Analysing the change in contrast sensitivity post-travoprost treatment in primary open-angle glaucoma patients using Spaeth Richman contrast sensitivity test

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ORIGINAL PAPER

Analysing the change in contrast sensitivity post-travoprost treatment in primary open-angle glaucoma patients using Spaeth Richman contrast sensitivity test

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Abstract

Objective To determine the ability of the Internet-based Spaeth/Richman Contrast Sensitivity (SPARCS) in assessing the change in contrast sensitivity (both central and peripheral) post-treatment with travoprost 0.004%.

Design This is a prospective observational study.

Methods and participants. Data of 62 eyes (33 patients) undergoing treatment for naïve POAG patients were analysed. Patients were followed up for a period of six months after starting topical travoprost (*Travatan* 0.004%, Alcon), and the change in central and peripheral CS was studied.

Results Mean total SPARCS score at baseline was 69 ± 10.99, improved to 74.62 ± 9.50 after 6 months of therapy (*p*: 0.001) in all the glaucoma severity groups. Mean SPARCS score at baseline in mild glaucoma group was 72.05 ± 9.87, in the moderate glaucoma group, it was 62.23 ± 9.2, and in the severe glaucoma group, it was 59.36 ± 11.65. After 6 months of treatment with travoprost, the CS improved to 76.05 ± 8.36 in mild group, 76.69 ± 8.82 in moderate group and 67.18 ± 11.15 in severe group (*p* value: 0.014). The percentage change in the CS from baseline showed significant improvement in the superotemporal quadrant at 1 month (*p* value: 0.032), superonasal quadrant (*p* value: 0.049), inferotemporal quadrant at 3 months (*p* value: 0.003) and 6 months (*p* value: 0.039). Inferonasal quadrant was affected most by glaucoma. A statistically significant correlation was seen between total SPARCS score with MD and PSD. Correlation was also seen between the percentage change in CS and average RNFL thickness at 3 and 6 months.

Conclusion Both central and peripheral CS improve following IOP reduction with travoprost. Change in the CS has a significant correlation with RNFL thickness and the perimetric indices.

Keywords Contrast sensitivity · Glaucoma · Travoprost · SPARCS

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Introduction

Glaucoma is an optic neuropathy where there is axonal injury causing deprivation of neurotrophic growth factors, ultimately leading to the death of

retinal ganglion cell (RGC) [1]. During the natural course of glaucomatous optic neuropathy (GON), functional vision loss such as alterations in contrast sensitivity (CS) may occur earlier before any visible nerve fibre layer damage [2, 3]. Glaucoma patients exhibit abnormal CS, both central and peripheral, where the peripheral CS is affected first, and thus, it can be used to assess the presence and the progression of the disease [2, 4]. Although the glaucomatous damage to visual function has been considered to be irreversible, several studies have reported partial recovery in visual field defects in POAG patients, which may be related to the reduction in IOP [5–8].

CS improvements have been noted in patients when treated with selective and non-selective beta blockers. Evans et al. studied the change in CS in glaucoma patients already on beta blockers. They experienced an improvement in CS at 3 cycles per degree (cpd) ($p = 0.03$) on shifting to latanoprost possibly due to its effects on optic nerve and macular circulation [9]. All studies which evaluated change in visual function following treatment ascertained changes only in central CS, but peripheral CS was not assessed. Knowing the degree and pattern of change in peripheral CS is more important as this may be an indicator of early glaucomatous visual function defect [2].

In the present study, we used the Spaeth Richman Contrast Sensitivity Test (SPARCS), an Internet-based test, which uses low spatial frequency (0.4 cpd), to determine the change in both central and peripheral CS following treatment with topical travoprost 0.004% in treatment naïve Indian POAG patients.

Methods

Patient enrolment

This prospective observational study enrolled consecutive treatment naïve POAG patients who presented to the Glaucoma Clinic of Department of Ophthalmology, Government Medical College and Hospital, Sector 32, Chandigarh. The study was approved by the institutional ethics committee and was registered with Clinical Trials Registry of India (CTRI) available online at https://www.ctri.nic.in (CTRI Number: CTRI/2019/06/019849). A written, informed consent was obtained prior to enrolment. The diagnosis of POAG was made if the patient had gonioscopically open angle and evidence of optic nerve damage from either or both optic disc/RNFL structural abnormalities and reliable reproducible visual field defects measured on Humphrey's SITA FAST 24-2 test. The defects were considered suggestive of glaucoma when either defects of three or more points in cluster with a probability of less than 5% in a non-edge localization at the pattern deviation plot are observed or a pattern standard deviation index with a probability of less than 5% is found or outside normal limit result is obtained in the glaucoma hemifield test [10].

