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Original Article

Causes of excessive blinking in children aged 4-12 years

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Abstract: The current study aimed to investigate causes of excessive blinking in children aged 4 to 12 years, providing evidence for clinical treatment of abnormal blinking in children. A total of 578 children complaining of excessive blinking were recruited. Moreover, a total of 370 children without excessive blinking served as controls. Results showed that children with excessive blinking might have a single etiology or multiple etiologies together. Occurrence of excessive blinking was negatively correlated with age (P<0.001) and affected by sex (P=0.008). There were significant differences in tear break-up times (P<0.001), allergic conjunctivitis (P<0.001), corneal epithelial injuries (P=0.013), diopters of children with ametropia (P=0.001), and times of video display terminal (P<0.001) between three age groups. Allergic conjunctivitis (P<0.001), positive corneal fluorescein staining (P<0.001), conjunctival lithiasis/trichiasis (P<0.001), and times of video display terminal (P<0.001) had a negative relationship with breakup times of tear film. Allergic conjunctivitis and conjunctival lithiasis/trichiasis showed positive relationships with corneal fluorescein staining (P<0.001). Times of video display terminal were positively related to diopters of myopia-related ametropia (P=0.001). All subjects had mild ametropia. In addition, there were significant differences in breakup times of tear film between children with excessive blinking and controls (P=0.047). Thus, ocular surface diseases, refractive problems, times of video exposure, and tic disorders are causes of excessive blinking. Of these factors, ocular surface diseases and times of video exposure have relationships with breakup times of tear film. Moreover, these factors may interact with each other, causing deterioration of excessive blinking.

Keywords: Child, blinking, breakup times of tear film, ocular surface disease, times of video display terminal, tic disorders

Introduction

Blinking occurrence is normally about 10-15 blinks/minute. Each blink lasts for 0.3-0.4 seconds, with an interval of 3-4 seconds between blinks. Blinking is a natural neural reflex of the eyelid. It plays an important role in adaptive human behaviors [1]. Excessive blinking is defined as a frequency of blinking higher than 15 blinks/minute [2, 3]. Excessive blinking is often accompanied by ocular symptoms (such as itchy eyes, foreign body sensation of the eyes, ocular fatigue, and photophobia) and characterized by excessive unilateral or bilateral eyelid closure and opening with or without abnormal eyeball movement. Excessive blinking is often intermittent and recurrent. It is difficult to control. In addition, it may be attenuated during gazing and disappear after blinking for several weeks or months. It may recur after disappearance [4]. Some children with excessive blinking develop other symptoms, such as crowing the eyebrows, wrinkling the forehead, and sucking the nose. Excessive blinking has become a common disease in the Department of Pediatric Ophthalmology. In some children, excessive blinking is misdiagnosed as infectious keratoconjunctivitis, causing long term use of eye drops after misdiagnosis. This may increase incidence of ocular discomforts and injuries. It may even cause side effects of some drugs [5, 6]. Some parents do not pay attention. This may contribute to deterioration of the disease and delay correct treatment. In addition, some parents become nervous about this disease and misdiagnose it as "tic disorder". Thus, some inhibitory drugs have been used for treatment of excessive blinking. These may not only cause side effects, but also bring adverse somatic and psychological effects [7]. It usually causes significant psychological burden to children and their parents. Doane and others [8, 9] aimed to identify the mechanical properties of blinking. Blinking phenomena have been exten-

sively studied in various contexts of disease, such as dry eyes and visual tasks, as well as systemic disease [10, 11]. Causes of excessive blinking are complex. They may include ocular disease, systemic disease, and psychological disease [12]. Excessive blinking has significantly affected the learning abilities of children. Despite a plethora of information concerning blinking disorders in adulthood, relatively little information exists for evaluation and management of children presenting with blinking disorders. Nonstandard diagnosis and treatments of excessive blinking also cause significant adverse effects in children and their families. Therefore, more attention should be paid to the diagnosis and treatment of children with excessive blinking. Thus, it is imperative to investigate and identify causes of excessive blinking, taking targeted treatment. This may assist in avoiding misdiagnosis and mistreatment.

