Electromyographic Evidence that FL-41 Tinted Spectacles Decrease Blink Frequency and Force in Benign Essential Blepharospasm

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Abstract

Background: We have previously shown that over 90% of patients with benign essential blepharospasm (BEB) are more light sensitive than control subjects and as light sensitive as patients with migraine. We have also shown that patients with BEB prefer wearing a special rose-colored tint, FL-41, over standard gray lenses. These subjects reported that wearing FL-41 reduced their light sensitivity and improved the frequency and severity of their spasms compared to wearing gray sunglasses. The purpose of this study was to use electromyography to determine if FL-41 tinted lenses are effective in reducing blink frequency, duration, or force (root mean square) in subjects with BEB when compared with rose-tinted or gray-tinted lenses.

Methods: We recruited a total of 52 subjects to participate in two clinical trials. In both the first and second trials, thirteen subjects with BEB and thirteen controls were recruited to determine if FL-41 tinted lenses affected blink frequency, duration, or amplitude while subjects read. In the first trial, FL-41 tinted lenses were compared to rose-tinted lenses. In the second trial, FL-41 tinted lenses were compared to gray-tinted lenses. In both trials, blink frequency, duration, and root mean square were measured using surface electromyography of the orbicularis oculi muscle. The data were analyzed with a customized, Windows-based software program.

Results: Compared to the rose tint, FL-41 reduced the mean blink rate by 7.0 blinks/minute ($p=0.002$). FL-41 also reduced mean eyelid contraction force by 6.6 μV ($p=0.013$). There was no statistically significant difference in blink duration. Compared

to gray tint, FL-41 reduced the mean blink rate by 6.3 blinks/minute (p=0.003). There was no statistically significant difference in blink duration or force.

Conclusions: Spectacle lens tinting with FL-41 reduce the frequency and force of eye closure in subjects with BEB. These results are consistent with the subjective benefit patients experience, and suggest physicians should recommend this tint to their BEB patients. These results highlight the importance of photophobia in BEB, and indicate surface EMG is a useful, objective measure of BEB severity.

Introduction

Photophobia is a general term used to describe light sensitivity or abnormal intolerance to light. Patients with photophobia avoid light because of pain or discomfort. Although photophobia is most commonly associated with inflammatory conditions of the eye, it is also frequently reported by patients with blepharospasm, migraine, meningitis, sub-arachnoid hemorrhage, and head injury. The mechanism of photophobia is thought to involve the trigeminal pathway and possibly input from the occipital lobe and thalamus. Irritation to any region supplied by the trigeminal nerve can facilitate photophobia. [1]

Benign essential blepharospasm (BEB) is a movement disorder characterized by involuntary spasmodic contraction of the eyelids. [2] Patients often report that their symptoms are initiated and exacerbated by sensitivity to both ambient and bright light. [3] We have reported that photophobia occurs in over 90% of patients with blepharospasm. [4] The spasms are physically and socially debilitating and have a significant adverse effect on quality of life. [5,6,7] We have previously shown that BEB also interferes significantly with normal activities such as reading, driving, and working. [4] In severe cases the patient can be rendered functionally blind.

Photophobia is experienced by 90% of migraine sufferers, and is a significant source of discomfort among these patients.. [8] Another University of Utah study demonstrated that BEB patients are more light sensitive than age-matched control subjects and that the degree of light sensitivity in these patients was similar to that of migraine patients. [9] This study also showed that tinted lenses improved light sensitivity in BEB patients.

FL-41 is a rose-colored tint that blocks visible light at the blue end of the spectrum. It was first described in a study of migrainous school children. Children who wore FL-41 tinted spectacles experienced a significant improvement in their migraine symptoms. It has been recently shown that subjectively, BEB patients seem to prefer FL-41 compared to a variety of other tints NEED REFERENCE(Yen, 2005). In a companion article, we asked 30 subjects with BEB to wear either FL-41 or standard, gray tinted spectacles for a period of two weeks each. Subjects filled out questionnaires at the end of each segment of the trial. Our subjects reported significant improvements in several of their BEB-related symptoms when wearing FL-41.

The mechanism of the subjective benefit associated with FL-41 is unclear. The purpose of this study was to objectively determine if FL-41 tinted lenses affect blink frequency, duration, or force of contraction in patients with BEB.

