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***Retrospective Study***

**Comparison of ocular axis and corneal diameter between entropion and non-entropion eyes in children with congenital glaucoma**

Wang Y *et al*. Epiblepharon in congenital glaucoma

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**Abstract**

BACKGROUND

Children with congenital glaucoma are often accompanied by acquired epiblepharon in the lower eyelid, which causes entropion of the lower eyelid and damages the cornea.

AIM

To infer the possible causes of lower eyelid entropion by comparing the difference of ocular axis and corneal diameter between inverted and non-inverted ciliary eyes in children with congenital glaucoma.

METHODS

A total of 15 patients (11 males and 4 females) diagnosed with congenital glaucoma between July 2016 and January 2019 at Tongren Hospital were included. Five patients had bilateral glaucoma, and ten had unilateral glaucoma. Each patient had only one eye with lower eyelid entropion which is associated with congenital glaucoma. All the patients had no entropion in another eye. The clinical data were collected. Main outcome measures were the ocular axis and corneal diameter.

RESULTS

The average age of the 15 patients was 1.85 ± 0.49 years. Paired *t*-test showed that the average ocular axis of congenital glaucoma eyes with lower eyelid entropion (24.86 ± 3.44 mm) was significantly longer than that of congenital glaucoma eyes without lower eyelid entropion (20.79 ± 1.34 mm; *P* < 0.001). The average corneal diameter of congenital glaucoma eyes with lower eyelid entropion (13.61 ± 0.88 mm) was also significantly greater than that of congenital glaucoma eyes without lower eyelid entropion (11.63 ± 0.48; *P* < 0.001).

CONCLUSION

The rapid growth of the ocular axis and corneal diameter may be the main cause of congenital glaucoma with acquired lower eyelid entropion. Therefore, children with poor control of intraocular pressure and excessive growth of ocular axis and corneal diameter must be observed for the existence of acquired epiblepharon.

**Key Words:** Acquired epiblepharon; Congenital glaucoma; Entropion; Ocular axis; Corneal diameter; Congenital epiblepharon

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**Core Tip:** Children with congenital glaucoma are often accompanied by acquired epiblepharon in the lower eyelid. This study investigated the ocular axis and corneal diameter of eyes with acquired epiblepharon in the lower lid among patients with congenital glaucoma and explored the cause of acquired epiblepharon in congenital glaucoma patients.

**INTRODUCTION**

Congenital glaucoma with lower eyelid entropion, due to trichiasis friction of the cornea, causes corneal damage and thus corneal nebula, corneal macula, and corneal leukoplakia. Children not only develop photophobia but also have corneal tears. These factors can affect the development of vision and quality of life. Congenital epiblepharon is characterized by a skin fold under the orbicularis muscle that tilts the lashes, pushing them against the globe[1,2]. It may cause keratopathy and astigmatism, and surgical correction is recommended[3]. Congenital glaucoma develops within the first few years of life and may cause megalocornea, corneal edema, or buphthalmos[4-7]. Acquired epiblepharon in the lower eyelid is also one of the clinical features of patients with congenital glaucoma. This kind of acquired epiblepharon frequently requires early surgical correction due to the risk of severe keratopathy. In children with congenital glaucoma, acquired epiblepharon commonly develops. What is the pathogenesis?

To the best of our knowledge, only a few cases of acquired lower eyelid epiblepharon have been described in patients with congenital glaucoma. Mandal *et al* reported a case of unilateral congenital glaucoma associated with asymmetric congenital lower lid entropion in a 2-year-old girl[8]. In addition, no studies have evaluated the ocular axis and corneal diameter of eyes with acquired epiblepharon in patients with congenital glaucoma.

We investigated the ocular axis and corneal diameter of eyes with acquired epiblepharon in the lower lid among patients with congenital glaucoma and explored the cause of acquired epiblepharon in these patients. The ocular axis and corneal diameter were compared between entropion and non-entropion eyes in children with congenital glaucoma, and the results may lead to a better understanding of the cause of acquired epiblepharon in patients with congenital glaucoma.

