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Research Article

A Cross-Sectional Study to Compare the Effects of Chewing Versus Smoking Tobacco on Corneal Endothelial Health

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Abstract

Purpose: Tobacco smoking is known to trigger an increase in levels of oxygen radicles in aqueous humor and other ocular tissues, decreased levels of antioxidants such as ascorbic acid. This study aims to compare effects of chewing versus smoking tobacco on corneal endothelial health.

Materials and Methods: This cross-sectional study was conducted at tertiary hospital which included 273 participants divided into three cohorts: 91 tobacco smokers, 91 tobacco chewers, and 91 non-tobacco users. They were evaluated for demographic data, history of systemic comorbidities. Corneal endothelial evaluation done by non-contact specular microscopy. Endothelial cell density, coefficient of variation in cell size, % hexagonality, maximum cell area, minimum cell area and standard deviation of cell area recorded and compared among three groups. Categorical data was represented in the form of frequencies and proportions. Chi-square test or Fischer's exact test (for 2x2 tables only) was used as test of significance for qualitative data. Continuous data was represented as mean and standard deviation. ANOVA was used as the test of significance to identify the mean difference between three groups. MS Excel and MS word was used to obtain various types of graphs. P value <0.05 was considered as statistically significant after assuming all the rules of statistical tests.

Results: Out of 273 participants, 126 (46.1%) were male and 146 (53.4%) were females. Mean age was 58 ± 2 years in all three groups. ECD and hexagonality was highest among non-tobacco users and least among tobacco chewers. All other endothelial parameters were highest among tobacco chewers compared to tobacco smokers and non-tobacco users.

Conclusion: The effects of tobacco chewing, in addition to smoking on corneal health cannot be underrated. This study points to evidence that chewers may be at a higher risk of corneal endothelial changes as compared with smokers. Therefore, it becomes imperative that these patients must undergo extensive pre-surgical evaluation in terms of a thorough corneal endothelial structural analysis when planning for a vision-improving surgery such as cataract surgery.

Keywords: *Tobacco Chewers; Tobacco Smokers; Endothelial Cell Parameters; Specular Microscopy*

Introduction

Tobacco consumption is a major public health concern worldwide at present. In India, it was estimated that one-third of women and two-thirds of men consume tobacco in some form, either smoking or smokeless tobacco [1]. Although smoking is the most prevalent form of tobacco consumption, other forms of tobacco use are also significant. Smokeless tobacco, with contents like nicotine, and other carcinogens imposes major medical, financial and social burden especially in south and south-east Asian regions [2]. India accounts for 70% of global smokeless tobacco consumption, which is prevalent in all age groups and accounts for a major public health concern in this country and the surrounding regions.

Tobacco smoking, known to trigger an increase in levels of oxygen radicles in aqueous humor and other ocular tissues, and also decreased levels of antioxidants such as ascorbic acid [1,2]. Additionally induced hypoxia and a chronic inflammatory milieu have been implicated to cause corneal endothelial damage over time [3-5]. The resultant peripheral vasoconstriction and oxidative stress caused by nicotine, impairment of collagen synthesis causing delayed wound healing, alterations in the Descemet membrane, and direct toxicity of nicotine on the corneal surface are primarily responsible for corneal damage.

Various corneal changes such as an increase in the central corneal thickness (CCT), a loss of hexagonal endothelial cells, tear film instability and susceptibility to infections leading to persistent corneal defects have been attributed to long-term tobacco usage [6].

Although much was known about the effects of tobacco smoking on ocular health, there is paucity of literature on head-to-head comparison between different forms of tobacco consumption in this regard. It has been reported that the blood levels of nicotine are twice the amount for smokeless when compared with tobacco smokers, which can potentiate the toxic effects in the tissues, including the eye [7,8]. Literature search shows decreased corneal endothelial cell count in smokers when compared with non-smokers [1-8].

Aim of the Study

In this study we aim to compare the effects of chewing versus smoking tobacco on corneal endothelial health.

Materials and Methods

This cross-sectional observational hospital-based study was conducted on 273 participants divided into three cohorts: 91 tobacco smokers, 91 tobacco chewers and 91 non-tobacco users fulfilling the inclusion criteria in the department of Ophthalmology at R.L.J. Hospital and Research Centre attached to Sri Devaraj Urs Medical College, Kolar for a period from October 2024 to March 2025. This study was performed according to the guidelines of the Declaration of Helsinki, and all subjects gave their written informed consent to participate, which was approved by the Institutional Ethics Committee.

Inclusion criteria:

1. Patients with ophthalmic condition (other than exclusion criteria) from age groups ranging from 20 years to 70 years of either sex, who consume tobacco either in form of smoking or chewing.
2. Healthy controls of same age group with no history of tobacco use in any form are included in this study.