Methods

This study was approved by the University of Utah Institutional Review Board (IRB) and all study procedures were performed in accordance with prevailing HIPAA regulations. Informed consent was obtained from each subject prior to participation.

Subjects were recruited from the clinics one of the authors (KBD, JEAW, BJK), from subjects who had participated in prior University of Utah BEB studies, and from attendees of the 2005 annual meeting of the Benign Essential Blepharospasm Research Foundation (Park City, UT). Recruited subjects were required to have a history of involuntary contraction of the orbicularis oculi muscles for one year or more. Spasms had to be evident on clinical examination. Patients with other eye conditions that could cause photophobia, such as iritis, were excluded. Subjects who already wore FL-41 lenses were not excluded from the study. Subjects filled out a baseline questionnaire to evaluate the severity of their symptoms, and the effect these symptoms have on their quality of life. The baseline severity of each subject's symptoms and the effect of light sensitivity on ADLs were ascertained with a questionnaire. The questionnaire contained items similar to those used in previous studies of light sensitivity and blepharospasm conducted at our institution (Adams, 2006; Judd, 2006; Blackburn 2006). The questionnaire contained questions designed to assess light sensitivity and the effect of light sensitivity on activities of daily living (ADLs). Some of these questions were derived from a Mayo Clinic Survey on eyelid spasms (Chapman, 1999). The questionnaire also contained questions

designed to assess eyelid spasm severity, based on a Blepharospasm Movement Scale developed by Fahn (1989).

FL-41, rose-tinted, and gray-tinted lenses were examined for spectral characteristics using a Perkin-Elmer spectrophotometer and the absorption spectrums were compared. All lenses were custom tinted to have similar overall transmission across the visible spectrum, but differed in their spectral characteristics. In other words, all lenses transmitted the same amount of light overall, but differed in their transmission of various colors within the visible spectrum (Figure 1). The rose-tinted spectacles were tinted in such a way as to be indistinguishable from FL-41 to both the investigators and the subjects. The gray-tinted spectacles were chosen to match those used in our previous investigations of BEB and to be representative of standard tinted spectacles that one might purchase over-the-counter. All lenses were manufactured as “clip-ons” so they could be easily mounted over subjects’ usual reading spectacles. Standard lenses were also used for subjects who did not customarily wear a reading correction.

Surface electromyography (EMG) was recorded from the left orbicularis oculi using 2 mm disc electrodes. A ground electrode was placed on the left earlobe. The EMG signal was collected using a Synergy EMG machine using a low frequency filter of 20 Hz and a high frequency filter of 20 kHz. (Viasys Health Care, Madison, WI). A five minute recording was obtained under each condition. Blink frequency was calculated over the entire five minute epoch. A customized, Windows-based software program was used to measure the duration and root mean square (RMS) of twenty randomly

selected individual blinks WAS THIS REALLY RANDOM – IF NOT IT CREATES A SELECTION BIAS..

Two trials were performed, each with different subjects. In the first trial, 13 subjects with BEB and 13 controls were tested. Each subject wore either FL-41 or rose-tinted spectacles, in random order. Randomization was performed by using R Statistical Software. This was done to keep approximate balance between which lenses were selected first at all points in the study. In the second trial, 13 subjects with BEB and 13 controls were tested. Each subject wore wither FL-41 or gray-tinted spectacles, in random order. Subjects were asked to read under calibrated, ambient light for a period of five minutes with one of the tinted lenses. Next, the subjects were asked to read for 5 minutes with no tint, wearing only their usual reading spectacles. Finally, the subjects read for 5 minutes using the other tint. Total testing time for each subject was approximately 15 minutes. Subjects were compared with themselves as data were analyzed because so much variability exists among patients. The differences in blink rate, frequency, and RMS from each subject while reading with the different lenses were then averaged with the group.

NEED STATISTICAL METHODS

Results

Table 1 summarizes the demographics of the subjects tested who participated in the first trial (FL-41 vs. rose tint). Mean blink frequency, duration, and RMS for control subjects are reported in Table 2 IS THIS TABLE REALLY NECESSARY?. In control subjects, there were no significant differences in blink frequency, duration, or amplitude when FL-41 and rose-tinted lenses were compared. Data from the BEB subjects are reported in Table 3. In BEB subjectsFL-41 lenses reduced the mean blink rate by 7.0 blinks/min compared to rose tint(Wilcoxon signed-rank test $p< 0.002$). There was also a significant reduction in blink RMS of 6.6 μvolts ($p<0.013$). There was no significant difference in blink duration.