POAG was classified based on the age of onset as juvenile open-angle glaucoma (JOAG/onset at 10–35 years) and adult-onset POAG (after the age of 35 years). The latter was further classified as high-tension glaucoma (HTG) and normal tension glaucoma (NTG). NTG refers to patients with glaucoma, an open angle, characteristic visual field defect and an IOP < 22 mm Hg without treatment [11].

In order to avoid multiple etiologies of decreased CS or factors that could preclude the patient from providing reliable and valid data, patients with a history of incisional surgery in the past 6 months or any cause for visual impairment (like cataract [nuclear sclerosis equal to or more than grade 2 using LOCS III grading], diabetes mellitus, neurological diseases) best-corrected visual acuity (BCVA) of less than 20/80 or patients who had undergone refractive surgeries were excluded. We did not include any patients with multifocal IOLs as they may alter the CS.

This was a pilot study; hence, a prior sample size calculation was not done. We enrolled 64 eyes of 34 newly diagnosed adult-onset POAG patients of high-tension type (22 males;12 females, 4 single eyed) out of which 1 patient (2 eyes) was excluded from the study due to uncontrolled IOP. Data of 62 eyes were analysed.

All patients underwent a detailed clinical examination. IOP was recorded with a calibrated Goldmann Applanation tonometer (GAT), and the visual field was examined using a 24-2 SITA Fast protocol using a Humphrey Visual Field Analyser (HVF 750i II, Carl Zeiss Inc.). The Disc Damage Likelihood Scale (DDLS) was used to evaluate the amount of optic disc damage (neural rim loss) caused by glaucoma [12].

Severity of glaucoma was graded using the visual field defect-based Hodapp Anderson and Parrish (HAP) grading system [13]. Main parameters used for

staging were the mean deviation (MD), the number of test points depressed below predefined probabilities on the pattern deviation (PD) plots and loss of threshold sensitivity within the central 5° of the visual field (Supplementary Table 1).

RNFL thickness was measured using SDOCT (Cirrus 5000, Carl Zeiss Meditec AG). Optic Disc Cube 200 × 200 protocol of Cirrus HD-OCT version 5.0.0.326 was used for scan acquisition. CS was assessed using SPARCS at baseline, at 3 months and at 6 months after the initiation of therapy with prostaglandin analogue, travoprost (0.004%) as topical eyedrops.

The branded travoprost used for the study was *Travatan* (Alcon Inc., contains travoprost 0.04 mg/mL with Polyquad 0.001% as preservative) to avoid any variability due to excipients and quality control with different generic versions of travoprost. Patients were advised to instil the medication daily at bedtime and re-examined two weeks after the start of therapy to record the IOP reduction. Cases of uncontrolled IOP with travoprost and those who required additional medical therapy were excluded from the study.

Contrast sensitivity assessment

CS was assessed using SPARCS via https://www.sparcscontrastcenter.com, where each patient was given a unique identification number. SPARCS was performed in the glaucoma clinic, on a standard computer with Internet access. It is designed to be used on a monitor set to 1024 × 768 resolution, 256 grey levels and a size of at least 22 cm width and 26.5 cm height. The SPARCS website provided the instructions on how to take the test. Patients were seated 50 cm from the computer monitor. At this testing distance, the test occupied 30° of vision horizontally and 23.5° of vision vertically. The central test area subtends 5° horizontally and 3.5° vertically. Monocular testing was performed on each eye with the subject's habitual eyeglasses given in patients already using it. Patients were then instructed to fixate on the central area of the testing screen and identify which of the areas appeared different. When patients were ready, they clicked on the central area to activate the test. To avoid learning effects, two practice trials were conducted before the first baseline measurement and one before each subsequent visit [14].

SPARCS evaluates CS in five areas of visual field: the left upper quadrant (LUQ), left lower quadrant (LLQ), right upper quadrant (RUQ), right lower quadrant (RLQ) and the central area. Vertical square wave gratings with a spatial frequency of 0.4 cpd appear for 0.3 s in one of the five tested areas while the other four areas stay a similar colour to the background. Patients then temporarily break fixation to select the area that shows the contrast gratings. Subsequently, patients fixate again on the central area and click it to activate the programme to show the next image. The area with the gratings appears at random. Correct and incorrect responses are recorded by SPARCS until the contrast threshold is determined in each area. During the test, the luminance of the gratings is gradually decreased. The contrast threshold is determined using a staircase strategy with reversals. Initial correct responses advance four levels until an incorrect response is made. After the incorrect response, the contrast level presented is two levels easier. Thereafter, the algorithm advances or regresses one level at a time until two incorrect responses are made at a specific level, which establishes the threshold. If a patient stops trying to guess the correct area and simply clicks the same location again and again, the test terminates and explains to the patient to attempt to choose the location the image appeared. The range of contrast tested is from 100 to 0.45% (log CS 0.00 to 2.35) and decreases by approximately 0.15 log units between levels. The contrast value is calculated by Weber contrast. The central area and four peripheral areas each receives separate scores. Each log-based score is then scaled out of 20 by dividing by 2.35 and multiplying by 20. A total SPARCS score is summated from each of the five areas, making 100 the perfect summed score from all five areas.

