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Recent trend of increasing myopia can be traced to infancy

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ABSTRACT

In recent years, a trend has been noted for increasing numbers of myopia cases found globally, which could potentially be indicative of a bigger problem. However, the cause of this trend remains unknown and in addition, we have yet to be able to establish a reliable method for preventing the onset of myopia. Furthermore, previous myopia studies have not paid adequate attention to hyperopia. That is to say, it has been suggested that the development of refraction in infancy and the onset of myopia are distinct from emmetropization. However, myopia studies also need to focus on the development of refraction in infancy, which involves hyperopia. Based on this viewpoint, our new hypothesis is that the trend towards myopia is associated with changes during the infancy period. The supporting evidence for these changes can be found in four areas, epidemiology of hyperopia, relationship with body height, incidence of esotropia, and birth month research. If this hypothesis is true, we need to investigate why there has been a decrease in hyperopia patients rather than why there has been an increase in myopia patients.

Introduction

Myopia is a refractive error in which light from a distance cannot be focused on the retina owing to excessive extension of the axial length [1]. Recently, there has been a global trend for increases in the number of myopic patients, which could potentially be indicative of a bigger problem [2]. However, the reasons for these increases are unknown, and as of yet there has not been any reliable way established for preventing the onset of myopia.

It has been previously speculated that the onset of myopia might be associated with performing near vision tasks over a long period of time [3]. For example, highly educated people have a higher myopic prevalence rate [4], and experimental studies have shown that myopia arises in animals when they wear minus lenses that simulate near vision work [5]. Therefore, it appears logical that increases in near vision work due to the recent modernization of life have caused this increased trend of myopia. Alternatively, however, while many basketball and volleyball players are tall, this does not necessarily mean that there is a causal relationship between jumping movement and height. Moreover, it cannot be shown that the recent global trend towards taller individuals has been caused by increases in daily jumping movement. Furthermore, although an enormous number of studies have examined myopia over the years, they still have not proven there is a causal relationship between near vision work and the onset of myopia.

Another environmental factor that has been suspected as affecting myopia onset is the light environment. A previous study has shown that sunlight suppressed the progression of myopia [6], while another study found that breeding animals under various light environments could produce myopia [7]. Also, the relationship between circadian rhythm and refraction cannot be ignored [8]. In addition, there have been concerns that night light pollution due to recent urbanization might adversely affect overall health [9]. Furthermore, the possibility exists that changes in the light environment could be associated with the increasing tendency of myopia globally.

In general, infants are hyperopic at birth, and then rapidly develop towards emmetropia in infancy [10,11]. After this period of emmetropization, myopia typically develops starting when children reach school age. Inevitably, most studies on myopia have examined the actual onset and progress of myopia. This is because many researchers have imagined the following implicit refraction development model to study myopia [10].

Refraction = Early Variation + Emmetropization + Myopic Onset (Model 1; Fig. 1)

As this model indicates, myopia research is based on the idea that the onset of myopia stems from the development that occurs before emmetropization. However, by adding the concept of hyperopia and its development from a continuous perspective from infancy, this leads to a new hypothesis.

New model on refractive development

In our refractive development model, eyeball growth from 0 years of age to adulthood is modified by emmetropization. This model can be stated as follows:

Refraction = Early Variation + Growth (k) + Emmetropization (e) (Model 2; Fig. 2)

