

Association between personality traits and experience of adverse periocular reactions to topical prostaglandin analogues

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To cite: Kishimoto N, Noro T, Kodaka F, *et al.* Association between personality traits and experience of adverse periocular reactions to topical prostaglandin analogues. *BMJ Open Ophthalmology* 2022;**7**:e000946. doi:10.1136/bmjophth-2021-000946

► Additional supplemental material is published online only. To view, please visit the journal online (<http://dx.doi.org/10.1136/bmjophth-2021-000946>).

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Received 25 November 2021
Accepted 11 June 2022



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ABSTRACT

Background Aesthetically unappealing adverse periocular reactions to prostaglandin (PG) eye-drops are a major challenge in glaucoma treatment. This study analysed the personality traits of patients with glaucoma based on a five-factor model and examined the associations between these factors and adverse periocular reactions.

Methods One hundred and forty-seven patients with glaucoma were surveyed anonymously regarding their personality traits and how often adverse periocular reactions were experienced.

Results The analysis included 117 valid responses (71 men and 46 women, age: 61.9±11.5 years). Patients who experienced hypertrichosis of the eyelashes scored significantly higher on extraversion ($p<0.05$), with no significant differences in the other four personality traits. Patients who experienced eyelid hyperpigmentation and deepening of the upper eyelid sulcus showed no significant differences in any of the personality traits. Younger patients scored significantly higher on hypertrichosis ($p<0.05$).

Conclusion The experience of adverse reactions differed according to patient age and personality traits. Therefore, eye-drops should be chosen based on these factors.

Trial registration number UMIN000035155.

INTRODUCTION

Although topical prostaglandin (PG) analogues are quintessential for glaucoma treatment, their aesthetic adverse effects can decrease the rate of treatment adherence. The major adverse effects of PG eye-drops include eyelash hypertrichosis, eyelid hyperpigmentation and deepening of the upper eyelid sulcus (DUES). Subjective experiences related to medical problems can be associated with personality traits.¹ In the field of psychology, a five-factor model (the Big Five personality traits) is used to explain human personality through a combination of five personality traits: extraversion, agreeableness, conscientiousness, neuroticism and openness to experience.² Extraversion is the tendency

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Previous research aimed to ascertain patient personality traits and tailor treatment strategies to individuals to provide better treatment.

WHAT THIS STUDY ADDS

⇒ Analysis of the personality traits of patients with glaucoma revealed that extraversion scores were associated with the experience of adverse periocular reactions to topical prostaglandin analogues.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Ascertaining patient personality traits may help the continued treatment of chronic diseases such as glaucoma.

to be interested in or concerned with the external world; agreeableness is the tendency to act in a balanced and accommodating manner; conscientiousness is the tendency to be responsible, sincere and serious; neuroticism is the tendency to become depressed and emotionally unstable; and openness to experience tends to reflect a notable interest in knowledge and beauty.³ A previous study reported that neuroticism from the Big Five personality traits was associated with dropout from glaucoma treatment, suggesting that personality traits affected the subjective experiences of patients in terms of adverse effects.⁴ However, little is known about the association of personality traits with aesthetic adverse effects.

In the present study, we investigated the personality traits associated with the subjective experience of aesthetic adverse effects. We conducted a self-report questionnaire survey including subjective experience of aesthetic adverse effects (eyelash hypertrichosis, eyelid hyperpigmentation and DUES) and Big Five

personality traits in patients with glaucoma who were users of PG eye-drops.

