# Pretarsal skin height changes in children receiving topical prostaglandin analogue therapy for primary congenital glaucoma

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**PURPOSE** To compare pretarsal skin height (PTSH), as proxy indicator of deepening of the upper eyelid sulcus, in children with primary congenital glaucoma (PCG) treated with topical prostaglandin analogues (PGAs) with PTSH in healthy children (control group 1) and children with PCG but not using PGAs (control group 2).

**METHODS** We recruited children with PCG who had been using PGAs for at least 6 months (PCG/PGA group). PTSH in all participants was measured using ImageJ software from photographs taken in a standardized manner. The PTSH was compared for the PCG group and both control groups.

**RESULTS** A total of 34 children with PCG and 41 controls (31 in group 1; 10 in group 2) were included. The difference in PTSH between children in the PCG/PGA group and both control groups was statistically significant (mean difference, ≥1.7 mm [$P < 0.01$]).

**CONCLUSIONS** The PTSH was significantly greater in children with PCG using PGAs compared to children with PCG not using PGAs and healthy children. Children and their parents should be counseled about lid abnormalities prior to commencing treatment with PGAs. (J AAPOS 2018;22:290-293)

The use of topical prostaglandin analogues (PGAs) to control intraocular pressure in primary congenital glaucoma (PCG) is increasing.[1] However, there are some side effects of long-term use of topical PGAs in adults including dermatochalasis (excess upper eyelid skin), hyperpigmentation of periorbital skin, and increased eyelash length and discoloration.[2-5] Lid changes and deepening of the lid sulcus has been well described in adults.[6-8] Although hyperpigmentation of the periorbital tissues has been described in children,[9,10] deepening of the upper lid sulcus has not been studied. To our knowledge, changes in periorbital fat tissue using quantitative measures following PGA treatment in children and its comparison to healthy children and those with PCG but not using PGAs has not been reported in the literature.

Anatomically the upper lid crease is formed by the attachments of the levator aponeurosis to the upper eyelid skin. We hypothesized that if PGA treatment resulted in atrophy of the preaponeurotic pad, the lid crease would move posteriorly and the pretarsal skin height (PTSH) would increase. This hypothesis is supported by previous reports demonstrating an increase in PTSH in eyes treated with PGA unilaterally based on photographs of adults with prostaglandin orbitopathy.[11] The current study investigated whether PTSH could be used as an objective measure of early sulcus changes in children. To study PTSH as a proxy indicator for deepening of the upper eyelid sulcus, we compared the PTSH of Saudi children with PCG after topical PGA treatment of at least 6 months' duration and compared it to PTSH in healthy Saudi children. We also studied factors associated with increased PTSH in children with PCG using topical PGAs, including age, sex, and duration of PGA use.

## Subjects and Methods

The King Khaled Eye Specialist Hospital Institutional Research Board approved this study, which conformed to all local laws and was compliant with the principles of the Declaration of Helsinki. Consecutive PCG patients ≤18 years of age treated with topical PGAs (PCG/PGA group) for at least 6 months were eligible for inclusion and recruited prospectively from the glaucoma clinics at our institution. In children with bilateral PCG, only data from the right eye were included. Two control groups were also recruited: normal healthy children (control group 1)

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and children with PCG but not using PGAs (control group 2). For control groups, only data from the right eye were used. Children using contact lenses and children with ptosis at baseline were excluded.

For this preliminary study, we aimed to recruit a minimum of 30 children with PCG and a similar number of children without PCG (control group 1). For comparison of the findings of children with PCG using PGAs, we recruited 10 children of similar age for control group 2; fewer children were allowed in this group to facilitate recruitment, because most of the children at our institution had advanced disease, often presented late, and were already using PGAs. Only a small proportion of our children with PCG were not using PGA.