The current study investigated children with excessive blinking. Possible causes of excessive blinking were explored in these children, aiming to provide evidence for clinical treatment of abnormal blinking in children.

Materials and methods

General characteristics

This study adhered to the tenets of the Declaration of Helsinki and was approved by the Institutional Review Board of Children's Hospital, Chongqing Medical University. Consent for publication was obtained from all participants.

This study was conducted on children presenting to the Ophthalmology Clinic with excessive blinking. The study was conducted between December 2016 and November 2018. A total of 578 children, including 341 boys and 237 girls, with excessive blinking ages from 4 to 12 years old, served as the observation group. In addition, 370 matched children without excessive blinking, including 220 boys and 150 girls, were randomly recruited as controls.

Inclusion criteria: (1) Children with excessive blinking as the chief complaint; (2) Informed consent was obtained from parents or guardians; (3) Children cooperated with examinations; and (4) Children did not receive prior treatment for excessive blinking.

Exclusion criteria: (1) Children did not cooperate with examinations; (2) Parents or guardians refused to participate in this study; (3) Children were allergic to fluorescein; and (4) Children received treatment for excessive blinking before the study.

Methods and data processing

The following information was collected by interviewing parents or guardians: (1) Gender, age, duration, and frequency of signs and symptoms; (2) History of allergies, including the family history of allergies and allergic diseases; (3) Concomitant focal and systemic symptoms during excessive blinking; (4) Diagnosis of tic disorders; (5) Prior diagnosis and treatment of excessive blinking and use of eye drops or antibiotics; and (6) Times of video display terminal (VDT) each day.

Slit-lamp examination: (1) Routine eye examination: Eyelids, eyelashes, conjunctiva, and cornea were examined for papilla, follicles, stones, injury, inflammation, foreign bodies, and scars; (2) Tear meniscus height (TMH): Abnormal tear secretion was defined as TMH lower than 0.3 mm; (3) Breakup times of tear film (BUT): BUT was measured thrice and the mean was calculated. Decreases in tear film stability were defined as BUT lower than 10 seconds; and (4) Corneal fluorescein staining (FLS): Positive staining suggests corneal epithelial injury [13].

Allergen examination: Skin prick tests were employed to examine common inhaled allergens. A positive reaction is defined as a light yellow rash with surrounding erythema. History of allergies, family history of allergies, eye examinations, and allergen examinations were employed for diagnosis of allergic conjunctivitis (AC) [14].

Vision examination: The International Visual Chart was used for vision examinations. When visual acuity was ≤0.6 for children aged 4 years and ≤0.8 for children aged ≥5 years, abnormal visual acuity was diagnosed [15].

Autorefractor (RK-8100; Topcon, Tokyo, Japan): This was performed three times and the mean was calculated. When vision examinations and autorefractors indicated abnormal, cycloplegic retinoscopy procedures were performed.

Table 1. Numbers of TD and AC of 3 groups in the observation group

			TD		AC	
Group	Boy	Girl	Boy	Girl	Boy	Girl
4-6 y	171	100	8	3	116 (67.84%)	48 (48.00%)
7-9 y	114	92	5	2	52 (45.61%)	34 (36.96%)
10-12 y	56	45	3	2	20 (35.71%)	13 (28.89%)
Total Number	341	237	16	7	188 (55.13%)	95 (40.08%)
Proportion	59.00%	41.00%	2.77%	1.22%	32.52%	16.43%
Total proportion	100.00%		3.99%		48.95%	

Notes: observation group: children with excessive blinking; AC: allergic conjunctivitis; TD: Tic disorder.

Cycloplegic retinoscopy: 1% Atropine sulfate eye gel was used three times a day for 3 days to the children <7 years; 1% cyclopentolate was used three times with the interval of 10 minutes for children ≥7 years. Pupillary reactions were then tested. Cycloplegia is defined as absence of pupillary light reflex. Streak retinoscope (YZ24; Six Six Vision Corp, Suzhou, China) was used for retinoscopy [16].