Fluorescent lighting was used in a room without daylight to minimize glare, reflections and to ensure uniform testing conditions. IOP measurement was reassessed 2 weeks, 3 months and 6 months after initiation of therapy. SPARCS was repeated at 3 months and at 6 months after initiation of therapy. Normality of CS score was checked by Kolmogorov–Smirnov test. If scores were normally distributed, the Student's paired t test was used; otherwise, Wilcoxon signed-rank test was used for comparing the measurement changes between the baseline, 3 months and 6 months post-treatment visits. The Spearman rank correlation test was performed to

analyse the correlation between changes in CS and IOP. The measurable variables were subjected to normality. Normally distributed variables were then subjected to ANOVA/post hoc test. Skewed variables were subjected to Kruskal–Wallis ANOVA and Mann–Whitney test for pairwise comparison.

To see the trend in CS using SPARCS before and after the treatment with prostaglandins for a period of 6 months, we used repeated measure ANOVA with Bonferroni correction. All statistical tests were two-sided and performed at a significance level of $p = 0.05$. The statistical analysis was carried out using IBM Statistical Package for Social Sciences (SPSS Version 21 for Windows).

Results

Data of 62 eyes were analysed out of which thirty-eight eyes (61.5%) had mild glaucoma, 13 (21%) had moderate glaucoma while 11 (17%) had severe glaucoma. Majority of the study subjects were > 50 years of age with mean age (± SD) of 60 years (± 10) in the mild group, 58 years (± 13) in moderate and 63 years (± 17) in severe group. The study groups had no statistical difference between the age (p value: 0.827) or gender (p value: 0.573). Out of 62 eyes examined, 11 eyes were pseudophakic (where no cataract surgeries were done within the 6-month period of patient selection) with monofocal intraocular lens possessing no UV filter.

Visual acuity

Kruskal–Wallis H test showed that the distribution of BCVA was not similar across the glaucoma severity groups at all time periods (at baseline, Chi-square: 11.44; p value: 0.003, at 3 months Chi-square = 10.64; p value: 0.005 and at 6 months, Chi-square = 12.31; p value: 0.002). Pairwise comparison using Bonferroni correction showed there was significant difference in BCVA score between mild versus severe (at baseline p value: 0.010, at 3 months p value: 0.003 and at 6 months p value: 0.001) and between moderate versus severe groups (at baseline, p value: 0.027 and at 6 months, p value: 0.029).

Optic nerve head (ONH)

The mean DDLS in the mild group was 5.79 ± 1.55, in the moderate group, it was 6.54 ± 1.71, and in severe group, it was 7.27 ± 1.61. As expected in pairwise analysis, the DDLS score was significantly higher in the severe group as compared to the mild group, which was statistically significant (p value: 0.026).

Intraocular pressure (IOP)

The mean of the baseline IOP was taken in all groups and was found to be higher in the severe group (23.82 ± 3.6 mm Hg) as compared to the mild (22.26 ± 2.5 mm Hg) and the moderate groups (23.08 ± 5.1 mm Hg), but the difference was not statistically significant (p value: 0.369). IOP decreased in all study subjects after 6 months (mild glaucoma:11.13 ± 0.8 mm Hg, moderate glaucoma: 11.38 ± 1.7 mm Hg and severe glaucoma: 12.09 ± 1.1 mmHg). One-way ANOVA test showed that the intragroup IOP variation was statistically significant at 6 months (p value: 0.040). In pairwise analysis using Bonferroni correction, the mild glaucoma group versus severe glaucoma group, IOP difference was statistically significant (p value: 0.035).

Contrast sensitivity

The mean total SPARCS score at baseline was 69 ± 10.99, which had a statistically significant improvement after 6 months to 74.62 ± 9.50 (p value: 0.001) (Fig. 1). Table 1 shows percentage change in CS and the quadrantwise change of the same among the study groups at various time periods.

By comparing the study groups using the post hoc test and using Bonferroni correction, there was significant difference between the total score at baseline versus 6 months, 1 month versus 6 months (p value: 0.001) and 3 months versus 6 months (p value: 0.002). Considering the glaucoma severity groups, the mean SPARCS score at baseline in the mild glaucoma group was 72.05 ± 9.87, in the moderate glaucoma group, it was 62.23 ± 9.2, and in the severe glaucoma group, it was 59.36 ± 11.65.

