

EVALUATION OF THE EFFECTS OF MODERATE TO SEVERE SMOKING ON RETINAL NERVE FIBRE LAYER THICKNESS

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ABSTRACT

BACKGROUND

Smoking causes serious health problems worldwide. This study was intended to evaluate the possible structural changes like thickness in the retinal nerve fibre layer (RNFL) of moderate to heavy smokers and compare them with those of healthy non-smokers using time domain optical coherence tomography (TD-OCT).

MATERIALS AND METHODS

We included 100 active smokers (35 cases are heavy smokers and 65 cases are moderate smokers) and 100 age- and sex-matched healthy non-smokers between 20 years to 50 years for this cross-sectional study. After a full ophthalmological examination, TD-OCT was done for all participants and peripapillary RNFL thickness was measured in all four quadrants in both the groups and then compared.

RESULTS

Mean age of smokers was 38.65±8.18. Mean ages of severe smokers (SS), moderate smokers (MS) and non-smokers (NS) were 43.2±7.09 years, 39.85±7.59 years and 36.11±8.06 years respectively. Age matched analysis of RNFL thickness showed significant difference between smokers and non-smokers. It showed significant decrease in average thickness specially over inferior (129.82±19.9), superior (123.48±20.48) and nasal quadrants (82.57±21.69) (p values <0.001). Severe smokers have significant RNFL thinning over nasal quadrant (p <0.001) than moderate smokers. However, temporal quadrant showed no difference in both the cases and controls.

CONCLUSION

Smoking causes significant RNFL thinning in chronic, healthy cigarette smokers. OCT could be a useful tool for early detection of ocular damage in chronic healthy smokers. However, no significant correlation was found between number of cigarettes smoked per day and RNFL thinning.

KEYWORDS

Smoking, RNFL Thickness, OCT, WB.

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BACKGROUND

In addition to promoting atherosclerosis, myocardial infarction and sudden cardiac death, tobacco smoking also causes cancer of different system of body.¹ Up to 90% cases of Chronic Obstructive Pulmonary Disease (COPD) are related to cigarette smoking. Epidemiological data link cigarette smoking to many ophthalmic disorders. Toxic compounds affect ocular tissues, mainly through ischemic or oxidative mechanism.² Some common eye diseases, such as

cataract,³ age related macular degeneration,⁴ retinal vein occlusion,⁵ anterior ischemic optic neuropathy,⁶ thyroid ophthalmopathy,⁷ and primary open angle glaucoma,⁸ have been found to be associated with cigarette smoking. Diffusely decreased retinal sensitivity and peripheral scotoma have been found in the visual fields of the healthy heavy smokers.⁹

Optical coherence tomography is a technique that provides graphical information of retinal nerve fibre layer thickness. It provides an objective measure of retinal ganglion cell axonal presence in normal eyes and their loss by means of RNFL thickness. The normal range of RNFL thickness in adults has been measured by several investigators using OCT.¹⁰ However, to the best of our knowledge, no study in this region has evaluated the effects of chronic smoking on RNFL thickness in healthy subjects.

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Present study aimed to explore the effects of moderate to heavy smoking on RNFL thickness and compare it with age matched non-smoker healthy individuals.

MATERIALS AND METHODS

This cross-sectional study was conducted between January 2016 to June 2017 in the outpatient clinic of a tertiary eye care hospital in West Bengal on a consecutive volunteer basis. Informed consent was obtained from all subjects. The study included 200 eyes of 100 smokers of which 35 cases were heavy smoker and 65 cases were moderate smokers. Chronic, heavy smokers are defined as smokers, taking more than 20 cigarettes per day for the last 5 years or more and moderate smokers as persons taking 10 to 20 cigarette per day for at least 5 years. The control group comprised of 200 eyes of 100 healthy, non-smoking subjects.

Total 200 eyes of moderate to heavy smokers are compared with 200 eyes of healthy controls. Approval from the institutional ethical committee was obtained. In both the groups, only the subjects with small refractive errors (-1D to +1D spherical equivalent) and best corrected visual acuity (BCVA) $\geq 6/6$ according to Snellen chart tests were selected for the study. Young, healthy, heavy smokers with age between 20 years to 50 years were included in the study.