Hyperopia is defined as spherical degree ≥ +2.00 D. Myopia is defined as spherical degree ≤-0.50 D. Astigmatism is defined as absolute cylindrical degree ≥1.00 DC. The diopter is represented by Spherical equivalent refraction (SER). Diopters ≤-3.00 D is mild refractive error, -3.00 D~-6.00 D is moderate refractive error, and ≥-6.00 D is high refractive error. The distribution of refraction is expressed as $\bar{x} \pm s$ [17-19].

Statistical analysis

Children with excessive blinking in the observation group were divided into three age groups, including the 4-6 group, 7-9 group, and 10-12 group. Children without excessive blinking served as controls. All data were categorically recorded, listed, and subjected to statistical analysis with SPSS version 22.0. Count data are expressed as rates (%). Measurement data are described by $\bar{x} \pm s$.

Spearman's rank correlation analysis was adopted to investigate the relationships of BUT, allergic conjunctivitis, conjunctival lithiasis or trichiasis, positive FLS, times of video display terminal, diopters of ametropia, and tic disorders between the 3 age groups. Relationships between gender, allergic conjunctivitis, conjunctival lithiasis or trichiasis, positive FLS, times of video display terminal, diopters of ametropia, and tic disorders with BUT were also explored. Relationships between allergic conjunctivitis, conjunctival lithiasis/trichiasis with positive FLS, and times of video display terminal with types of ametropia were also explored. P<0.05 indicates statistical significance.

Pearson's correlation analysis included the amount of frequent blinking and ages of the children. BUT and times of video display terminal were also included, as well as times of video display terminal and diopters of ametropia. P<0.05 indicates statistical significance.

Paired-t tests were employed for comparisons of BUT between children with and without excessive blinking, as well as gender. P<0.05 indicates statistical significance.

Results

A total of 578 children with excessive blinking were enrolled as the observation group. This group included 341 boys (59.00%) and 237 girls (41.00%). The mean age was (6.99±2.26) years old (4-12 years). In addition, there were 370 children without excessive blinking serving as the control group. This group included 220 boys (59.45%) and 150 girls (40.55%). The mean age was (7.02±2.30) years old (4-12 years).

Of children with excessive blinking, allergic conjunctivitis was found in 283 children (48.95%; 188 boys and 95 girls) (**Table 1**). Allergen examinations showed that most children were allergic to dust mites (61.23%) (dermatophagoides pteronyssinus and dermatophagoides farinae). Conjunctival lithiasis/trichiasis was noted in 37 children (6.40%; 22 boys and 15 girls). Tic disorders (TD) were found in 23 children (3.99%; 16 boys and 7 girls) (**Table 1**). Positive FLS was shown in 247 children (42.73%; 143 boys and 104 girls) (**Table 2**).

Ametropia was observed in 78 children (13.49%; 45 boys and 33 girls). All cases were mild ametropia. Diopters of ametropia in the three groups were, respectively, (1.47±1.61) D,

Table 2. FLS and conjunctival lithiasis/trichiasis of 3 groups in the observation group

Group	FLS		Lithiasis/trichiasis	
	Boy	Girl	Boy	Girl
4-6 y	79 (46.20%)	52 (52.00%)	11 (6.43%)	7 (7.00%)
7-9 y	45 (39.47%)	38 (41.30%)	8 (7.01%)	5 (5.43%)
10-12 y	19 (33.92%)	14 (31.11%)	3 (5.36%)	3 (6.66%)
Total Number	143 (41.93%)	104 (43.88%)	22 (6.45%)	15 (6.32%)
Proportion	24.74%	17.99%	3.81%	2.59%
Total proportion	42.73%		6.40%	

Notes: observation group: children with excessive blinking; FLS: fluorescein staining.

Table 3. Ametropia and VDT times of 3 groups in the observation group

Group	Boy	Girl	Hypermetropic	Myopic	Diopter (D)	VDT (h/d)
4-6 y	20 (11.69%)	12 (12.00%)	26 (9.59%)	6 (2.21%)	1.47±1.61	1.27±0.55
7-9 y	9 (7.89%)	8 (8.69%)	7 (3.40%)	10 (4.85%)	-0.49±1.37	2.08±0.87
10-12 y	16 (28.57%)	13 (28.88%)	4 (3.96%)	25 (24.75%)	-1.00±1.10	2.82±0.94
Total	45 (13.19%)	33 (13.92%)	37 (6.40%)	41 (7.09%)		
Proportion	13.19%	13.92%	6.40%	7.09%		

Notes: observation group: children with excessive blinking; VDT: video display terminal.