MATERIALS AND METHODS

Subjects

The potential participants were patients with glaucoma seen as outpatients by an ophthalmologist at the Jikei University School of Medicine Hospital between December 2018 and March 2019. A total of 147 patients who consented to participate in this study completed a self-administered questionnaire during their visit and returned it to the physician in the examination room. The survey asked the patients for their age and sex and included a brief measure of the Big Five personality traits (the Japanese version of the Ten-Item Personality Inventory (TIPI-J)) and also inquired whether they had used PG eye-drops and the duration of treatment (<3 months, 3 months–1 year, 1–3 years and >3 years). The questionnaire did not include items related to glaucoma severity, such as the visual field. To determine if they had experienced adverse periocular reactions, the patients were asked, ‘Do you think that your eyelashes have thickened or lengthened/the colouring of your eyelids has increased/your eyes have become sunken since you started using eye drops?’. The patient responses were scored 1 point for ‘No’, 2 for ‘A little’, 3 for ‘Somewhat’, 4 for ‘Quite a bit’ and 5 for ‘A lot’. Patient responses were analysed, with an experience score of 1 indicating no adverse reactions, and a score of 2–5 indicating adverse reactions. To determine how they felt about these adverse reactions, the patients were asked, ‘How do you feel about your eyelashes/rings around your eyes/your sunken eyes?’. The possible responses were ‘Minor discomfort is an inevitable part of treatment’, ‘[I] want to switch to a different medication’ and ‘[I am] not particularly concerned’. To determine how often they consulted a physician regarding their adverse reactions, the patients were asked, ‘Have you consulted your doctor regarding your eyelashes/rings around your eyes/your sunken eyes?’. The possible responses were ‘Yes’ or ‘No’ (figure 1).

Big Five personality traits and the TIPI-J

The Ten-Item Personality Inventory (TIPI) is a questionnaire specifically used to evaluate the ‘Big Five’ personality traits.^{2 4 5} The Big Five personality traits³ are as follows:

1. Extraversion.
2. Agreeableness.
3. Conscientiousness.
4. Neuroticism.
5. Openness to experience.

The TIPI consists of 10 statements, to which participants indicate their agreement or disagreement by rating the statements from 1 (strongly disagree) to 7 (strongly agree). The TIPI items are as follows.

1. Extraverted, enthusiastic.
2. Critical, quarrelsome.

- A** 1. Do you think that your eyelashes have thickened or lengthened since you started using the eye drops?

No	A little	Somewhat	Quite a bit	A lot
1	2	3	4	5

2. How do you feel about your eyelashes?

- Minor discomfort is an inevitable part of treatment
 Want to switch to a different medication
 Not particularly concerned

3. Have you consulted your doctor about your eyelashes?

- Yes
 No

B

1. Do you think that the coloring of your eyelids has increased since you started using the eye drops?

No	A little	Somewhat	Quite a bit	A lot
1	2	3	4	5

2. How do you feel about the coloring of your eyelids?

- Minor discomfort is an inevitable part of treatment
 Want to switch to a different medication
 Not particularly concerned

3. Have you consulted your doctor about the coloring of your eyelids?

- Yes
 No

C

1. Do you think that your eyes have become sunken since you started using the eye drops?

No	A little	Somewhat	Quite a bit	A lot
1	2	3	4	5

2. How do you think about your sunken eyes?

- Minor discomfort is an inevitable part of treatment
 Want to switch to a different medication
 Not particularly concerned

3. Have you consulted your doctor about your sunken eyes?

- Yes
 No

Figure 1 Questionnaire regarding adverse reactions characteristic of topical PG. Patients were asked about eyelash hypertrichosis (A), hyperpigmentation of the eyelids (B), and DUES (C) in simple terms. Adverse reactions were scored from 1 (none) to 5 (severe) (A-1, B-1, C-1). Feelings (A-2, B-2, C-2) and actions (A-3, B-3, C-3) regarding adverse reactions were selected from the options below. DUES, deepening of the upper eyelid sulcus; PG, prostaglandin.

3. Dependable, self-disciplined.
4. Anxious, easily upset.
5. Open to new experiences, complex.
6. Reserved, quiet.
7. Sympathetic, warm.
8. Disorganised, careless.
9. Calm, emotionally stable.
10. Conventional, uncreative.