Exclusion criteria:

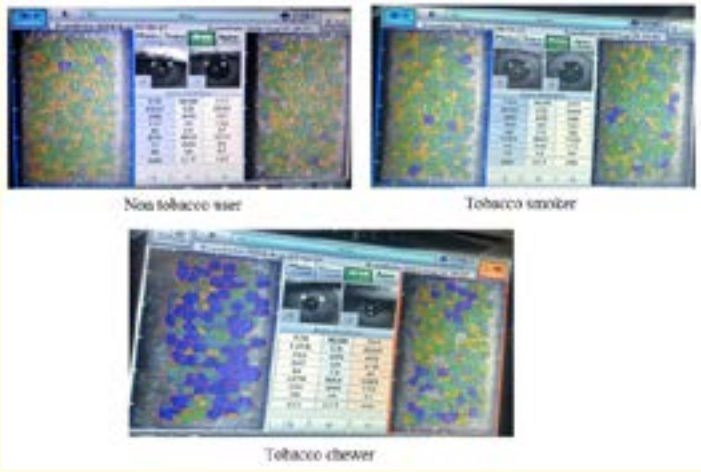
1. Mixed use of tobacco
2. Corneal endothelial dystrophies
3. Prior ophthalmic surgeries
4. Severe ocular trauma, chemical injury
5. Dry eye syndrome

6. Past/present history of corneal infection
7. Prolonged contact lens use
8. Raised intraocular pressure
9. High myopia
10. Pterygium.
11. Systemic illness that is known to impair tear function such as rheumatoid arthritis and other connective tissue diseases
12. Patients with diabetes mellitus.

Patients those selected as per the inclusion criteria were assessed regarding their demographic details, history and subjected to a detailed ocular examination of both the eyes for visual acuity by Snellen's chart for distant vision, near vision by Jaeger chart, anterior segment assessment by slit lamp biomicroscope, fundus examination by + 90D lens assisted slit lamp biomicroscope and direct ophthalmoscopy, intraocular pressure measurement by Goldmann applanation tonometry.

Assessment of endothelial cell parameters by Tomey's non-contact specular microscopy for:

1. Endothelial cell density (ECD)
2. Percentage of Hexagonality (HEX)
3. Average cell area (AVG)
4. Maximum cell area (MAX)
5. Minimum cell area (MIN)
6. Standard deviation of cell area (SD)
7. Coefficient of variation in cell area (CV).



Figure

Sample size calculation

Was estimated by using the difference in mean ECD between non tobacco, tobacco smoker and tobacco chewers from the study Jha A., *et al.* as 2488.7 ± 305.5, 2396.63 ± 221.13 and 2283.24 ± 341.9. Using these values at 95% Confidence limit and 90% power sample size of 82 was obtained in each group by using the below mentioned formula and Med calc sample size software. With 10% nonresponse sample size of 82 + 8.2 ≈ 91 minimum subjects were included in each group.

Sample size estimation formula: $N = \frac{3SD^2(Z_{\alpha/2} + Z_{\beta})^2}{d^2}$

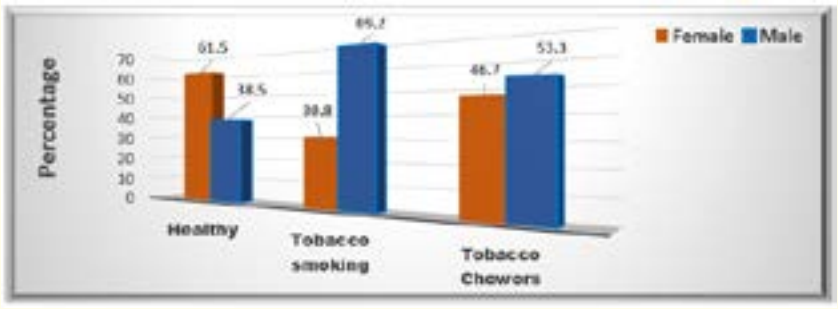
- Where $Z_{\alpha/2}$ is the critical value of the Normal distribution at $_{\alpha/2}$ (e.g. for a confidence level of 95%, **α** is 0.05 and the critical value is 1.96).
- Z_{β} is the critical value of the Normal distribution at β (e.g. for a power of 90%, ß is 0.1 and the critical value is 1.28).
- SD is the standard deviation from previous study population variance, and
- d is the largest difference among three groups.

Statistical analysis

Data was entered into Microsoft excel data sheet and was analyzed using SPSS 22 version software. Categorical data was represented in the form of frequencies and proportions. Chi-square test or Fischer's exact test (for 2x2 tables only) was used as test of significance for qualitative data. Continuous data was represented as mean and standard deviation. ANOVA was the test of significance to identify the mean difference between three groups. P value <0.05 was considered as statistically significant after assuming all the rules of statistical tests.