Table 4. BUT and TMH of 2 groups in the observation group

Age	Total (n)		BUT (s)		TMH	
	Observation (n=578)	Control (n=370)	Observation (n=578)	Control (n=370)	Observation (n=578)	Control (n=370)
4-6 y	271	173	8.57±2.77	9.34±2.14	0.32±0.040	0.33±0.023
7-9 y	206	129	8.44±2.49	8.89±1.65	0.33±0.043	0.32±0.033
10-12 y	101	68	7.87±1.86	8.25±1.93	0.32±0.041	0.32±0.039

Notes: observation group: children with excessive blinking; BUT: breakup time of tear film; observation: children with frequent blinking as the observation group; control: children without frequent blinking as the control; TMH: tear meniscus height.

(-0.49±1.37) D, and (-1.00±1.10) D (**Table 3**). Times of video display terminal in the three groups were, respectively, (1.27±0.55) h/d, (2.08±0.87) h/d, and (2.82±0.94) h/d (**Table 3**).

In children with excessive blinking, BUT was, respectively, (8.57±2.77) s, (8.44±2.49) s, and (7.87±1.86) s. BUT in children without frequent blinking was, respectively, (9.34±2.14) s, (8.89±1.65) s, and (8.25±1.93) s (**Table 4**). TMH of all was higher than 0.3 mm (**Table 4**).

The course of the disease in children with frequent blinking was (1-90) days.

Children with frequent blinking may have a single cause or multiple causes (**Table 5**). In children with excessive blinking, occurrence of frequent blinking was negatively correlated with age and affected by sex (**Figure 1**). **Table 6** outlines correlation analysis statistics of different groups and correlative factors.

Discussion

Reports of excessive blinking in children are infrequent. Very little guidance exists concerning how to evaluate and manage children with excessive blinking. However, excessive blinking has become a common disease in the Department of Pediatric Ophthalmology. In this study, it was found that occurrence of excessive blinking was negatively correlated with age. Excessive blinking decreases with increases in age. This is mainly due to the blink reflex and childhood anatomy, as well as physiological characteristics. The sensor of the blinking reflex is the cornea. It is controlled by the central nervous system [20]. In children, the cere-

Table 5. Causes of excessive blinking

Causes of excessive blinking	Number	Proportion
Simple shortened BUT	121	20.93%
Shortened BUT and positive FLS	61	10.55%
AC and shortened BUT	104	17.99%
AC, shortened BUT and positive FLS	154	26.64%
AC, and ametropia	6	1.04%
AC, ametropia and shortened BUT	3	0.52%
AC, ametropia, shortened BUT and positive FLS	4	0.69%
AC and TD	2	0.35%
AC, TD and shortened BUT	3	0.52%
AC, lithiasis/trichiasis and shortened BUT	4	0.69%
AC, lithiasis/trichiasis, shortened BUT and positive FLS	3	0.52%
Lithiasis/trichiasis and shortened BUT	5	0.87%
Lithiasis/trichiasis, shortened BUT and positive FLS	25	4.33%
Ametropia	65	11.25%
TD	18	3.11%
Total number	578	100%

Note: BUT: breakup time of tear film; FLS: fluorescein staining; AC: allergic conjunctivitis; TD: Tic disorder.