Table 4 summarizes the demographics of the subjects who participated in the second trial (Fl-41 vs. gray tint). Mean blink frequency, duration, and RMS for control subjects are reported in Table 5. In control subjects, there were no significant differences in any parameter when FL-41 and gray-tinted lenses were compared. Data from the BEB subjects are reported in Table 6. In BEB subjects, compared to the gray tint, FL-41 lenses reduced the mean blink rate by 6.3 blinks/min ($p < 0.003$). There was no significant difference in blink duration or amplitude when the two tints were compared.

Discussion

These findings indicate that LF-41 lenses reduced blink frequency compared to both rose and grey tint lenses. The reduction in the RMS of individual blink responses when comparing FL-41 to rose tinted lenses suggests a reduction in the strength of the abnormal contraction given RMS is proportionate to force of contraction. In a companion article (Blackburn 2006), we report that BEB patients experienced subjective reductions in blink spasm frequency and severity with improvement in reading, writing and driving with use of FL-41 lenses compared to gray tinted lenses. Two limitations of the companion study are that there was no objective measure of blink frequency or force and that the study was not masked. The present study addresses both limitations by using an objective method of assessing spasm frequency, duration, and force and by employing a rose colored lens specifically designed to imitate the appearance of FL-41, thereby masking both investigator and subject.

It should be noted that not every BEB subject experiences an objective improvement in spasm parameters when wearing FL-41 tinted lenses. This finding agrees with our observations in the companion study that demonstrated that *most* subjects preferred FL-41 tinted lenses, but not all. BEB subjects who do experience a reduction of spasm symptoms with FL-41 tinted lenses only show a modest improvement in blink frequency. Therefore, FL-41 tinted lenses should not be used as the only treatment for BEB but as an adjuvant to commonly accepted medical or surgical therapies such as botulinum toxin injections and myectomy.

A wide variation in blink parameters was observed in all groups, including the control groups. Some of the variation in parameters observed in the BEB subjects is probably due to different treatments each subject was receiving. The variation in the control group likely reflects both genetic and environmental influences. This wide variation in blink parameters explains why the data could not be averaged for the entire group and why blink parameters were measured, compared, and analyzed for each subject THIS IS CONFUSING, YOU NEED TO OUTLINE YOUR STATISTICAL METHODS.

The reason FL-41 lenses are effective in reducing the symptoms of BEB remains speculative. Subjects with BEB appear to have a particular sensitivity to that part of the visible spectrum that is attenuated by FL-41. Because no significant changes were observed in blink parameters among control subjects, it appears that control subjects do not share this same sensitivity. Thus it appears that there is a physiologic difference between BEB and control subjects. It is possible that that this physiologic difference involves some mechanism within the eye that transduces these wavelengths of light into a painful or uncomfortable sensation (photophobia) in BEB subjects.

BEB subjects in a previous, uncontrolled study also seemed to prefer FL-41 over a variety of other tints (Herz and Yen, 2005). FL-41 was also shown to be preferred over a standard, gray tinted lens in our companion study (Blackburn, 2006) Together with the present study, we conclude that FL-41 lenses are better than other tints at blocking frequencies of light that aggravate BEB symptoms. It is reasonable to assume that there may be other tinted lenses that are as effective as or more effective than FL-41 lenses.

Future studies could be directed at experimenting with other tints that more sharply attenuate the frequencies of light blocked by FL-41 tinted lenses.

Conclusion

This is the first study to quantify the effect FL-41 tinted lenses have on blink frequency, duration, and amplitude in BEB subjects. FL-41 tinted lenses appear more helpful in reducing eyelid spasms than neutral rose tint, neutral gray tint, or no tint in the greatest number of BEB subjects. Spectacle lens tinting with FL-41 appears to be an effective treatment in BEB. To determine if this inexpensive and non-invasive treatment is effective for an individual patient, physicians should recommend this tint to their BEB patients. FL-41 tint is commercially available through Brain Power, Inc. (www.callbpi.com), Phantom Research Laboratories, Inc. (www.phantomresearch.com), and the John A Moran Eye Center Optical Shop (www.insight.med.utah.edu/jmec/optical_shop/optical_shop.htm).