Volunteers were excluded if they were under local or systemic medication, had been exposed to any kind of toxic substances (alcohol), had a history of systemic diseases like diabetes, hypertension or any neurological disorders, any family history of glaucoma or intra ocular pressure >21 mmHg along with previous or current history of ocular diseases, trauma, intraocular surgery or any media opacities. All subjects underwent a complete ophthalmological examination including slit lamp examination, applanation tonometry (Goldmann), optic disc evaluation with +90D lens, automated perimetry (24-2 SITA standard) by Humphrey visual field analyser and Indirect ophthalmoscopy.

Each subject underwent OCT for assessment of peripapillary RNFL thickness after dilating the pupil with mydriatics. OCT is an optical signal acquisition and processing imaging allowing extremely high quality micrometer resolution. The fast RNFL scan protocol consists of 3 consecutive 360° scans with a diameter of 3.4 mm centered on the optic nerve head. The RNFL thickness

parameters calculated by the Stratus- OCT software (version 4.0.1) were average thickness (360° scan), temporal (316°-45°), superior (46°-135°), nasal (136°- 225°) and inferior thickness (226°-315°). Good-quality scans featured focused images and signal strength equal to or higher than 7 as well as a centered ring around the optic disc for RNFL scans. It uses three color-coded modalities to represent RNFL thickness: a wave chart or temporal-superior-nasal-inferior-temporal (TSNIT) graph, a radial diagram and a table.

Mean data of all subgroups (i.e. moderate smoker vs severe smoker or non-smoker) were compared along with comparison between two major groups (i.e. smoker vs non-smoker). Comparison of the means done by chi square test, independent samples t test and Kruskal Wallis test wherever applicable using the software Statistical Package Program for Windows (SPSS Inc., Chicago, IL, USA), (version 13). Differences were considered significant at $P < 0.05$.

RESULTS

We included 100 active smokers (35 cases are heavy smoker and 65 cases are taken as moderate smoker) and 100 age- and sex-matched healthy non-smokers. Age of smokers and non-smokers ranged between 23 years to 50 years. Mean age of smokers was 38.65 ± 8.18 . Mean age of severe smokers (SS), moderate smokers (MS) and non-smokers (NS) were 43.2 ± 7.09 , 39.85 ± 7.59 and 36.11 ± 8.06 respectively.

All patients were male. Both study and control subjects had VA $\geq 6/6$, with small refractive error ranging from -1D to +1 D.

Severe smokers had smoked an average of 22.19 ± 1.10 cigarettes per day (range, 21–30) and moderate smokers had smoked an average of 16.04 ± 1.98 (range, 10-20). The mean smoking duration of the severe smokers was 9.73 ± 2.41 years and mean smoking duration of the moderate smokers was 6.62 ± 1.05 years.

Using independent samples t test average RNFL thickness was found to be significantly less ($p < 0.001$) in smokers than in non-smokers. Statistically significant RNFL thinning was seen in all quadrants, except in temporal quadrant. (table 1)

| Group Statistics | Non-Smoker (Number=100) | Smoker (Number=100) | P-Value |
|--|-------------------------|---------------------|---------|
| Retinal Nerve Fibre Layer Thickness | | | |
| A. Inferior Quadrant | 140±16.32 | 129.82±19.9 | <0.001 |
| B. Superior Quadrant | 134.21±19.22 | 123.48±20.48 | <0.001 |
| C. Nasal Quadrant | 93.75±20.61 | 82.57±21.69 | <0.001 |
| D. Temporal Quadrant | 72.72±13.84 | 68.47±15.36 | 0.004 |
| E. Average | 110.22±9.19 | 101.05±12.62 | <0.001 |

