation between continuous variables was measured using Pearson's correlation. Level of significance is set at 5%

Results: In the present cross sectional study, of the total 160 participants, 64 participants were tobacco users and 96 were tobacco non-users (total 160). Table 1 shows the subject characteristics with respect to tobacco use. Table 2 shows the mean ± SD values of ACE-R (total and subscale) scores in tobacco users Vs non-users and smoked tobacco users Vs smokeless tobacco users. Results of two-way ANOVA for differences in ACE-R (total and subscale) scores between the three groups are presented in table 4.The mean ACE-R score was highest among tobacco non-users, decreased in smokeless tobacco users and was least among smokers. The variation of ACE-R score between the three groups was statistically significant ($p<0.001$). Similar pattern of statistically significant variation of mean score was observed among attention and orientation, memory and verbal fluency and the variations were statistically significant. Pearson's correlation coefficients were calculated to examine associations between Fagerstrom and ACE-R (total and subscale) scores in tobacco users. The results are summarized in table 5.

Table 1: Subject characteristics with respect to tobacco use

	Smoked tobacco (N=32)	Smokeless tobacco (N=32)
Age at first tobacco use	23.09±6.007	18.38±6.194
Years of tobacco use	24.13±6.020	15.16±8.588
Fagerstrom score	6.41±2.138	5.94±2.488
ACE-R score	82.72±2.29	85.78±2.67

Table: 2 Comparison of age and ACE-R (total and subscale) scores between smoked tobacco users, smokeless tobacco users and tobacco non-users

Parameters	Smoked tobacco users (n=32)	Smokeless tobacco users (N=32)	P value	Tobacco users (n=64)	Tobacco non-users (n=96)	P value
Age	41.47±5.55	38.97±5.80	0.08	40.22±5.77	40.31±5.46	0.92
ACE-R	82.72±2.29	85.78±2.67	**<0.001**	84.25±2.91	88.71±2.63	**<0.001**
Orientation and attention	18.22±1.13	18.91±0.99	**0.012**	18.56±1.11	19.70±1.52	**<0.001**
Memory	22.59±1.81	23.22±1.16	0.105	22.91±1.54	23.69±1.40	**0.001**
Verbal fluency	4.91±1.06	6.34±1.47	**<0.001**	5.63±1.46	6.91±1.31	**<0.001**
Language	22.75±1.59	22.63±1.24	0.726	22.69±1.41	22.38±1.42	**0.003**
Visuo spatial	14.25±1.16	14.69±1.18	0.140	14.47±1.18	15.04±0.93	**0.001**

p<0.05 is statistically significant

Table3: Results of two-way ANOVA for differences in ACE-R (total and subscale) scores between the three groups

		Sum of Squares	df	Mean Square	F	p value
ACER score	Between Groups	913.32	2	456.66	68.69	**<0.0001**
	Within Groups	1043.77	157	6.64		
	Total	1957.10	159			
Attention and orientation	Between Groups	57.06	2	28.53	15.42	**<0.0001**
	Within Groups	290.42	157	1.85		

	Total	347.49	159			
Memory	Between Groups	29.68	2	14.84	7.06	**0.001**
	Within Groups	329.81	157	2.10		
	Total	359.50	159			
Verbal Fluency	Between Groups	96.10	2	48.05	28.56	**<0.0001**
	Within Groups	264.09	157	1.68		
	Total	360.19	159			
Language	Between Groups	18.40	2	9.20	4.54	**0.012**
	Within Groups	318.00	157	2.02		
	Total	336.40	159			
Visuospatial	Between Groups	15.66	2	7.83	7.37	**0.001**
	Within Groups	166.70	157	1.06		
	Total	182.37	159			

p<0.05 is statistically significant

Table 4: Pearson Correlation coefficients of Fagerstrom and ACE-R (total and subscale) scores in tobacco users

	Fagerstrom score	ACER score	Attention and orientation	Memory	Fluency	Language	Visuo spatial
Fagerstrom score	1	-.417*	-.025	-.331	-.196	.221	-.405*
		.017	.893	.064	.281	.224	.021
ACER score	.005	1	.174	.469*	.335	.335	.306
	.978		.340	.007	.061	.061	.089
Attention and orientation	.304	.138	1	-.129	.045	-.023	-.436*
	.090	.453		.483	.808	.903	.013
Memory	.202	.402*	.102	1	-.105	-.317	.019
	.266	.023	.577		.569	.077	.917
Fluency	-.131	.733*	-.197	-.008	1	-.149	.072
	.475	.000	.279	.967		.416	.695
Language	-.156	.325	-.265	-.301	.338	1	-.052
	.395	.069	.143	.094	.058		.776

Visuospatial	-.117	.501*	-.108	.170	.232	-.216	1
	.523	.003	.554	.351	.202	.235	

Correlations above the diagonal (smoked tobacco users N=32), below the diagonal (smokeless tobacco users N=32). In each cell upper value is r (Pearson Correlation coefficient) and lower value is p.