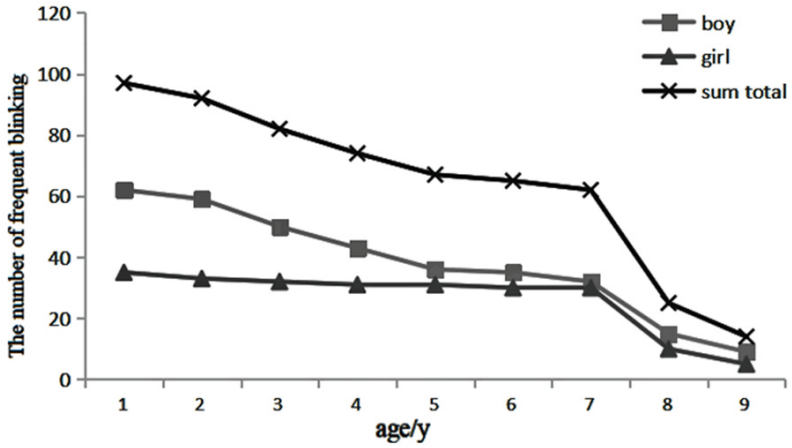

Figure 1. Number of frequent blinking increased with age and sex. Of children with excessive blinking, the occurrence of frequent blinking was negatively correlated with age (r=-0.944, p=0.000) and affected by sex (T=3.54, p=0.008).

bral cortex is immature. Thus, over-reaction to a stimulation is very common. The cornea is rich in sensory nerve endings and sensitive to stimulation. Corneal sensitivity is high in childhood, but decreases with age.

Ocular surface disease: Tear film locates on the surface of the cornea and provides a moist environment for the epithelium of cornea and conjunctiva. This may reduce friction during blinking and eyeball movement [21]. Positive FLS is negative with BUT ($p<0.05$). When BUT reduces, the friction may increase during eyeball movement. This may cause damage to the corneal epithelium. BUT in children with excessive blinking was lower than controls. However, TMH showed no significant differences between two groups. This indicates that tear secretion is normal and tear film instability is a major cause of excessive blinking. When tear stability reduces, the cornea becomes dry soon after the eyelid opens. Excessive blinking is helpful for the reconstruction of tear film. Tear instability may cause excessive blinking. Kashkouli et al. [22] and Nosch et al. [23] found that tear film stability directly affected the frequency of blinking, in accord with present findings. Thus, BUT can be used to reflect the frequency of blinking. Correlation levels of BUT with other factors should be further studied. Results showed that BUT had no relationship with gender, consistent with findings reported by Pauline et al. [24]. BUT is negatively correlated with age, consistent with findings reported by Cho et al. [25].

Allergic conjunctivitis has become a common disease and a major cause of excessive blinking in children. Incidence of infectious diseases has decreased, but incidence of allergic diseases has increased with improvements in living environments, development of health care, and increased air pollution [26]. Present results show that allergic conjunctivitis was negatively related to BUT and positively to positive FLS. When mast cells and eosinophils become activated, they release many inflammatory factors. This causes damage to corneal and conjunctival epithelial cells and goblet cells. This may result in a lack of mucus layer,

Table 6. Correlation analysis statistics

Different groups	Correlative factor	Statistical value	P
3 groups of observation	BUT	r=-0.175	P<0.001
	AC	r=-0.192	P<0.001
	FLS	r=-0.103	P=0.013
	Diopter of ametropia	r=-0.607	P=0.001
	Time of VDT	r=0.626	P<0.001
	Conjunctival lithiasis/trichiasis	P>0.05	
	TD	P>0.05	
Correlative factors of observation	AC and BUT	r=-0.814	P<0.001
	FLS and BUT	r=-0.748	P<0.001
	Conjunctival lithiasis/trichiasis and BUT	r=-0.311	P<0.001
	Time of VDT and BUT	r=-0.307	P<0.001
	AC and FLS	r=0.769	P<0.001
	Conjunctival lithiasis/trichiasis and FLS	r=0.153	P<0.001
	Time of VDT and diopter of myopia	r=-0.141	P=0.001
	Sex and BUT	P>0.05	
	TD and BUT	P>0.05	
Observation and control group	BUT	t=-4.43	P=0.047
	TMH	P>0.05	
	Age	P>0.05	
	Gender	P>0.05	

Notes: Observation: children with excessive blinking; control group: children without excessive blinking; BUT: breakup time of tear film; FLS: fluorescein staining; AC: allergic conjunctivitis; TD: Tic disorder; TMH: tear meniscus height. There were significant differences in BUT, allergic conjunctivitis, corneal epithelial injury, diopter of children with ametropia and time of VDT among the three groups, but no difference in conjunctival lithiasis/trichiasis and tic disorder. Allergic conjunctivitis, positive FLS, conjunctival lithiasis/trichiasis, and time of VDT had a negative relationship with BUT, but TD and sex had no relationship with BUT. AC and conjunctival lithiasis/trichiasis had positive relationships with FLS. Time of VDT was positively related to the diopter of myopia-related ametropia, and all were mild ametropia. In addition, there was a significant difference of BUT between children with excessive blinking and without; The indexes of TMH, age, and gender showed no significant differences between two groups. P<0.05 indicates statistical significance.