Table 1

Significant thinning of RNFL was found when compared between non-smokers with moderate smokers and with severe smokers. However, there is no significant difference between moderate smokers and severe smokers, except in RNFL thickness of nasal quadrant ($p = < 0.001$). (Table 2)

| Group Statistics | Non-Smoker (Number=100) | Moderate Smoker (Number=65) | Severe Smoker (Number=35) | p-Value |
|--|----------------------------|--------------------------------|------------------------------|---------------------------------|
| Retinal Nerve Fibre Layer Thickness | | | | |
| A. Inferior Quadrant | 140±16.32 | 129.50±17.29 | 130.4±24.15 | 1=<0.001 2=0.003 3=0.785 |
| B. Superior Quadrant | 134.21±19.22 | 123.47±18.13 | 123.48±24.39 | 1=<0.001 2=0.001 3=0.998 |
| C. Nasal Quadrant | 93.75±20.6 | 78.22±20.36 | 90.64±21.90 | 1=<0.001 2=0.301 3=<.001 |
| D. Temporal Quadrant | 72.72±13.84 | 68.96±15.27 | 67.57±15.60 | 1=0.024 2=0.016 3=0.546 |
| E. Average | 110.22±9.19 | 100.07±10.99 | 102.86±15.12 | 1=<0.001 2=<0.001 3=0.176 |
| Table 2. Comparison of RNFL Thickness (mean ±SD) of Non-smoker, Moderate and Severe Smoker | | | | |
| 1=comparison between non-smoker and moderate smoker, 2=comparison between non-smoker and severe smoker, 3= comparison between moderate and severe smoker | | | | |

Age matched analysis of RNFL thickness showed thinning in different quadrants in different age groups between smokers and non-smokers. It showed significant thinning in inferior (p= .04), superior (p<0.001), nasal quadrants (p= .005) along with average thickness (p< 0.001) in 21-30 years age group, inferior (p=.009), superior (p 0<0.001), nasal (p<0.001) and average (p<0.001) thickness in 31-40 years age groups and inferior (p<0.001), temporal (p=.011) and average (p<0.001) thickness in 41 to 50 years age group. (Table 3)

| Parameter | Non-smoker | | | Smoker | | | p-Value |
|--|----------------------------------|----------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|----------------------------------|
| | 21- 30 yrs. (x ₁) | 31- 40 yrs. (y ₁) | 41-50 yrs. (z ₁) | 21-30 yrs. (x ₂) | 31-40 yrs. (y ₂) | 41-50 yrs. (z ₂) | |
| Retinal Nerve Fibre Layer Thickness | | | | | | | |
| A. Inferior Quadrant | 139.64±15.3 | 137±14.46 | 145.17±18. | 132.33±13.5 | 130.03±16.3 | 129.24±22.2 | 1=0.039 2=0.012 3=<.001 |
| B. Superior Quadrant | 140.51±14.9 | 135.65±22.9 | 125.8±14. | 125.45±13.1 | 122.98±16.3 | 123.30±23. | 1=<.001 2=<.001 3=.373 |
| C. Nasal Quadrant | 93.11±20.42 | 98.08±20.7 | 87.41±19.1 | 78.75±20.4 | 81.5±20.16 | 83.75±22.5 | 1=0.006 2=<0.001 3=.266 |
| D. Temporal Quadrant | 76.01±11.57 | 70.22±14.6 | 73.55±14 | 73.87±13.6 | 68.94±14.78 | 67.23±15.7 | 1=.506 2=.619 3=.008 |
| E. Average | 112.36±9.39 | 110.35±9.2 | 107.95±8.5 | 102.69±8.1 | 100.8±9.9 | 100.8±14.2 | 1=<0.001 2=<0.001 3=<0.001 |
| Table 3. Comparison of RNFL Thickness and Central Macular Thickness (in Microns) (Mean ±SD) of Smoker and Non-smoker of Different Age Groups by Independent Sample t Test | | | | | | | |
| 1=comparison between x ₁ and x ₂ , 2=comparison between y ₁ and y ₂ , 3=comparison between z ₁ and z ₂ | | | | | | | |

Sub group analysis between different age groups (i.e. 21-30 years, 31-40 years, 41-50 years) of severe smoker as well as moderate smoker did not show any statistically significant difference.