**MATERIALS AND METHODS**

***General information***

A total of 15 patients (30 eyes, 11 males and 4 females) diagnosed with congenital glaucoma between July 2016 and January 2019 at Tongren Hospital were included. Five patients had bilateral glaucoma, and ten had unilateral glaucoma. All the 15 eyes with lower eyelid entropion were associated with congenital glaucoma. All the patients had lower eyelid entropion only in one eye and no entropion in another eye. Congenital glaucoma infants with lower eyelid entropion show varying degree of corneal damage due to high intraocular pressure (IOP) and trichiasis, such as corneal edema with corneal epithelial injury, corneal nebula, corneal macula, and corneal leukoplakia. The degree of corneal injury was recorded (Table 1). This study was a retrospective study conducted in accordance with the principles of the Helsinki Declaration and approved by the Institutional Review Board of the Ethics Committee of Beijing Tongren Hospital, Capital Medical University (TRECKY2020-063).

***Diagnostic criteria for primary congenital glaucoma***

Congenital glaucoma was confirmed by a glaucoma doctor, and lower eyelid entropion was diagnosed by an ocular plastic surgeon. Primary congenital glaucoma (PCG) refers to simple anterior chamber angle dysplasia without other anterior segment abnormalities. Its diagnosis is based on at least two of the following clinical features: (1) Neonatal corneal diameter ≥ 11 mm; increased corneal diameter > 12 mm in infants within 1 year old; corneal diameter in children of any age > 13 mm; and elevated IOP (> 21 mmHg); (2) Haab's striae; (3) Corneal edema; and (4) Increased optic nerve cup / disc ratio[9].

***Inclusion criteria and exclusion criteria***

**Inclusion criteria:** Congenital glaucoma was diagnosed in one or both eyes, with one eye with lower eyelid entropion and the other eye without.

**Exclusion criteria:** Congenital epiblepharon and secondary glaucoma, such as traumatic, surgical, and hormonal drug-induced glaucoma.

***Main outcome measures***

Main outcome measures were the ocular axis and corneal diameter in patients with congenital glaucoma. The ocular axis was measured by color Doppler ultrasound, and the corneal diameter was measured with a ruler during general anesthesia for the operation of congenital glaucoma.

***Statistical analysis***

SPSS version 26.0 (SPSS, Inc., Chicago, IL, USA) was used to conduct the statistical analyses. Kolmogorov-Smirnov test was used to estimate the normality of distribution of the measured variables. Values are presented as the median or mean ± SD. Categorical data were tested using the chi-square test. The *t*-test was used for parametric continuous variables and Mann–Whitney’s test for nonparametric continuous variables. For paired samples, the pairwise *t*-test was utilized. A *P*-value < 0.05 was considered statistically significant.

**RESULTS**

The average age of the 15 patients was 1.85 ± 0.49 years. There are different degrees of corneal damage in children with congenital glaucoma with lower eyelid entropion, for example, diffuse corneal epithelial damage, corneal nebula, corneal macula, and corneal leukoplakia. There were nine (60%) cases of diffuse corneal epithelial damage, three (20%) cases of corneal nebula, two (33.3%) cases of corneal macula, and one (6.7%) case of corneal leukoplakia. Paired *t*-test showed that the average ocular axis of eyes with congenital glaucoma with lower eyelid entropion (24.86 ± 3.44 mm) was significantly longer than that of eyes without lower eyelid entropion (20.79 ± 1.34 mm; *P* < 0.001, Table 2). The average corneal diameter of congenital glaucoma eyes with lower eyelid entropion (13.61 ± 0.88 mm) was also significantly greater than that of congenital glaucoma eyes without lower eyelid entropion (11.63 ± 0.48 mm; *P* < 0.001).

**DISCUSSION**

Epiblepharon is a condition in which a fold of the skin and the underlying pretarsal orbicularis muscle overlap the eyelid margin and push the eyelashes inward against the cornea. It is a common congenital eyelid abnormality in Asian children[2,10,11]. Congenital epiblepharon usually involves the medial one-third or one-half of the lower eyelids and usually occurs on both sides. Hayasaka *et al*[3] reported that the incidence of lower lid epiblepharon decreased with age in Japanese children; the incidence was 24% at age 1, 20% at age 2, and 17% at ages 3-4. The prevalence of lower eyelid epiblepharon is high in Chinese preschool children, particularly among boys and younger children. In a previous study, the prevalence of lower eyelid epiblepharon was 26.2%, which decreased with age, with prevalence rates of 30.6%, 28.0%, 15.0%, and 14.3% in children at 3, 4, 5, and 6 years old, respectively[12]. A high prevalence of epiblepharon has also been reported among individuals with congenital glaucoma. In a previous study, the prevalence of lower eyelidacquired epiblepharon was higher among patients with congenital glaucoma than among control patients (40.7% *vs* 13.3%, *P* < 0.001). Asymmetric lower lid epiblepharon was more frequent in patients with congenital glaucoma. In addition, unilateral epiblepharon was associated with unilateral buphthalmos and unilateral glaucoma[13].