After 6 months of treatment with topical travoprost, the CS improved to 76.05 ± 8.36, 76.69 ± 8.82 and 67.18 ± 11.15 in mild, moderate

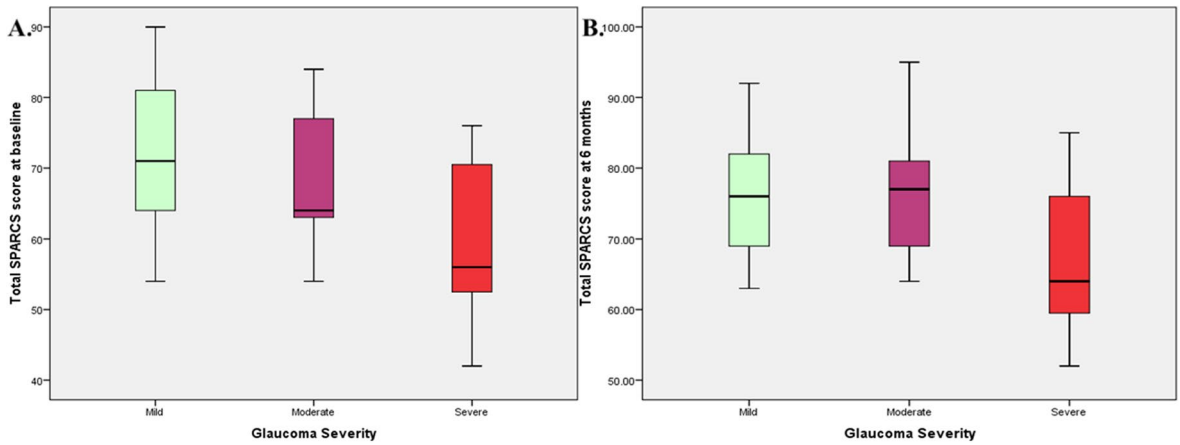

Fig. 1 Box plot showing the comparison between the total SPARCS scores at baseline and at 6 months in the glaucoma severity groups

Table 1 Baseline characteristics of all subjects

Mean baseline	Mild ($n=38$)	Moderate ($n=13$)	Severe ($n=11$)
IOP (mmHg)	22.26 ± 2.46	23.08 ± 5.09	23.82 ± 3.57
RNFL (microns)	79.32 ± 11.15	75.46 ± 21.99	63.73 ± 8.39
MD (dB)	2.23 ± 1.87	7.89 ± 1.45	16.67 ± 3.38

and severe glaucoma groups, respectively. The change in CS was statistically significant at 6 months (p value: 0.014). The difference was statistically significant in mild versus severe (p value: 0.003) and in moderate versus severe (p value: 0.045) groups.

When the individual quadrant of the test was analysed, a statistically significant improvement in SPARCS score was found in central quadrant and in at least 2 peripheral quadrants in all subjects. The inferonasal quadrant of the SPARCS test screen had the lowest scores. The inferonasal quadrant was affected in 40.3%, 32.3% and 38.7% of the study population at baseline, at 3 months and at 6 months, respectively. Figure 2 shows distribution of SPARCS score at baseline, at 3 months and at 6 months according to individual patients. Interestingly, it shows improvement in the total SPARCS score at both follow-ups in 50 of 62 eyes.

Percentage change of contrast sensitivity

The percentage change in the CS from baseline in various study groups across the time with treatment using Kruskal–Wallis H test showed significant improvement in the superotemporal quadrant at 1 month (p value: 0.032), superonasal quadrant (p value: 0.049), inferotemporal quadrant at 3 months (p value: 0.003) and 6 months (p value: 0.039) (Table 2).

RNFL thickness

The average OCT RNFL thickness at baseline showed that the mild group (79.32 ± 11.15 microns) had a better RNFL thickness as compared to the moderate (75.46 ± 21.99 microns) and severe group (63.73 ± 8.39 microns), and the difference was statistically significant (p value: 0.006). Supplementary Table 2 shows OCT average RNFL thickness of study groups across the time period.

Visual field indices

The baseline mean deviation (MD) showed significant field defects in the severe glaucoma group (16.67 ± 3.38) as compared to the mild glaucoma (2.23 ± 1.87) and the moderate glaucoma groups (7.89 ± 1.45) (p value: 0.001). The pattern standard deviation (PSD) also showed significant variation in the severe group (11.13 ± 2.08) as compared to the mild (2.74 ± 1.95) and the moderate groups