Data analysis

All data analyses were performed using IBM SPSS Statistics for Windows, V.27.0 (IBM Corp, Armonk, New York, USA). The two-sided level of statistical significance was

set at $p < 0.05$. The following calculation⁵ was used to evaluate each of the Big Five personality traits: extraversion: item 1 + (8 – item 6); agreeableness: (8 – item 2) + item 7; conscientiousness: item 3 + (8 – item 8); neuroticism: item 4 + (8 – item 9); and openness to new experience: item 5 + (8 – item 10).

Associations between the Big Five personality traits and experiencing adverse reactions

To investigate the personality traits that were associated with the experience of each aesthetic adverse effects, we performed a two-sample t-test to compare the Big Five personality traits between patients who had and had not experienced each aesthetic adverse effect. The level of statistical significance was set at $p = 0.01$ because the five subitems on personality traits exist in the TIPI-J. We then performed a logistic regression analysis to identify the personality traits that were associated with each aesthetic adverse effects, in which the independent variables were sex (%female), age and the subitems from the TIPI-J and the dependent variables were the presence or lack of experience of aesthetic adverse effects.

Associations between the degree of each personality trait and experience of adverse reactions

To investigate the type of the aesthetic adverse effects that were associated with the degree of each component of the Big Five personality trait, we performed a multiple regression analysis, in which the independent variables were sex (%female), age and the presence or lack of experience of aesthetic adverse effects and the dependent variable was the degree of each personality trait.

Associations of sex and age with experiencing adverse reactions

To investigate the association of age and sex with the degree of aesthetic adverse effect, we performed a multiple regression analysis, in which the independent variables were sex (%female) and age and the dependent variable was the degree of experience score of each adverse effect.

RESULTS

Patient characteristics

Of the 147 patients who responded to the survey, 16 with missing TIPI-J or sex data and 14 who had never used PG were excluded; therefore, responses from 117 patients were analysed (figure 2). The study included 71 men (60.7%) and 46 women (39.3%). The mean age was 61.9 ± 11.5 years. Of the 117 patients who had used PG, 88 (75.2%) had used PG for > 3 years. This was a voluntary questionnaire and the patients were not forced to complete all answers. Therefore, 47 patients (40.2%) reported all three side effects, which were analysed independently. If a patient responded to any of the three adverse reactions, their responses were analysed. In this study, 108, 108 and 106 patients responded to questions regarding hypertrichosis of the eyelashes,

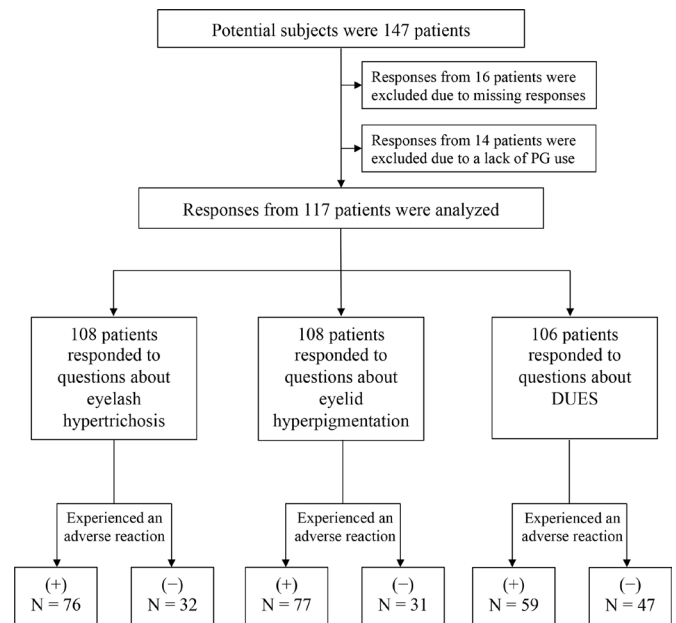


Figure 2 Summary of questionnaire responses. DUES, deepening of the upper eyelid sulcus; N, number of patients; PG, prostaglandin.

hyperpigmentation of the eyelids and DUES, respectively. When asked whether they had experienced adverse reactions to PG, 76 patients (70.4%) responded that they had experienced hypertrichosis of the eyelashes, 77 (71.3%) responded that they had experienced eyelid hyperpigmentation and 59 (55.7%) responded that they had experienced DUES.