In congenital epiblepharon, the suggested pathogenic mechanisms are: (1) Redundant skin; (2) a weak attachment of the pretarsal orbicularis muscle and skin to the underlying tarsus; and (3) hypertrophy and overriding of the orbicularis oculi muscle[14-16]. Mandal *et al* proposed that retractor aponeurosis disinsertion is the most likely cause of congenital low lid entropion[8]. Corneal trauma can result from this condition, making retractor aponeurosis disinsertion an important potential cause of corneal ulceration in infants. An association of congenital corneal ulceration with congenital entropion has been reported[17]. Corneal erosions were frequently found in the group with epiblepharon and rarely found in the group without epiblepharon, suggesting that most corneal erosions are caused by not only congenital glaucoma but also epiblepharon. Buphthalmos pushes the lower lid downward and alters the balance of forces between the anterior and posterior lamella. This imbalance might lead to acquired epiblepharon. Buphthalmos was more frequently found in the group with epiblepharon than in the group without epiblepharon[13].

Congenital glaucoma eyes with uncontrolled IOP in young children are subject to enlargement of the axial length and cornea[18]. Our results showed that the axis and corneal diameters of eyes with congenital glaucoma and acquired lower eyelid epiblepharon were significantly larger than those of the contralateral eyes without lower eyelid epiblepharon. The rate of enlargement of the ocular axis and corneal diameter exceeds that of the development of the lower eyelids, causing the lower eyelids to bear the pressure, especially tension, and when tension is incurred over a long time, lower eyelid entropion easily develops. Epiblepharon in congenital glaucoma appears to be associated with exophthalmos caused by buphthalmos. High IOP causes buphthalmos, and this condition usually persists even after the IOP has lowered because the sclera loses its elasticity and does not readily contract[19]. Buphthalmos pushes the lower lid downward and alters the balance of forces between the anterior and posterior lamella. This imbalance might lead to epiblepharon. A high prevalence of epiblepharon has also been reported in thyroid-associated orbitopathy[20].

In our study, the ocular axis of congenital glaucoma with entropion eyes was 24.86 ± 3.44 mm, while that of congenital glaucoma without entropion eyes was 20.79 ± 1.34. The ocular axis of the entropion eyes was significantly larger than that of the non-entropion eyes. The extrapolated mean axial length at birth was 16.8 mm, and there was rapid initial axial growth, with a mean axial length of 20 mm at 12 mo of age and 21 mm at the age of 4 years[21]. The average ocular axis was 23.3 mm (range, 21.4–27.2 mm) in normal children ranging in age from 7 to 9 years[22]. Dogan *et al*[23] found that among children aged 6-10 years, the ocular axis was 23.13 ± 0.55 mm. The average age of the children in our study was only 1.85 ± 0.49 years, but the ocular axis of the entropion eyes of the congenital glaucoma patients was larger than that of the normal children. Kiskis *et al*[24]found that both the corneal diameter and ocular axis in congenital glaucoma eyes are usually larger than those in normal children.

We hypothesized that one possible mechanism for this lower eyelid-acquired epiblepharon is that the eyeball becomes enlarged, placing pressure on the lower eyelid and lower eyelid retractor. These factors can cause the posterior lamella of the lower eyelid to tighten and shorten, pulling the posterior lamella without affecting the anterior lamella and eventually causing lower eyelid acquired epiblepharon. Another reason is the enlargement of the cornea; the eyeball is enlarged and protrudes forward due to the enlargement of the cornea. The cilia are then easily pushed against the cornea. Finally, high IOP in children with congenital glaucoma leads to corneal epithelial edema and thus photophobia. Because of photophobia, children are willing to close their eyes. However, due to the enlargement of the cornea and eyeballs, it is often difficult for children to close their eyes completely, so they try to squeeze their eyes frequently to reduce the symptoms of photophobia. Frequent eye squeezing can lead to blepharospasm. Blepharospasm can cause the orbicularis oculi muscle in front of the tarsal plate to move forward, the anterior layer of the eyelid to place pressure on the posterior layer, and the development of lower eyelid entropion. The rapid growth of the eye axis and corneal diameter is likely responsible for the development of acquired lower eyelid epiblepharon in patients with congenital glaucoma.