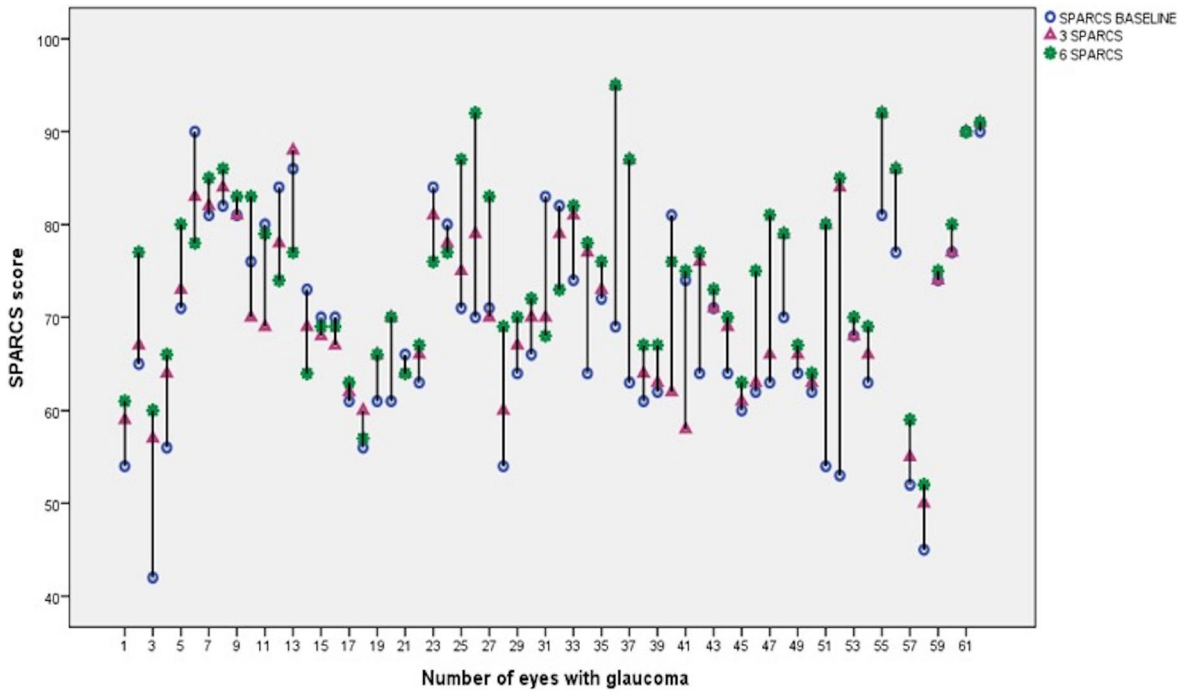

Fig. 2 Distribution of SPARCS score at baseline, at 3 months and at 6 months according to individual patients

(6.94 ± 3.42) (p value: 0.001), and the distribution of the scores in the three groups was statistically significant (p value: 0.001).

Using regression models, the Spearman's rank coefficient at baseline and at 3 months showed high degree of correlation between the total SPARCS score with MD and PSD. There was also correlation between the percentage change in CS and average RNFL thickness at 3 months and 6 months. Table 3 shows correlation between CS, perimetric indices and RNFL thickness. If we consider change in SPARCS score versus change in MD and PSD at 3 months, the correlation coefficients were 0.276 ($p = 0.031$) and 0.0193 ($p = 0.133$), and at 6 months, correlation coefficients were 0.306 ($p = 0.016$) and 0.233 ($p = 0.068$).

Discussion

Even in early stages of glaucoma, patients often complain of much worse 'subjective/functional' vision than what would be expected based on their good 'objective' visual acuity and this apparent discrepancy may be explained by the decrease in visual function caused by glaucoma. The ability to see in low-illumination conditions and the ability to detect low-contrast objects are two important daily life functions that are compromised in patients with peripheral vision loss due to glaucoma [15]. CS is a psychophysical parameter which has a strong correlation with vision-related quality of life in glaucoma patients [16, 17]. Several studies have shown evidence of cell shrinkage before cell death in experimental glaucoma [17]. It was postulated that the RGCs in glaucoma patients which were functioning suboptimally prior to treatment ('sick' RGCs) showed an improvement in CS with treatment [6]. This, however, did not suggest that improvements would be progressive, but most likely in a stepped response to the therapy [17].