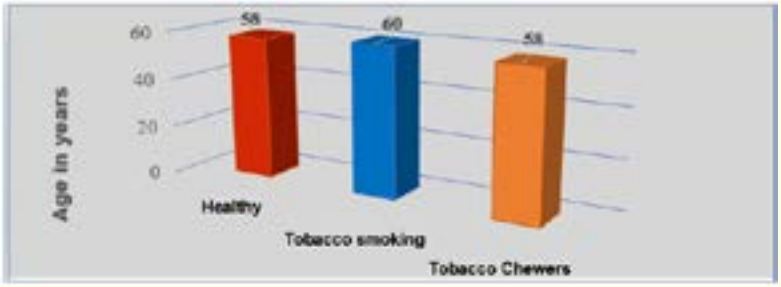
Results

There were total of 273 patients divided into three cohorts: 91 tobacco smokers, 91 tobacco chewers, and 91 non-tobacco users aged between 20 and 70 years.



Graph 1: *Distribution of subjects according to gender among the groups.*

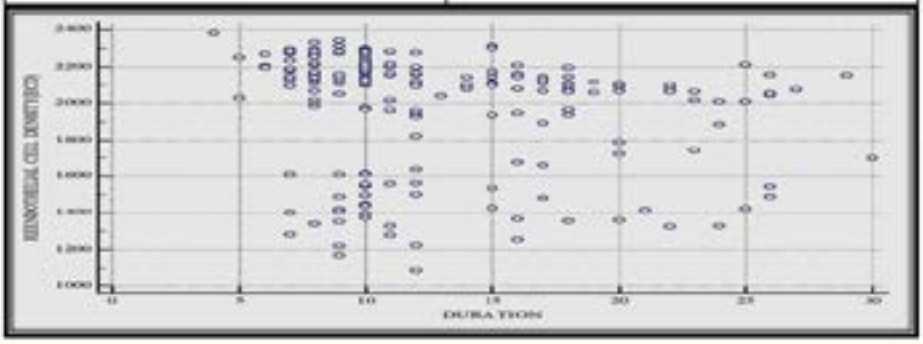
P value was 0.001, hence there was a statistically significant difference found between groups with respect to sex with male preponderance in both tobacco smokers and chewers.



Graph 2: *Comparison of age among the groups.*

P value was 0.148, so there was no statistically significant difference found between groups with respect to age.

Correlation coefficient r	**-0.1489**
Significance level	P=0.0454
95% Confidence interval for r	-0.2885 to -0.003130



Graph 3: *Endothelial cell density has reduced with increased duration of tobacco usage, there was significant reduction of ECD after tobacco usage for more than 10 years.*

	Healthy		Tobacco smoking		Tobacco chewers		P value
	Mean	**SD**	**Mean**	**SD**	**Mean**	**SD**	
RE ECD	2520	193	2171	87	1749	338	<0.01
RE HEX %	43	5	40	5	38	6	<0.01
RE AVG	399	30	458	22	602	167	<0.01
RE MAX	970	205	1153	266	1518	558	<0.01
RE MIN	96	19	112	22	155	92	<0.01
RE SD	156	23	187	26	269	85	<0.01
RE CV	39	4	41	5	45	8	<0.01

Table 1a

	Healthy vs tobacco smoking	Healthy vs tobacco chewers	Tobacco smoking vs chewers
RE ECD	<0.01	<0.01	<0.01
RE HEX %	<0.01	<0.01	<0.01
RE AVG	<0.01	<0.01	<0.01
RE MAX	0.004	<0.01	<0.01
RE MIN	0.139	<0.01	<0.01
RE SD	<0.01	<0.01	<0.01
RE CV	0.103	<0.01	<0.01

Table 1b

Table 1a and 1b: *Comparison of various corneal endothelial parameters of "Right eye" among three groups.*

Endothelial cell density and % hexagonality were more in non- tobacco users, whereas lowest in tobacco chewers which was statistically significant (P < 0.01). All others parameters were highest among chewers which was statistically significant (P < 0.01).

	Healthy		Tobacco smoking		Tobacco chewers		P value
	Mean	SD	Mean	SD	Mean	SD	
LE ECD	2504	201	2394	2221	1816	394	<0.01
LE HEX %	43	5	41	5	38	7	<0.01
LE AVG	400	43	461	25	572	149	<0.01
LE MAX	1012	234	1128	225	1441	463	<0.01
LE MIN	99	17	104	22	144	64	<0.01
LE SD	158	23	190	26	260	102	<0.01
LE CV	39	4	41	5	45	9	<0.01

Table 2a

	Healthy vs tobacco smoking	Healthy vs tobacco chewers	Tobacco smoking vs chewers
LE ECD	1.00	0.01	0.01
LE HEX %	0.001	0.011	0.018
LE AVG	<0.01	<0.01	<0.01
LE MAX	0.051	<0.01	<0.01
LE MIN	1.00	<0.01	<0.01
LE SD	<0.01	<0.01	<0.01
LE CV	0.081	<0.01	<0.01

Table 2b

Table 2a and 2b*: Comparison of various corneal endothelial parameters of "Left eye" among three groups.*

Endothelial cell density and % hexagonality were more in non- tobacco users, whereas lowest in tobacco chewers which was statistically significant (P < 0.05). All others parameters were highest among tobacco chewers which was statistically significant (P <0.05).