In patients with congenital glaucoma, epiblepharon is associated with corneal erosions. Therefore, in patients with congenital glaucoma, whether epiblepharon exists should be evaluated, especially in patients with accompanying buphthalmos or corneal erosion. This investigation was a retrospective study. Our study was limited by the sample size. A prospective study with a large sample size and long-term follow-up is warranted to elucidate the risk factors and natural course of lower eyelid acquired epiblepharon in congenital glaucoma.

**CONCLUSION**

The rapid expansion of the ocular axis and corneal diameter in children with congenital glaucoma easily causes acquired epiblepharon of the lower eyelid, which leads to entropion of the lower eyelid and corneal erosions. Therefore, entropion of the lower eyelid must not be ignored in children with congenital glaucoma and rapid growth of the ocular axis and corneal diameter.

**ARTICLE HIGHLIGHTS**

***Research background***

Children with congenital glaucoma are often accompanied by acquired epiblepharon in the lower eyelid, which causes entropion of the lower eyelid and damages the cornea. Few studies have evaluated the ocular axis and corneal diameter of acquired epiblepharon in patients with congenital glaucoma.

***Research motivation***

Acquired epiblepharon in patients with congenital glaucoma could affect the development of vision and quality of life. Children with congenital glaucoma are easy to accompany with acquired epiblepharon.

***Research objectives***

This study aimed to infer the possible causes of lower eyelid entropion by comparing the difference of ocular axis and corneal diameter between inverted and non-inverted ciliary eyes in children with congenital glaucoma.

***Research methods***

A total of 15 patients, including five with bilateral glaucoma and ten with unilateral glaucoma, only had one eye with lower eyelid entropion associated with congenital glaucoma. Main outcome measures were the ocular axis and corneal diameter.

***Research results***

The average ocular axis of congenital glaucoma eyes with lower eyelid entropion was 24.86 ± 3.44 mm and without lower eyelid entropion was 20.79 ± 1.34 mm. The average corneal diameter of congenital glaucoma eye with lower eyelid entropion was 13.61 ± 0.88 mm and without lower eyelid entropion was 11.63 ± 0.48 mm.

***Research conclusions***

The rapid growth of ocular axis and corneal diameter may be the main cause of congenital glaucoma with acquired lower eyelid entropion.

***Research perspectives***

Children with poor control of intraocular pressure and excessive growth of the ocular axis and corneal diameter must be observed for the existence of acquired epiblepharon. This study was limited by its size. A prospective study with a large sample size and long-term follow-up is needed.

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**Footnotes**

**Institutional review board statement:** The study was reviewed and approved by the Beijing Tongren Hospital Institutional Review Board.

**Informed consent statement:** All study participants, or their legal guardian, provided informed written consent prior to study enrollment.

**Conflict-of-interest statement:** None of the authors has a financial interest in any of the products, devices, or drugs mentioned in this manuscript.

**Data sharing statement:** No additional data are available.

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**Table 1 Degree of corneal injury in congenital glaucoma with lower eyelid entropion, *n* (%)**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Corneal damage** | **Diffuse corneal epithelial damage** | **Corneal nebula** | **Corneal macula** | **Corneal leukoplakia** | **Total** |
| Number of cases | 9 (60) | 3 (20) | 2 (33.3) | 1 (6.6) | 15 (100) |

**Table 2 Comparison of ocular axis and corneal diameter of eyes in congenital glaucoma patients with and without lower eyelid entropion**

|  |  |  |  |
| --- | --- | --- | --- |
| **Variable** | **Congenital glaucoma with lower eyelid entropion patients (*n* = 15)** | **Congenital glaucoma without lower eyelid entropion patients (*n* = 15)** | ***P* value** |
| Ocular axis | 24.86 ± 3.44 mm | 20.79 ± 1.34 mm | < 0.001 |
| Corneal diameter | 13.61 ± 0.88 mm | 11.63 ± 0.48 mm | < 0.001 |