SPARCS was validated by the USFDA in January 2015 as a user-friendly, highly specific and sensitive method of determining CS, with 79% sensitivity, 93% specificity and with high test–retest reliability [18]. Patients with glaucoma demonstrate CS loses at spatial frequencies between 0.25 and 8 cpd [19]. Many individual as well as stimulus variables affect CS. Stimulus variables include the luminance level, contrast, exposure time and target motion while

Table 2 Percentage change of contrast sensitivity in the study groups across the time period

% Change of contrast sensitivity	Mild ($n=38$) median (IQR)	Moderate ($n=13$) median (IQR)	Severe ($n=11$) median (IQR)	p value
Total SPARCS score				
1 month	0.00 (−0.29–2.56)	2.47 (0.00–6.76)	3.70 (0.00–9.43)	0.084
3 months	1.63 (−2.59–5.74)	4.76 (1.42–15.23)	8.20 (0.00–12.86)	0.137
6 months	4.94 (−1.43–12.90)	11.69 (3.96–24.83)	12.86 (2.82–15.56)	0.149
SPARCS (ST)				
1 month	0.00 (−5.84–0.00)	0.00 (0.00–7.37)	4.57 (0.00–17.23)	0.032
3 months	0.00 (−0.45–10.75)	0.00 (−7.63–14.86)	3.25 (−6.65–17.23)	0.816
6 months	3.56 (0.00–17.22)	13.46 (0.00–29.44)	10.02 (0.00–17.22)	0.435
SPARCS (SN)				
1 month	0.00 (0.00–5.62)	0.00 (−0.29–22.07)	0.00 (−6.27–10.89)	0.800
3 months	0.00 (0.00–11.78)	7.13 (0.00–38.88)	5.01 (0.00–30.37)	0.492
6 months	0.00 (0.00–10.43)	16.26 (0.00–38.88)	13.28 (0.00–30.37)	0.049
SPARCS (CC)				
1 month	0.00 (−0.50–1.48)	0.00 (−6.51–0.00)	0.00 (−13.74–10.02)	0.809
3 months	0.00 (−4.77–9.72)	6.09 (−17.82–19.44)	0.00 (−2.29–14.32)	0.945
6 months	7.13 (0.00–14.62)	7.13 (−13.77–24.63)	0.00 (0.00–17.23)	0.988
SPARCS (IT)				
1 month	0.00 (−2.15–6.00)	0.00 (−13.14–23.69)	0.00 (0.00–23.25)	0.366
3 months	0.00 (−9.72–8.77)	0.00 (−1.25–15.68)	20.89 (7.13–30.37)	0.003
6 months	0.00 (−0.68–23.82)	17.22 (0.00–32.16)	20.23 (11.45–40.89)	0.039
SPARCS (IN)				
1 month	0.00 (−5.85–0.00)	0.00 (−5.13–10.94)	0.00 (0.00–14.15)	0.674
3 months	3.17 (0.00–11.27)	7.13 (0.0026.98)	8.99 (0.00–47.32)	0.614
6 months	9.06 (0.00–27.91)	11.42 (0.00–43.79)	0.00 (0.00–47.32)	0.614

ST Superotemporal, *SN* superonasal, *CC* central component, *IT* inferotemporal, *IN* inferonasal

Table 3 Correlation between functional and structural parameters

Time period	Total SPARCS score and MD correlation coefficient (p value)	Total SPARCS score and PSD correlation coefficient (p value)	Total SPARCS score and average RNFLT correlation coefficient (p value)	% Change in CS and average RNFLT correlation coefficient (p value)
Baseline	−0.459 (0.001)	−0.283 (0.026)	0.187 (0.146)	−0.124 (0.336)
3 months	−0.350 (0.006)	−0.280 (0.028)	0.020 (0.877)	−0.316 (0.012)
6 months	−0.192 (0.135)	−0.222 (0.083)	0.011 (0.930)	−0.371 (0.003)

MD Mean deviation, *PSD* Pattern standard deviation, *RNFLT*etinal nerve fibre layer thickness

the individual variables include training, retesting, individual differences and adaptation. SPARCS has several advantages over the previously available chart and computer-based tests for CS assessment in glaucoma patients. Since it is a computer-based test, it eliminates the problem of chart fading. It does not use objects or letters, which reduces the confounding effects of literacy, culture and intelligence. It measures CS in both central and peripheral areas and thus correlates well with the early pattern of glaucomatous damage [18]. While interpreting a patient's results on SPARCS, attention should be paid to the total scores and the scores of the individual areas. It is possible that the total score may mask a low score in the peripheral quadrant; however, this can occur only 5% of the time. A total

SPARCS score < 67 has a sensitivity of 84.4% and a specificity of 70% for detecting glaucoma patients [20]. As with other tests for glaucoma, there can be some overlap between normal and glaucoma patients; however, some individuals with minimal optic nerve damage still score well [18].

There may be an overlap in what the Standard Automated Perimetry (SAP) assesses and what SPARCS detects as both have contrast appreciation as the basis of target detection. SAP uses a white stimulus presented on a white background at discrete spatial points in the visual field, which can be defined by Weber contrast (which is most useful in context of lighting). SAP performance is location-specific, and studies have noted the poor structure–function consistency [21]. Even in disease-free eyes, contrast thresholds are highly variable for the size III stimulus, and the nature of this variability is consistent with the effects of ganglion cell saturation causing SAP to overestimate loss in more severely damaged areas. Any visual damage in the neurological functioning of the RGCs can be demonstrated only when test–retest variability is extremely low. SPARCS is also based on Weber's contrast and employs a sensitive bracketing technique to determine the contrast threshold. It assures central fixation because the testing image only appears when the subject is fixating centrally. The authors believe that the concurrent use of SAP and SPARCS may add insight to visual function in glaucoma patients.