Comparison of RNFL thickness between right and left eyes of all smokers showed no significant differences ($p > .05$) (Table 4).

| Parameters | Right Eye | Left Eye | P Value |
|--|--------------|--------------|---------|
| Retinal Nerve Fibre Layer Thickness | | | |
| A. Inferior Quadrant | 129.45±20.50 | 130.19±19.39 | P=0.467 |
| B. Superior Quadrant | 120.43±18.75 | 126.53±21.74 | P=0.001 |
| C. Nasal Quadrant | 85.74±22.30 | 79.4±20.68 | P=0.004 |
| D. Temporal Quadrant | 67.15±15.40 | 69.8±15.29 | P=0.419 |
| E. Average | 100.73±12.39 | 101.36±12.91 | P=0.430 |

Table 4. Comparison of RNFL Thickness (Mean ±SD) of Right and Left Eye of Smokers

DISCUSSION

This study was conducted to evaluate the effects of smoking on RNFL thickness. Our results showed that the RNFL thickness was significantly decreased in smokers when compared with non-smokers. The analysis of the quadrants revealed that inferior, superior and nasal RNFL were thinner in smokers than in non-smokers. Temporal quadrant also showed RNFL thinning but it was not statistically significant. This study showed severe neurological damage to the eye in the form of RNFL thinning. Neurological damage caused by smoking is showed by Akarsu C et al,¹¹ They concluded that smoking causes neurological damage by affecting central visual field of moderate smokers with significantly lower foveal thresholds ($p=0.001$) and mean retinal sensitivity ($p=0.02$) on white on white (W-W) perimetry. On the other hand, Uz E et al¹² opined that chronic heavy smokers have reduced ($p<0.023$) contrast sensitivity values, which are associated with low levels of serum Mn (manganese) and Zn(zinc). Gundogan FC et al¹³ reported that cigarette smoking increases P50 amplitude and decreases N95 latency in habitual smokers in pattern electroretinogram (PERG) PERG has been reported to be a valuable clinical and research tool that enables evaluation of macular and retinal ganglion cell function. They concluded that, these results may be related to the deleterious effects of smoking on the ocular circulation along with arousal modulation and Carbon monoxide toxicity. Moreover, Gundogan FC¹⁴ showed that, cigarette smoking causes a stimulant effect on mfERG in central retinal areas. Our results showed no significant difference between moderate smokers and severe smokers except in RNFL thickness of nasal quadrant ($p=<0.001$). This deviates from the results reported by Hepsen IF and Evereklioglu C.⁹ They evaluated the central 30–2 threshold tests of W-W perimetry and found differences between the visual fields of moderate and heavy smokers. Comparison of RNFL thickness between right and left eyes of all smokers showed no significant differences between two eyes ($p > .05$), which proves that the effect of smoking is bilaterally symmetrical. Subgroup analysis of RNFL thickness between different age groups of moderate and severe smokers showed no correlation between duration of smoking and RNFL thickness. OCT has proved to be a useful tool for detecting early changes in glaucoma in form of reduction in macular volume and RNFL thickness.¹⁵ Thinning

of RNFL may be a precursor of altered electroretinogram, decreased retinal sensitivity and visual field disturbances. Our finding is very valuable for the patients suffering from glaucoma, as retinal nerve fibre layer was found to be significantly thinner in them compared to normal eyes.¹⁶

We measured RNFL thickness of all our cases and controls in time domain OCT, which is the major drawback in this study along with small sample size. All the cases in our study were males. This could be due to the fact that tobacco smoking is more prevalent in males and there is a reluctance to disclose the fact of smoking for the females. We recommend further studies using spectral domain OCT with a larger sample. We can also analyse the effects of passive smoking and other forms of smoking and their correlation with duration of smoking.

CONCLUSION

Tobacco smoking, the leading preventable cause of disease and disability, causes significant RNFL thinning in smokers. We presume smoking definitely causes subclinical damage to ocular structures which is not detected by standard automated perimetry. The present study also suggests a possible role of OCT in early detection of tobacco induced ocular damage. The results of the present study emphasize on avoidance of tobacco smoking and proper counselling and stimulate further studies in this regard.

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