Discussion

The results of this study suggested that tobacco chewers have a significant impact on the corneal endothelial parameters when compared with tobacco smokers and non-tobacco users which was similar to Jha., *et al.* study [1]. Cross-sectional observational hospital-based study was conducted on 273 participants aged between 20 and 70 years, divided into three cohorts: 91 tobacco smokers, 91 tobacco chewers and 91 non-tobacco users at R.L. Jalappa Hospital and Research Centre attached to Sri Devaraj Urs Medical College, Kolar for a period 6 months. Mean age was found to be 58 ± 2 years in all the three cohorts and male preponderance was seen in both tobacco smoking and chewing groups; whereas female preponderance was seen in non-tobacco group.

The cornea, avascular tissue is a highly specialized structure on the anterior surface of the eye that forms the main refractive element and accounts for approximately two-thirds of the total optical power [3]. It consists of five anatomical distinctive layers: epithelium, Bowman's membrane, stroma, Descemet's membrane, and endothelium. The corneal endothelium, the most posterior layer of the cornea, consists of a monolayer of uniformly sized hexagonal-shaped cells that principally maintain corneal transparency by regulating fluid and nutrient balance. Because corneal endothelial cells (CECs) have limited proliferative potential, multiple factors, including endothelial dystrophies, surgical trauma, age and smoking contribute to corneal endothelial cell loss and decreased corneal endothelial cell density [6]. Specular microscopy is a non-invasive tool that can be used for evaluation of healthy and diseased corneal endothelium and diagnosis of several endothelial disorders through visualization of endothelial cell characteristics.

The World Health Organization estimates that tobacco use is accountable for more than 8 million deaths worldwide each year [7]. Tobacco contains more than 4500 substances, including reactive free radicals, which induce carcinogenic and proinflammatory reactions and decrease the antioxidant level in the ocular tissue, aqueous humor, and blood [8]. These toxic substances in tobacco can cause acute or chronic effects mainly through ischaemic or oxidative mechanisms. Tobacco smoking may impair the wound healing process in the cornea, making it more susceptible to complications following surgeries like cataract surgery. Although much was known about the effects of tobacco smoking on ocular health, there is a paucity of literature on head-to-head comparisons between different forms of tobacco consumption in this regard. This study was conducted to compare the effects of chewing versus smoking tobacco on corneal endothelial health.

Endothelial cell density (ECD) was found to be statistically significant ($P < 0.01$) in tobacco users when compared to non-tobacco users which was similar to study done by Ilhan N [3]. ECD was lowest among tobacco chewers when compared to tobacco smokers which was statistically significant ($P < 0.01$). Endothelial cell density (ECD) is primary indicator of endothelial health, with a lower count suggesting a compromised cornea.

Verma A., *et al*. found that % hexagonality (HEX) was significantly reduced in tobacco chewers, when compared with tobacco smokers and non-tobacco users which was similar to this study ($P < 0.01$) [2]. Smoking effects corneal endothelial cells morphology with respect to size and shape, cells become larger and irregular in shape. This impairs their ability to maintain fluid balance in the cornea effectively. Hence tobacco chewing causes greater corneal endothelial dysfunction.

Ilhan N stated that there was no statistically significant difference in CV among smokers and non-smokers which was not same as this study [3]. This study found out that tobacco chewers had highest CV followed by tobacco smokers and least among non-tobacco users, which where statistically significant ($P < 0.05$).

A study by Sayin N., *et al*. suggest that there was no statistically significant difference in the mean endothelial cell density (ECD), endothelial cell size, SD of size, CV of size between smokers and non-smokers ($P > 0.05$) which was not same in this study [4].

Kara S., *et al*. study found that there was no effect of tobacco on corneal endothelial parameters, whereas this study showed that there was statistically significant difference in corneal endothelial parameters due to tobacco usage [10].

Conclusion

In conclusion, the effects of tobacco chewing, in addition to smoking on corneal health cannot be underrated. This study points to evidence that chewers may be at a higher risk of corneal endothelial changes as compared with smokers. Therefore, it becomes imperative that these patients must undergo extensive pre-surgical evaluation in terms of a thorough corneal endothelial structural analysis when planning for a vision-improving surgery such as cataract surgery.

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Nil.

Conflicts of Interest

There are no conflicts of interest.

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