We enrolled 30 treatment naïve POAG subjects and started them on travoprost 0.004%. Since our centre is a tertiary care centre, we usually get referred patients. It is a common practice among most general ophthalmologists to start treatment based on a single, high reading of IOP and suspicious optic discs (with or without getting SAP testing); hence, many patients seeking opinion at our glaucoma service usually report with prior anti glaucoma medication. Most of the patients are started on topical beta blockers by the referring doctor. Therefore, to assess the true effect of travoprost on central and peripheral CS, we did not enrol these patients and took a pristine set of treatment naïve POAG patients, with no coexisting disorders that would influence CS. Although a larger sample would provide stronger data, the pristine sample and the strength of current data offer useful insight that can be developed in future studies.

The average age of our study population was 60 years (SD 12.31, range 26–84 years) which was similar to the study done by Evans and coworkers where the average age group of patients receiving latanoprost was also 60 years (SD 8.9) [9]. In our study, the average age was relatively more than the age of patients studied by Richman et al. (age 57 years) [18] and Arend et al. (age 55 years) [8]. The age of subjects is important as the CS declines with age. The difference between CS for 20-year-olds and 70-year-olds at approximately 8 cpd ranges from 0.2 to 0.57 log units [21]. The younger age groups tend to have better scores as they can understand the test better and also have better CS for their age. The current study included more of older subjects and there were no significant differences between the age groups of mild, moderate and severe glaucoma groups in our study. All patients in our study were Asian Indians, and thus, there was no racial difference.

Richman et al. have shown that progressive nerve damage causes decreased SPARCS score [18]. They have shown that all glaucoma patients with at least some rim tissue loss had lower SPARCS score than 95% of the controls. In our study, the optic disc damage as evaluated by DDLS was stable across the limited follow-up period of 6 months, which could be explained by attainment of target IOP with travoprost. A longer follow-up for both the CS and DDLS would add greater insight.

The mean IOP decreased in all study subjects after therapy with travoprost (0.004%) and was maintained across the 6-month follow-up period. Travoprost has been shown to provide a consistent diurnal IOP control with statistically significant IOP reductions persisting upto 84 h post-dose in previous studies. It is also known to increase the pulsatile ocular blood flow (pOBF) and provide IOP control for longer periods.

Percentage IOP reduction was more in the mild group (58%) followed by the severe group (50%) and then in the moderate group (48%). The mean IOP measured was higher for the severe group across all time periods, and the difference in IOP between mild versus severe was statistically significant (p value: 0.035). Increased IOP is a risk factor most often associated with glaucoma. Prata et al. have demonstrated strong association between CS changes and IOP reductions at frequencies of 3 cpd ($R^2 = 0.67$) and 12 cpd ($R^2 = 0.43$) after treating POAG patients randomly with timolol, brimonidine, travoprost [22]. The

temporal CS may be reduced in the early preperimetric phase where there is only raised IOP [23].

Gandolfi et al. have shown that the eyes with no VF defects on white-on-white SAP, but having an IOP ≥ 30 mmHg, show a decreased spatial CS (12 cpd) that can be improved after surgical reduction of IOP [5]. Previous studies have hypothesized that improvements in RGC sensitivity may be associated with a reduction in IOP, improved tissue perfusion or neuroprotection [6, 7]. The choroidal system accounts for 90% of optic nerve blood flow. The extent of choroidal perfusion varies with the particular glaucoma treatment and this has a direct effect on ONH perfusion [24]. Therefore, anti-glaucoma treatments can influence long term tropism of the ONH [25]. Drug-induced increased blood flow may mediate improvements in CS. Nicola Cardascia et al. demonstrated the changes in pOBF with travoprost versus latanoprost in 18 POAG patients for short term therapy of 180 days. While comparing the pOBF between travoprost and latanoprost, they found that the flow was increased 44.9% by day 15 with travoprost and was maintained throughout the study (180 days). The pOBF was increased 47.9% by day 15 with latanoprost and was maintained at that level for 60 days, but then progressively decreased throughout the remainder of the study ($p < 0.01$ at all time points versus baseline) [26]. Considering the influence of IOP on pOBF, only travoprost increased pOBF, reducing IOP for a longer period. This consistent blood flow improvement caused by travoprost can explain why it may have a favourable profile for improved CS function.