Associations between the Big Five personality traits and experiencing adverse reactions

In eyelash hypertrichosis, the score of 'Extraversion' in patients who experienced aesthetic adverse effect was significantly higher than who had not (8.86 ± 2.68 vs 7.59 ± 2.34 , $p = 0.024$), but the statistical significance was disappeared after multiple comparison for five subitems. No significant differences in personality traits were noted in patients who experienced eyelid hyperpigmentation or DUES (table 1). No significant differences were observed in the background or demographics of patients with or without eyelash hypertrichosis, eyelid hyperpigmentation and DUES (online supplemental table 1).

Logistic regression analysis showed that 'Extraversion' was the only variable that expected the experience of eyelash hypertrichosis ($\beta = 0.24$, $z = 2.25$, $p = 0.024$).

Associations between the degree of each personality trait and experience of adverse reactions

There were no specific types of aesthetic adverse effects related to the degree of each personality traits.

Associations of sex and age with experiencing adverse reactions

Experience scores and sex were not significantly correlated. However, age and the experience score for

Table 1 Associations between Big Five personality traits and experiencing adverse reactions to topical PG

Experienced an adverse reaction	Eyelash hypertrichosis		P value*	Eyelid hyperpigmentation		p-value*	DUES		p-value*
	(+) n=76	(-) n=32		(+) n=77	(-) n=31		(+) n=59	(-) n=47	
Subitems from the TIPI-J									
Extraversion	8.86±2.68	7.59±2.34	0.024*	8.66±2.59	8.06±2.77	0.964	8.98±2.76	8.11±2.29	0.280
Agreeableness	10.64±1.64	10.94±1.90	0.304	10.64±1.65	10.94±1.92	0.493	10.78±1.49	10.72±1.98	0.796
Conscientiousness	9.66±2.29	9.16±2.02	0.156	9.53±2.28	9.48±2.05	0.719	9.78±2.25	9.32±2.10	0.255
Neuroticism	7.55±2.43	7.34±2.29	0.430	7.48±2.38	7.58±2.39	0.771	7.54±2.58	7.38±2.07	0.209
Openness to experience	8.93±2.44	8.59±2.40	0.519	9.12±2.31	8.10±2.56	0.108	9.22±2.39	8.49±2.31	0.280

*A two-sample t-test was used to examine Big Five dimensions measured with the TIPI-J. The data are presented as means±SD. The statistical significance of the test was set at <5%. DUES, deepening of the upper eyelid sulcus; N, number of patients; PG, prostaglandin; TIPI-J, Japanese version of the Ten-Item Personality Inventory.

hypertrichosis of the eyelashes were significantly negatively correlated ($p=0.031$) (table 2).

Patient feelings about and actions regarding adverse reactions

The patients were asked how they felt about the adverse reactions. The patients who responded that minor discomfort (adverse reactions) is an inevitable part of treatment included 26 patients (37.2%) who experienced hypertrichosis of the eyelashes, 32 (48.5%) who experienced eyelid hyperpigmentation and 21 (39.6%) who experienced DUES. The patients who responded that they wanted to switch to a different medication included one patient (1.4%) who experienced hypertrichosis of the eyelashes, three (4.5%) who experienced eyelid hyperpigmentation, and four (7.6%) who experienced DUES. Combined, 28 patients (38.6%) experienced hypertrichosis of the eyelashes, 37 (53.0%) experienced eyelid hyperpigmentation and 28 (47.2%) experienced DUES. Close to half of the patients were dissatisfied with the eye-drops due to the adverse of eyelid hyperpigmentation and DUES. Nevertheless, only one patient (1.4%) who experienced hypertrichosis of the eyelashes, two (3.0%) who experienced eyelid hyperpigmentation and one (1.9%) who experienced DUES consulted a physician regarding these adverse reactions (figure 3). The personality traits did not differ significantly between the group of patients who wanted to have their medication switched and the group who did not. The comparison of personality traits between patients who consulted their physicians about adverse reactions and those who did not meet the statistically valid number of cases.