***Statistically significant (p=<.05)**

Discussion: The most common method of using tobacco is in the form of manufactured cigarettes. The present study was designed to examine the effects of chronic tobacco use on neurocognition. Previous research investigating this issue has been restricted only to the use of smoked tobacco and indicates that chronic cigarette smoking is associated with diminished function of multiple neurocognitive abilities and neurobiological abnormalities[8,9]. This study adds to the existing literature by investigating the effects of tobacco use in both users of smoked tobacco and smokeless tobacco and comparing them with tobacco non-users.

In the present study the nicotine dependence was higher among smokers as compared to users of smokeless tobacco. This is similar to a study conducted among male industrial workers of West India[10] and in contrast to a study conducted among male workers in Urban Delhi[11]. This difference in dependence among smokers and and smokeless tobacco users is probably due to the socio economic status, cultural norms, dose and duration of tobacco use. The mean ACE-R score, the measure of cognitive performance was highest among tobacco non-users and lowest among users of smoked tobacco. There was statistically significant negative correlation between Fagerstrom score, the measure of nicotine dependence and ACE-R score in users of smoked tobacco. This is consistent with previous findings of an inverse relationship between level and chronicity of smoking and various domains of neurocognition in adults[12,13].

All subscales of ACE-R showed a negative correlation with Fagerstrom score among tobacco smokers with the exception of language which showed a positive correlation. In users of smokeless tobacco ACE-R score, attention & orientation and memory showed a positive correlation with Fagerstrom score. The group differences in various subscales of ACE-R may be the result of dose effect i.e less exposure to nicotine in users of smokeless tobacco. There are conflicting reports from previous studies. Some have reported no effect of cigarette smoking on specific neurocognitive functions like learning, memory, mental arithmetic and verbal fluency[14]. In a study from USA as compared to healthy controls, cigarette smokers had cognitive deficits in auditory-verbal and visuospatial learning, visuospatial memory, cognitive efficiency, executive skills, general intelligence and processing speed[15]. In another population based case control study from Germany significant deficit was observed among smokers for visual attention and cognitive impulsivity, while verbal episodic memory, verbal fluency and verba working memory did not differ between smokers and non smokers[16]. Heishman et al., in their 1994 study reported enhanced motor response, focused and sustained attention and recognition memory in smokers as compared to never-smokers. The results were further substantiated by the same authors in 2010. They concluded that the beneficial cognitive effects of nicotine might be reason for initiation of smoking and maintenance of dependence[17]. Literature also reports that low dose nicotine may be anantioxidant and neuroprotective,

whereas high dose nicotine may induce neurotoxicity through oxidative stress and cellular injury[18]. Reviews based on cumulative research suggest that chronic cigarette smoking is associated with deficiencies in auditory – verbal learning and / or memory, general intellectual abilities, visual search speeds, processing speed, cognitive flexibility, working memory and executive functions across a wide age range[19]. The adverse neurocognitive effects may be due to a large no. of potentially cytotoxic compounds (e.g. free radicals and their precursors, CO, Nitrosamines, phenolic compounds and other polynuclear aromatic compounds) present in cigarette smoke which may be directly cytotoxic, damage neural or glial cell organelles and promote oxidative damage[20].
The limitations of the study are that the actual mechanisms contributing to cognitive decline in tobacco users are still unclear. Certain premorbid variables like genetic vulnerabilities should also have been considered as a potential contributing factor. To better understand the potential mechanisms, longitudinal research combining neurocognitive assessment with neuroimaging, biochemistry and perfusion of brain is required.

Conclusion: Our results suggest that both smoked and smokeless tobacco are associated with diminished neurocognitive functions. The information could be used by various national, regional and local agencies to introduce regulatory reforms and increase public awareness of the risk of tobacco-caused cognitive impairment.

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