Richman et al. tested the CS using SPARCS of 261 eyes of 157 patients out of which 118 eyes were glaucoma, 18 were glaucoma suspects and 125 were controls. They found that the glaucoma patients scored less (59.4 ± 15.3) compared to the scores of controls (74.4 ± 5.0) and suspects (68.7 ± 10) [18]. In our study, the total SPARCS score was found to be less in the severe glaucoma group across all time periods.

Evans et al. compared the effects of latanoprost and timolol maleate in gelrite on CS in 20 POAG patients using CSV 1000E and found that the CS of subjects treated with latanoprost after being switched from timolol showed an improvement at 3 cpd; conversely, those treated with timolol after being switched from latanoprost demonstrated a significant loss in CS at 3 and 18 cpd. The changes in CS occurred without a corresponding change in the IOP [9]. Arend and coworkers studied the CS change using CSV 1000E in 14 POAG patients after treating them randomly on timolol, dorzolamide or latanoprost for 4 weeks and revealed a significant improvement with dorzolamide at 6 cpd compared to timolol ($p = 0.003$), whereas none of the other drug options differed from one another. This improvement can be due to the increased blood flow to the ocular tissues caused by dorzolamide [8]. Since these studies were based on latanoprost and the CS was evaluated using CSV 1000E, our results cannot be compared with them and hence are not interchangeable.

Prata et al. studied the CS using FACT in 54 POAG patients who randomly received 0.5% timolol (17 patients), 0.2% brimonidine (14 patients) or 0.004% travoprost (19 patients) for a period of 6 months. The IOP reduction with travoprost was more than brimonidine or timolol and the CS improved with all the three medications; however, they found no significant difference in CS when these medications were compared. The improvement in the CS at 18 cpd was found to be statistically significant (p value: 0.03) [23].

The total SPARCS score has better reproducibility than the individual areas of SPARCS [27].Gupta et al. studied the test–retest reliability for SPARCS and Pelli Robson chart. Of the 5 SPARCS areas, the central region had the highest test–retest agreement (ICC = 0.651) [27]. In the current study, the peripheral areas were also studied. Statistical improvement was seen in the CS of superotemporal quadrant after 1 month of treatment (p value: 0.032), inferotemporal region after 3 months (p: 0.003) and 6 months (p: 0.039), superonasal quadrant after 6 months of treatment (p: 0.049). There are no studies available in the literature which demonstrate the most affected peripheral region/quadrant in glaucoma. In our study, we assessed the lowest score of an individual SPARCS area across various time points and found that the inferonasal quadrant was affected the most by glaucoma (24 eyes, 38.7%).

Our results showed high degree of correlation between the percentage change in the CS and RNFL thickness at 3 months ($S = -0.316$, p value: 0.012) and at 6 months ($S = -0.371$, p value: 0.003). Hence, SPARCS may be predictive of RNFL damage in glaucoma. Our results support previous studies that have shown decreased CS in glaucoma and suggest that this loss results due to RNFL thinning [28, 29].

The evaluation of the visual field indices is another important aspect for the diagnosis and treatment of glaucoma. However, less attention has been placed on how perimetry results correlate with CS in patients with glaucoma. In our study, change in MD and PSD correlated with the change in the CS in the subjects across various time points. Our study showed a decrease in the perimetric indices in the groups over the period of 6 months which was statistically significant (p value: 0.001). There was a significant correlation between the MD and CS at baseline ($S = -0.459$, p value: 0.001), at 1 month ($S = -0.323$, p value: 0.011) and at 3 months ($S = -0.350$, p value: 0.006). Our results are consistent with studies done by Hawkins et al. [30] and Wilensky et al. [31] who reported a significant correlation ($r = 0.57$, $p < 0.001$, $n = 127$) between the MD as measured with the Humphrey perimeter and the Pelli Robson CS scores. In the subgroup of patients with open-angle glaucoma, the correlation between the visual field MD and the CS score was higher at 0.689 ($p \leq 0.001$, $n = 62$) [31]. The PSD in the current study showed significant correlation at baseline ($S = -0.283$, p: 0.026) and at 3 months ($S = -0.280$, p: 0.028). There are no previous studies which provide enough evidence to support the use of CS for the early detection of glaucoma. CS correlates with the perimetric deviation, and we believe that CS in conjunction with VF testing can be a promising method for detecting functional changes in glaucoma patients, even in those with good visual acuity. The findings of our study suggest that there is improvement in both central and peripheral CS in POAG patients with topical travoprost and this change in the CS has a correlation with RNFL thickness and the perimetric indices.

However, the correlation between changes in the OCT findings was not very consistent, and therefore, another study with larger sample size is needed. It is a standard issue to estimate the changes in the sensitivity in different points of the retina and that should be additionally measured by other means.

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Declarations

Conflict of interest The authors have not disclosed any competing interests.

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