DISCUSSION

The use of the five-factor model and TIPI-J allows scoring of a person's personality traits based on a combination of five factors.^{4,5} Previous studies in ophthalmology have reported that the subjective symptoms of dry eye and its severity were correlated with the neuroticism score.^{6,7} In the current study, patients who experienced hypertrichosis of the eyelashes had a significantly higher extraversion score. Golshani *et al*⁸ administered a personality test to patients undergoing plastic surgery (including plastic surgery on the face), reporting significantly higher scores for extraversion and agreeableness than their scores for other personality traits. In orthopaedic surgery, Hilliard *et al*⁹ reported that patients who adhered to postoperative rehabilitation had a higher score for extraversion. Highly extroverted people are highly interested in the external world and are, thus, reported to go out more often.¹⁰ Because of concerns about appearance, patients may be more likely to notice hypertrichosis of the eyelashes. No significant differences in the Big Five personality traits were observed in patients who experienced eyelid hyperpigmentation or DUES. The possible explanations for this finding include the following: eyelid hyperpigmentation and DUES may be less likely to be noticed than hypertrichosis of the eyelashes, the survey questions may

Table 2 Associations of sex and age with experiencing adverse reactions characteristic of topical PG

	Sex			Age		
	β	SE	P value*	β	SE	P value*
Eyelash hypertrichosis	0.544	0.310	0.082	-0.029	0.014	0.031*
Eyelid hyperpigmentation	0.114	0.270	0.675	-0.022	0.012	0.063
DUES	0.317	0.239	0.189	-0.019	0.010	0.069

*Multiple linear regression analysis using experience scores as the dependent variable. Statistical significance for the test was set at <5%. β , unstandardised regression coefficient; DUES, deepening of the upper eyelid sulcus; PG, prostaglandin.

have been difficult to understand or the sample size may have been too small. The development of methods for patients to better understand the survey questions, particularly by including photographs of a classic case of DUES, requires further study. In the case of multiple adverse reactions, many people may likely wish to switch eye-drops or consult a doctor; however, the current study could not analyse cases of multiple adverse reactions due to the limitations of the questionnaire format.

The authors previously reported high neuroticism scores among individuals with continued glaucoma

treatment.⁴ The results of the current study showed no significant differences in neuroticism with respect to any adverse reaction. A search of the literature yielded no studies that reported a difference in patient personality traits depending on where they were seen, for example, at a clinic or university hospital. The subjects in the current study were patients seen by a glaucoma clinic at a university hospital; therefore, presumably many desired aggressive treatment. Such individuals are highly interested in efficacy and worsening visual field loss rather than adverse reactions to eye-drops; therefore, the potential for selection bias cannot be ruled out. Differences in facilities are a topic for future study.

PG causes characteristic adverse periorbital reactions including hypertrichosis of the eyelashes, hyperpigmentation of the eyelids and DUES. A previous study reported that 8%–60% of patients using PG had experienced hypertrichosis of the eyelashes, 12%–58% had experienced hyperpigmentation of the eyelids and 10%–40% had experienced DUES.¹¹ In the current survey, 70.4% of patients had experienced hypertrichosis of the eyelashes, 71.3% had experienced hyperpigmentation of the eyelids and 55.7% had experienced DUES, higher percentages than previously reported. Among the patients in the current study, 75.2% had used PG for >3 years. The awareness of adverse reactions to prolonged treatment with PG and the potential dissatisfaction with and forbearance of treatment may have increased. Further studies are needed that consider the duration of eye-drop use. Moreover, the frequency and extent of DUES differ depending on the type of PG; a low percentage of patients (approximately 10%–20%) experience DUES relative to hypertrichosis of the eyelashes or hyperpigmentation of the eyelids.¹¹ Similarly, the current study showed that a lower percentage of patients experienced DUES than experienced hypertrichosis or hyperpigmentation and that DUES may be an adverse reaction that patients are less likely to notice. However, the current study did not examine PG analogues by type; thus, studies with additional detailed examinations are needed.