Contributors

RD Lamb participated in study design and collected the study data. KB Digre, JEA Warner, and AG Smith participated in study design, and provided patients and materials or other study-related resources. SD Nandedkar created the customized, Windows-based software program used to analyze the blink responses. BJ Katz participated in study design, provided patients and materials or other study-related resources, and conducted the literature searches. All authors contributed to data analysis and interpretation, writing and critical revision of the manuscript.

Conflict of interest statement

SD Nandedkar has a proprietary interest in the use of the electromyographic amplifier and customized, Windows-based software program used to analyze blink parameters. The other authors have reported no conflicts of interest.

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Table 1: Demographics of 13 blepharospasm subjects and 13 control subjects in the FL-41 versus rose-tinted lens trial.

	Blepharospasm	**Control**
Female	10	8
Male	3	5
Total Number	13	13
Average Age of Subject	62	47
Average Years With Blepharospasm	6 years	N/A
Range of Years with Blepharospasm	1-23 years	N/A
Number Currently Receiving Botulinum toxin injections	9	N/A
Surgical Treatment	3	N/A
Currently using FL-41 lenses	1	N/A

Table 2: **Control subject data for FL-41 versus Rose tinted lenses.** This table compares the blink frequency, blink duration, and blink amplitude for control subjects using FL-41, Rose tinted, and no tinted lenses. There was no statistically significant difference in blink frequency, duration, or amplitude in the control group.

	Blink frequency (blinks/min)			**Blink duration (ms)**			**Blink amplitude (μV)**		
Subject	**None**	**Rose**	**FL-41**	**None**	**Rose**	**FL-41**	**None**	**Rose**	**FL-41**
1	8.8	5.8	8.8	155.5	171.5	143.5	15.7	15.5	20.0
2	22.6	28.8	20.8	174.5	198.8	176.4	45.5	40.1	39.8
3	39.2	42.6	33.2	191.0	185.5	191.9	29.5	33.4	24.2
4	39.8	33.6	33.0	175.1	154.0	139.9	49.0	40.0	26.2
5	36.0	32.8	36.4	169.8	152.0	148.8	23.1	24.8	24.9
6	11.4	6.0	10.4	132.5	148.4	170.5	47.9	39.9	25.3
7	19.4	14.2	27.8	182.0	121.5	161.3	21.8	12.9	19.7
8	10.6	11.2	11.2	167.6	176.3	206.5	88.9	91.5	84.5
9	47.2	47.2	45.4	170.0	160.5	184.3	109.1	123.3	104.0
10	18.6	22.2	25.4	165.5	144.5	150.8	28.8	37.3	34.4
11	19.6	12.4	13.2	199.0	175.3	152.0	33.9	42.0	25.6
12	13.4	13.8	19.6	202.8	196.3	209.3	29.0	32.9	32.0
13	12.0	10.2	9.0	154.0	114.0	144.5	16.5	11.8	17.1

Table 3: **Blepharospasm subject data for FL-41 versus Rose tinted lenses.** This table compares the blink frequency, blink duration, and blink amplitude for blepharospasm subjects using FL-41, Rose tinted, and no tinted lenses. Compared to the rose tint, FL-41 reduced the mean blink rate by 7.0 blinks/minute (p=0.002). FL-41 also reduced mean eyelid contraction force by 6.6 μV (p=0.013). There was no statistically significant difference in blink duration.

	Blink frequency (blinks/min)			Blink duration (ms)			Blink amplitude (μV)		
Subject	**None**	**Rose**	**FL-41**	**None**	**Rose**	**FL-41**	**None**	**Rose**	**FL-41**
1	16.6	19.2	9.4	124.3	138.2	138.4	29.8	34.2	25.9
2	4.4	8.4	3.0	92.8	126.9	100.2	9.1	11.6	5.8
3	62.2	66.4	51.4	156.8	169.0	156.5	49.4	37.3	44.3
4	10.0	10.2	9.2	81.3	118.7	114.8	34.8	28.2	24.0
5	34.6	32.2	32.2	134.8	127.0	151.0	50.3	53.0	51.1
6	11.0	8.2	8.0	49.0	43.3	54.8	35.8	40.2	30.6
7	37.6	32.6	26.6	115.0	108.3	77.8	51.2	51.7	45.8
8	42.4	54.6	37.6	156.8	204.3	151.0	27.5	38.7	32.9
9	33.0	28.2	19.4	138.3	116.8	161.4	36.8	36.5	32.5
10	21.2	23.6	13.0	155.5	146.0	153.3	20.8	24.5	28.6
11	32.0	22.0	11.8	151.3	141.5	171.8	46.7	42.5	29.2
12	12.4	18.8	7.8	167.5	190.6	177.3	27.3	46.8	36.9
13	50.0	51.0	55.0	231.0	225.0	171.8	68.8	55.1	26.4

Table 4: Demographics of 13 blepharospasm subjects and 13 control subjects in the FL-41 versus gray-tinted lens trial.