Data on age, sex, duration of PGA use, type of PGA used and laterality of PCG were collected. Photographs of eyes and periorbital tissues were acquired with written parental consent. All photographs were taken in a standard manner at a distance of 30 cm using a digital camera with a shutter speed of 1/125 s and an f-stop value of 18. A ruler with millimeter markings was placed in each frame for reference (eFigure 1), and the maximum height of PTSH in each patient was measured manually using ImageJ software[12] by an oculoplastic surgeon, who was masked to the treatment status of the child, using the measurement rule in the photograph for reference. The use of this software is well-established for measuring ocular tissue parameters.[13,14]

### Data Analysis

The data were collected using pretested customized data collection forms. Statistical Package for Social Studies (SPSS 22) was used for statistical analysis (IBM Corp, Armonk, NY). For qualitative variables, frequencies, and percentage proportions were calculated and validated with 95% confidence intervals. The data of subvariables were compared using the two-tailed $P$ value (0.05). A Bonferroni correction was used ($\alpha = 0.025$) to account for two primary comparisons (PTSH of PCG/PGA group vs control group 1 and PTSH of PCG/PGA group vs control group 2). For quantitative variables, such as PTSH, duration of PGA use and age, a frequency distribution curve was plotted. Because the distribution of PTSH was skewed to the right, log values were calculated, and the mean and standard deviation of the log of PTSH computed. For comparison, we estimated the difference of means and the 95% confidence intervals. A parametric one-way variance analysis was performed. For the post hoc test, equal variance was not assumed, and significance level of 0.05 (two-sided) using Tamhane's $T2$ test was applied. To correlate PTSH to age and the duration of PGA use, bivariate correlation analysis was used (SPSS). Pearson's $r$ and the two-tailed $P$ values were calculated. To study the interaction between variables on PTSH, linear regression modeling was performed with SPSS and $R^2$ values, adjusted coefficient, and the 95% confidence intervals were calculated.

## Results

The PCG/PGA group comprised 34 children; control group 1, 31 children; and control group 2, 10 children. Baseline characteristics of participants are shown in Table 1. Children in control groups 1 and 2 were, on average, younger by 2.8 years ($P = 0.002$) and 7.9 years ($P < 0.0001$), respectively, than children in the PCG/PGA group. The proportion of boys in the PCG/PGA group was similar to those of control groups 1 ($P = 0.64$) and 2 ($P = 0.80$).

Table 1. Baseline parameters for children with primary congenital glaucoma using prostaglandin analogues and control children

| | PCG/PGA group | Control group 1[a] | Control group 2[b] |
|---|---|---|---|
| Number | 34 | 31 | 10 |
| Age, years, mean ± SD | 9.3 ± 4.0 | 6.5 ± 2.7 | 1.4 ± 1.3 |
| Boys:girls | 20:14 | 20:11 | 6:4 |

*PGA*, prostaglandin analogue; *PCG*, primary congenital glaucoma; *SD*, standard deviation.
[a]Healthy children.
[b]Children with PCG but not using PGAs.

Of 34 eyes of patients with PCG treated with PGAs, all eyes underwent glaucoma surgery before PGA treatment. The mean number of surgical procedures in the PCG/PGA group was similar to control group 2 (2.1 ± 1.1 vs 1.8 ± 0.8 [$P = 0.26$]).

The mean duration of PGA treatment in the PCG/PGA group was 14.6 ± 2 months. Seven eyes were treated with bimatoprost eye drops, 10 eyes with travoprost eye drops, and 17 eyes latanoprost eye drops.

PTSH in all groups is presented in Table 2. PTSH was statistically significantly greater in the PCG/PGA group compared to both control groups 1 and 2 ($P < 0.01$). Age (Pearson $r = -0.01$, $P = 0.9$) or duration of PGA treatment (Pearson $r = -0.1$, $P = 0.6$) was not significantly correlated with PTSH in the PCG/PGA group.

## Discussion

Our study demonstrated a significant increase in PTSH in children with PCG treated with PGAs for at least 6 months compared with children with PCG not treated with PGAs and with healthy Saudi children without glaucoma. Variation of PTSH by age, laterality, type of PGA, and duration of PGA use was not statistically significant.

PTSH has been used by facial cosmetologists to document changes in lid position relative to the skin crease after surgical intervention.[15,16] The present study used PTSH as an objective marker of lid changes following PGA use in children with PCG. Loss of anterior orbital fat through chronic PGA use causes a deepening of the upper lid sulcus[8] and a corresponding increase in PTSH.

Eyelid changes following prostaglandin use are well documented in adults.[3,4,6,11,17-21] Rabinowitz and colleagues[6] compared orbital and lid changes in one eye following prostaglandin use for 1 year with fellow eyes as controls and found the eyelid crease height to be, on average, 1.25 mm greater in the treated eye than in the fellow eye. They also found an increase in anophthalmias and marginal reflex distance. These changes are thought