Previous studies reported no significant sex or age differences in the experience of adverse reactions.^{11 12} However, the results of the current study showed significant differences in hypertrichosis of the eyelashes but not for eyelid hyperpigmentation or DUES. Thus,

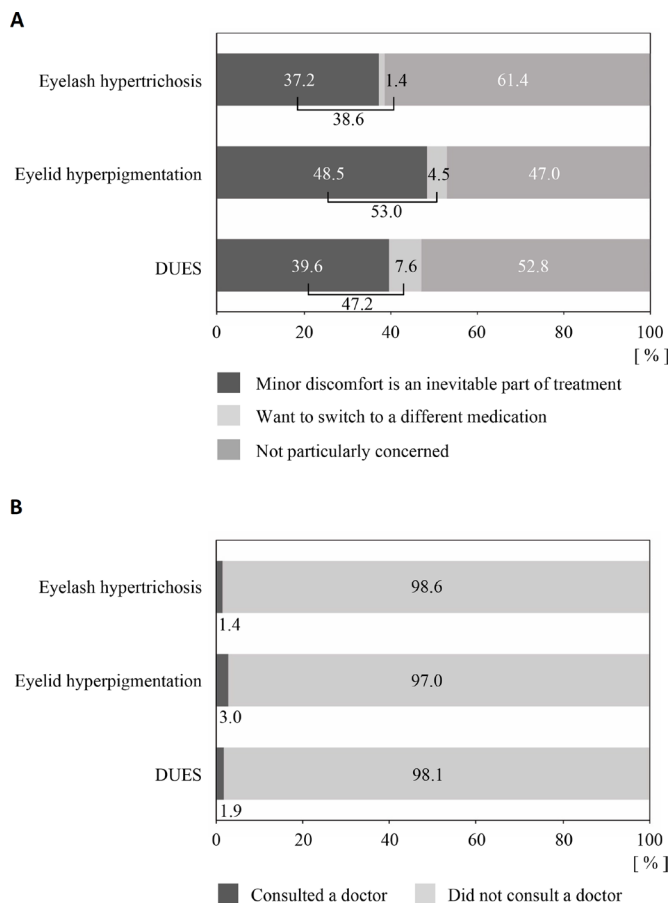


Figure 3 (A,B) Distribution of patient feelings (A) and actions (B) regarding adverse reactions to topical PG. The items in the questionnaire concerning adverse reactions are arranged vertically. The horizontal axis shows the percentages of patients who selected each response. DUES, deepening of the upper eyelid sulcus.



when eye-drops are prescribed to younger patients with glaucoma, medications that are less likely to cause hypertrichosis of the eyelashes should be chosen.

In total, 37%–49% of patients cited ‘Minor discomfort is an inevitable part of treatment’ as their reason for not consulting a physician regarding adverse reactions. Adverse reactions should be explained to patients before prescribing eye-drops, and they should fully understand those adverse reactions, which should facilitate their continuation of treatment. However, 7.6% of patients who experienced DUES reported wanting to switch to a different medication, indicating that they understood the adverse reaction but were dissatisfied with the eye-drops. Moreover, 97%–99% of patients did not consult a physician regarding their adverse reactions; therefore, their potential dissatisfaction with treatment did not translate into subsequent action. Having obtained informed consent, physicians may compel patients to endure adverse reactions or may create conditions where a patient is less likely to complain, a topic that requires further exploration. As current glaucoma treatment focuses on lowering intraocular pressure, adverse reactions may be disregarded. Although patients understand that lowering intraocular pressure is the biggest contributing factor to the treatment of glaucoma, adverse reactions should be actively discussed. Physicians need to create an environment in which patients feel free to discuss their illness and its treatment and to fully consider these feelings when developing treatment plans. Within the limited time of an outpatient visit, patients may not wish to express their dissatisfaction with treatment to a physician and may fear that expressing their dissatisfaction with a physician may become an obstacle to communication with the physician. These possibilities also warrant consideration. Because of these various circumstances, an anonymous survey of patient views and feelings is an effective way to ascertain what patients may have difficulty saying directly to their physicians. Poor adherence to eye-drops for the treatment of glaucoma increases the risk of blindness by 1.8-fold.¹³ Adverse reactions can reduce adherence to eye drops. To prevent this from occurring, physicians should implement an aggressive intervention regarding adverse reactions, such as taking photographs to objectively assess whether adverse reactions have occurred.