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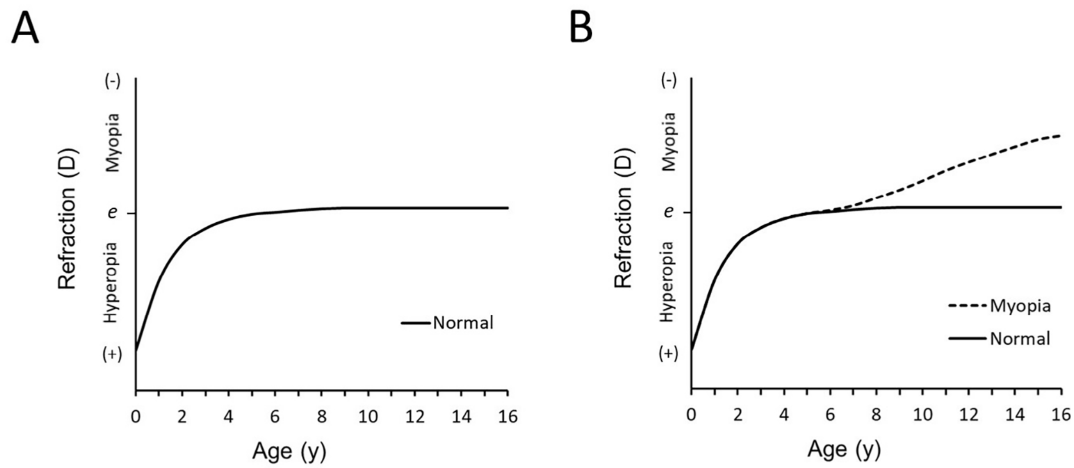

Fig. 1. Image of refractive development Model 1. This model assumes *e* is the target for emmetropization, which is approximately +0.5 D. The vertical axis shows the minus diopter on the upper side. (A) Normal refractive development. (B) Myopia deviates from (A) due to excessive near vision work.

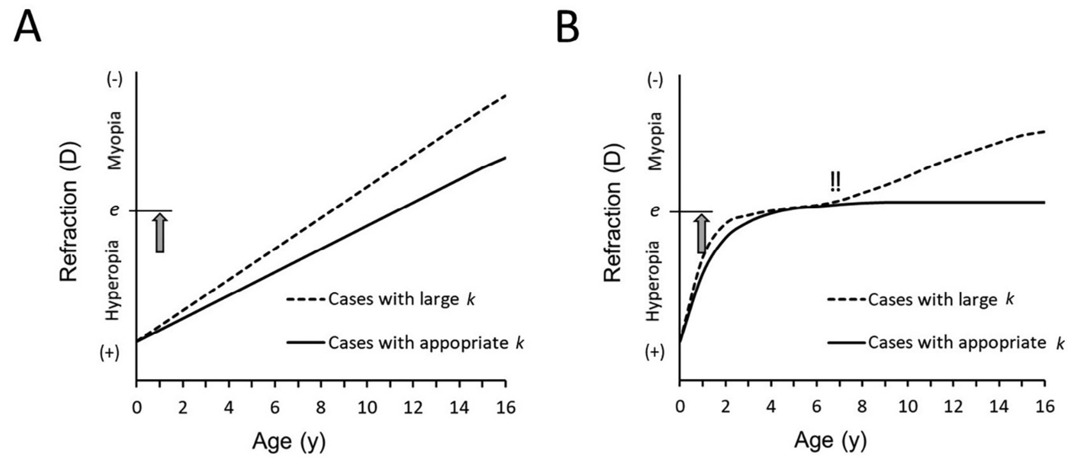

Fig. 2. Image of refractive development Model 2, which takes into consideration growth coefficient *k*. (A) Refractive development is based on the growth coefficient *k*, which is similar to the body height growth. In this case, the refraction is greatly dispersed, which is disadvantageous to survival. As a result, this suggests the development of an emmetropization mechanism towards *e*, as indicated by the arrow. (B) The observed refraction development is based on (A), which has subsequently undergone modification with emmetropization. Cases with a large *k* will develop myopia at the time point (!!) when it becomes impossible for the emmetropization mechanism to maintain *e*.

In this model, the growth term includes the growth coefficient *k*, and the emmetropization term includes the target value *e*. If we assume that the axial length that determines refraction also grows in conjunction with the height, then the growth term in Model 2 can be expressed by the Gompertz equation. Although the value of *k* is determined to some extent by a genetic factor, similar to the growth coefficient of height, it is considered not to be constant throughout life but to be variable in accordance with environmental factors that are present. However, the eyeball is a precise organ. Therefore, based on the growth term alone, ametropic changes can be a distinct disadvantage in survival competition, unless the refraction happens to be emmetropic. To overcome the survival disadvantages of these visual issues, it is thought that the process of evolution led to the development of the emmetropization mechanism. Emmetropization occurs by adjusting three elements that include refraction of the cornea, the crystalline lens, and the ocular axis. It acts like gravity by having an effect on the development of the hyperopic side with promotion of the target value *e*, while development of the myopic side requires suppression of the target value *e*. As a result, the refraction of the population becomes a high kurtosis distribution concentrated near emmetropia [10]. If the growth coefficient *k* is large and the emmetropization mechanism cannot maintain emmetropia, myopia will develop.