	Blepharospasm	**Control**
Female	12	7
Male	1	6
Total Number	13	13
Average Age of Subject	62	57
Average Years With Blepharospasm	14 years	N/A
Range of Years with Blepharospasm	2 - 60 years	N/A
Number Currently Receiving Botulinum toxin injections	11	N/A
Surgical Treatment	1	N/A

Table 5: **Control subject data for FL-41 versus gray-tinted lenses.** This table compares the blink frequency, blink duration, and blink amplitude for control subjects using FL-41, Gray tinted, and no tinted lenses. There was no statistically significant difference in blink frequency, duration, or force in the control group.

	Blink frequency (blinks/min)			Blink duration (ms)			Blink amplitude (μV)		
Subject	None	Gray	FL-41	None	Gray	FL-41	None	Gray	FL-41
1	27.0	33.8	28.4	176.0	187.3	255.8	33.5	42.0	38.1
2	10.6	15.0	9.2	200.5	187.7	224.4	15.1	17.8	14.6
3	22.0	17.6	13.0	271.0	251.7	282.5	23.4	23.5	26.9
4	16.6	18.6	20.8	189.5	201.5	224.8	21.8	30.8	24.3
5	13.2	16.0	14.4	158.3	127.0	179.5	18.4	17.0	20.7
6	34.4	31.0	21.8	234.5	226.3	265.5	31.3	32.4	34.0
7	29.2	38.5	34.8	203.0	224.0	194.8	17.2	15.7	25.9
8	32.6	13.8	29.0	197.8	198.5	185.0	13.8	15.6	16.0
9	27.6	20.4	17.4	194.0	182.1	240.9	20.1	13.5	32.2
10	8.6	9.2	7.2	155.5	164.0	183.0	89.0	55.4	180.4
11	16.6	19.6	7.4	149.0	151.0	144.6	40.4	28.5	47.3
12	65.4	55.0	49.6	163.3	147.5	153.5	32.8	42.4	36.1
13	23.8	12.0	28.2	213.8	214.8	174.8	21.9	21.0	26.6

Table 6. **Blepharospasm subject data for FL-41 versus gray-tinted lenses.** This table compares the blink frequency, blink duration, and blink amplitude for blepharospasm subjects using FL-41, Gray tinted, and no tinted lenses. Compared to gray tint, FL-41 reduced the mean blink rate by 6.3 blinks/minute (p=0.003). There was no statistically significant difference in blink duration or force.

	Blink frequency (blinks/min)			Blink duration (ms)			Blink amplitude (μV)		
Subject	None	Gray	FL-41	None	Gray	FL-41	None	Gray	FL-41
1	40.0	39.4	32.6	178.0	148.5	156.0	30.6	29.7	36.3
2	27.4	23.6	24.6	112.9	68.3	183.2	76.2	81.4	72.0
3	8.2	10.4	8.0	191.0	212.2	192.8	18.9	27.9	24.8
4	45.8	43.8	37.4	168.3	179.8	157.4	48.8	52.8	54.7
5	18.8	18.8	16.0	161.3	200.5	181.3	37.4	39.9	24.3
6	21.6	26.4	14.8	130.8	143.3	127.3	21.1	32.2	14.4
7	72.6	64.4	65.2	204.8	210.5	226.8	48.3	41.3	46.4
8	45.2	49.4	31.8	175.6	199.0	162.7	52.4	43.1	36.9
9	40.8	27.2	22.0	161.7	154.4	150.1	127.9	135.4	123.9
10	24.6	35.3	25.2	105.3	138.3	126.0	132.9	139.9	120.6
11	14.8	19.4	21.0	184.1	195.1	165.0	110.1	92.4	148.6
12	30.0	27.8	9.8	158.0	143.5	146.0	76.0	70.9	47.0
13	42.4	31.0	26.2	155.8	187.3	151.1	69.3	67.0	60.9

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