The current study surveyed patients with glaucoma regarding adverse reactions based on the Big Five personality traits. The results showed that the frequency with which adverse reactions were experienced and their extent differed depending on those traits. Based on these findings, eye-drops that are less likely to cause hypertrichosis of the eyelashes should be chosen for highly extroverted and younger patients. We observed no sex differences in the experience of adverse periocular reactions and almost none of the patients felt comfortable consulting a physician regarding their dissatisfaction with and adverse reactions to the eye-drops. Thus, treatment approaches

should be changed according to each patient’s personality traits, a concept known as personalised medicine, which may help improve treatment adherence.

Acknowledgements We would like to thank Ms Tomoko Kitazumi and Chihiro Saeki for their assistance in organising the data at the Department of Psychiatry, The Jikei University School of Medicine.

Contributors Study conception and design: NK, TNo, FK and TNa. Data acquisition: NK, MKur, YI, TW, MKu, and TNa. Data analysis and/or interpretation: NK, TNo, FK and KH. Manuscript drafting: NK, TNo and FK. Critical revision of the manuscript for important intellectual content: all authors. NK, TNo and FK contributed equally to this work as first authors. Guarantor: TNo. This study was conducted in collaboration with Jikei University School of Medicine and Santen Pharmaceutical Co, Ltd.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests KH is an employee of Santen Pharmaceutical Co, Ltd.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval All patients were registered in the study after providing informed consent. The study was conducted in accordance with the principles of the Declaration of Helsinki. This prospective observational study was approved by the Ethics Committee of Jikei University School of Medicine (approval no. 9205, Trial Registration no. 000035155). Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available on reasonable request.

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Supplementary Table 1. Background and demographics of patients who had or had not experienced adverse reactions to topical PG**Eyelash hypertrichosis**

Experienced an adverse reaction	(+) N=76		(-) N=32		p-value [†]
	Frequency	%	Frequency	%	
Age, mean±SD (years)	60.7±11.0		64.4±12.3		0.136
Sex:					0.137
Male	43	56.6	23	71.9	
Female	33	43.4	9	28.1	

Eyelid hyperpigmentation

Experienced an adverse reaction	(+) N=77		(-) N=31		p-value [†]
	Frequency	%	Frequency	%	
Age, mean±SD (years)	60.9±10.7		62.2±12.7		0.586
Sex:					0.919
Male	48	62.3	19	61.3	
Female	29	37.7	12	38.7	

DUES

Experienced an adverse reaction	(+) N=59		(-) N=47		p-value [†]
	Frequency	%	Frequency	%	
Age, mean±SD (years)	60.5±11.1		63.1±11.5		0.248
Sex:					0.182
Male	34	57.6	33	70.2	
Female	25	42.4	14	29.8	

†A two-sample *t*-test was performed to compare age of subjects with or without experiencing adverse reactions to topical PG. A chi-squared test was performed to compare the number of patients who experienced an adverse reaction by gender groups. The statistical significance of the test was set at less than 5%. PG, prostaglandin; SD, standard deviation; DUES, deepening of the upper eyelid sulcus; N, number of patients.