Model 2 can be used to easily interpret various animal studies of myopia. For example, with form deprivation myopia, the image is out of focus due to the scattering of the light. Therefore, the experiment is equivalent to deleting the intervention emmetropization term. In this case, when there is a constant environment, refraction develops the pattern seen in Fig. 2A due to only the genetic variation of *k*, and thus, the refraction should result in a normal distribution. The form deprivation method is suitable for selective breeding, as it has been shown to be able to easily cause myopia [12]. As compared to the form deprivation method, other myopia experiments that change variables in the light environment are considered to act on *k*. Since the emmetropization term is functioning in these cases, the emmetropia phase shown in Fig. 2B should be similar to that observed in the experimental results reported by Cohen et al. [7]. On the other hand, lens-induced myopia [13] can be interpreted as a replacement of the target value *e* of the emmetropization term. Normally *e* is approximately +0.5 D, but in conditions where animals wear a −5 D lens, the *e* will be set to −5 D. As the lens-induced myopia progresses, it is pulled by the attraction to the replaced target value *e*. As a result, the speed will be faster than the progression seen for the form deprivation experiment that lost attraction. Thus, the refraction will incorporate the power of the worn lens, with a resulting correlation of both values.

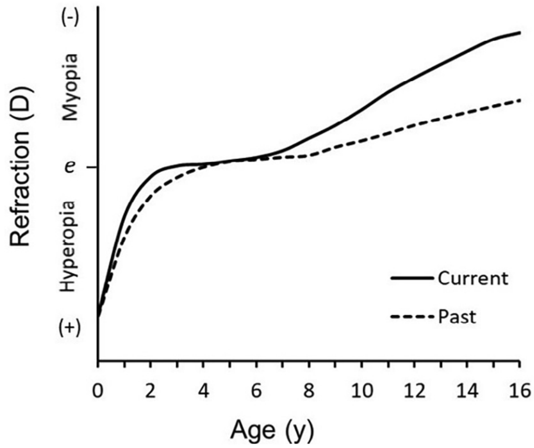

Fig. 3. Image of recent myopic trend based on the growth coefficient *k* of Model 2. The graph shows the change in the average refractive values of the population. The average *k* of the population has increased compared to the past due to changes in the light environment. In addition, there is a difference in the infantile hyperopia due to changes in the recent and past history. Moreover, the time point at which the emmetropization mechanism can no longer maintain *e* is accelerated, with the age of onset becoming younger, thereby leading to the increase in the degree of myopia.

Hsypothesis

Our new hypothesis states that the increasing tendency of myopic patients in recent years is due to the influences from the light environment, with these changes already having an effect starting from the infancy period. Thus, if these changes in the light environment are in fact the cause of this trend, then *k* is influenced not only at school age but also during the infancy period. As shown in Fig. 3, this effect should be able to be observed as a faster emmetropization. The important point that should be noted on the time axis of the refraction development that is shown in Fig. 3 is that the decrease in hyperopia is not a result of the increase in myopia. Although below we do describe the reasons for considering changes in the light environment as the cause of these increases in myopia, at the present time these factors cannot be deemed to be completely reliable. However, if more detailed epidemiological studies of hyperopia are carried out in the future, the basis of our current hypothesis should become more evident.