damage the corneal epithelium, and reduce tear film stability [27]. Results showed that allergic conjunctivitis had a negative relationship with age. Incidence of allergic conjunctivitis was higher in boys (32.52%) than girls (16.43%). This is consistent with Rhee's research [28]. Results may be related to the fact that boys have a matrilineal tendency and a wider range of activities. Thus, they are easily exposed to allergens [29].

Conjunctival lithiasis/trichiasis is also a cause of excessive blinking in children. Results suggest that conjunctival lithiasis/trichiasis was negatively related to BUT and positively to positive FLS. Mechanical stimulation induced by conjunctival lithiasis/trichiasis may cause damage to the ocular surface, reduce tear secretion, and damage tear stability, resulting in excessive blinking.

Ametropia: Simple ametropia was found in 65 children with excessive blinking. All cases were mild ametropia. Excessive blinking was shown to be related to refractive error. In mild ametropia, the visual organs are over-regulated for compensation, which leads to visual fatigue and frequent blinking. Coats et al. [2] speculated that ametropia without correction was a major cause of excessive blinking in children. After correction, excessive blinking was attenuated or even disappeared in about 87% of children. Abdi et al. found that correction of ametropia improved ocular symptoms in 94% of children, attenuated visual fatigue, and improved excessive blinking [30]. Thus, refractive problems are also important causes of excessive blinking in children.

Tic disorders: Tic disorders are causes of excessive blinking in children. Tic disorder refers to a

mental disease characterized by motor tics and/or phonic tics [31]. Incidence of TD in boys (2.77%) was higher than that in girls (1.22%). Kurlan et al. found that TD mainly occurred at 2-21 years. Incidence in males was higher than that in females [32], consistent with the current study. Some neuroleptics (mainly antipsychotic drugs) are effective in improving tic disorders. However, antipsychotic drugs have some side effects, including cognitive retardation, drug-induced irritability, anxiety, and depression, leading to adverse effects on the health of children [7]. Thus, treatment of tic disorders in children should be cautionary. Over-treatment should be avoided.

Times of VDT (video display terminal): Results showed that times of VDT were negatively related to BUT, but positively related to the diopter of myopia. With the development of market economy and the information era, VDT influences lives of people with its ample function. Long time use of VDT may increase exposure of palpebral fissure and promote the evaporation of tear film, which may cause dry eye and increase the frequency of blinking [33]. In addition, the characteristics of VDT may increase regulatory and convergence movements of the eyes for clear vision. This may cause eye discomfort and subsequent excessive blinking. You et al. found that myopia was related to the time interval between two rests during computer-related work [34]. Jordan et al. found that times of computer-related work in adolescences with myopia were 0.7-1.6 hours longer than in those with emmetropia [35], consistent with present findings.

Excessive blinking is also affected by sex ($p= 0.008$). It was hypothesized that this is related to causes of excessive blinking. It was found that allergic conjunctivitis (48.95%) was the cause of excessive blinking. Incidence of this disease was higher in boys than in girls.

In conclusion, correlation analysis showed that allergic conjunctivitis, corneal epithelial injury, conjunctival lithiasis/trichiasis, and times of video display terminal were related to BUT. The pathophysiology of these ocular surface diseases may affect ocular surface homeostasis and disrupt the stability of tear film, increasing the risk for excessive blinking. Causes of excessive blinking are complex in children. They may include ocular diseases, systemic diseases, and psychological diseases. There could be a single cause for excessive blinking in some children, but multiple factors are possible. Active identification of causes of excessive blinking and appropriate treatment methods are important. Clinicians should aim to avoid misdiagnosis, missed diagnosis, and over-treatment.

Disclosure of conflict of interest

None.

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