Supporting evidence

Epidemiology of hyperopia

Prevalence of hyperopia and prevalence of myopic patients are inversely related. For example, a report that compared urban and rural areas found that the percentage of hyperopia was as small as 7.1% in urban areas as compared to 30.8% in rural areas. In contrast, myopia was 13.9% in urban areas while it was 7.5% in rural areas [14]. Also, it is a well-known fact that as compared to Western populations, there are fewer hyperopia patients found in Asian populations, who have been shown to exhibit more myopia than Westerners. One important point that needs to be checked is whether or not the decrease in the tendency of hyperopia prevalence occurred at the same time as the recent increased tendency of myopia prevalence. Unfortunately, at the current time, epidemiological studies have yet to clarify this point [15]. The reason for this appears to be due to the fact that a reduction in the disease is less problematic than an increase, combined with that fact the decrease of hyperopic patients is considered to be a natural result of the increase of myopic patients. Thus, if the decrease of hyperopic patients is a natural result of the increase of myopic patients, the explanation for the increase in myopia should also be able to explain the decrease in hyperopia. That is, if the cause of myopia is due to near vision work, this should also lead to a reduction in the hyperopia. However, near vision work training has yet to be established or recommended as a treatment for hyperopia.

Signs that a subject will develop myopia in the future are thought to be present during the period when hyperopia is present (Fig. 2B). There have been reports that some populations with greater myopia were able to reduce hyperopia at a faster rate, for example, 10-, 20-, 30-, and 40-week-old infants in Hong Kong exhibited changes from +2.98 D, +1.97 D, +1.33 D, to +0.80 D, while in Italy the values in the same ages groups were +2.60 D, +3.00 D, +2.70 D, and +2.50 D [16]. Also, when comparing the average refractions of 6-year-old children in different countries, the refractions were, +0.96 D in Japan, +1.26 D in Australia, and +1.41 D in Northern Ireland, with the remaining hypermetric values before the development of myopia also shown to be less in the more myopic population [10]. As seen in Fig. 3, the recent refraction of infants should result in more myopia. Thus, do these results also demonstrate that there should be less hyperopia than was observed in the past? In other words, signs of myopic tendency should now be beginning to appear during infancy. Until the present, the existence of these events has rarely been investigated. When examining preschool children (average age 4.6 years) in Hong Kong, the average refraction between the 1996 group and the 2006 group exhibited a significant difference, changing from +0.92 D to +0.67 D [17]. Meanwhile, it has also been reported that the average refraction for Chinese children even now still remains at +1.44 D at the age of three and +1.33 D at the age of six [18]. Even so, comparison of these past and present reports cannot be made, as it is difficult to compare these studies due to differences in the examination methods [19–21].

Relationship with body height

Although it has been reported that refraction and height are related [22], the correlation is low [23]. The main reason for this has been considered to be due to the strong modification of emmetropization that can occur unlike that for body height. Since the axial length, which mainly determines refraction, is a physical dimension of the body, it is fully conceivable that refraction and body height might be common essential features. Body height is hereditary and correlated with the height of both parents. Moreover, people in urban areas are taller than that found in rural areas. In addition, body height has been shown to be correlated with the amount of exposure to the sun [24]. On the other hand, it is clear that refraction is also strongly hereditary, and that urban areas have higher myopic prevalence than rural areas. Furthermore, it has been reported that refraction is also related to the amount of exposure to the sun [25].

Body height at adulthood can be predicted by the amount growth that occurs up to 2 years of age [26]. In addition, the recent trend of higher heights has also been noted to appear during the growth period that occurs up to 2 years of age [27]. These features may also be applicable to the refraction and thus, perhaps future myopia can be predicted based on the development of refraction in children up to 2 years of age. Similar to the trends for higher heights, the recent myopia trend may be also be associated with changes in children up to 2 years of age. Furthermore, if the myopic tendency is associated with the height trend, environmental factors would be suspected to be altered in the light environment rather than associated with increases in the amount of near work, which is not related to height [25]. Since the amount of sunlight does not tend to fluctuate over the years, these changes are thought to be due to changes in the light at night caused by artificial lighting associated with urbanization [28].

Incidence of esotropia

Esotropia, especially the accommodative type, has links to hyperopia. In recent years, it has been suggested that the incidence of esotropia has decreased. In West Berkshire in the UK, the incidence of esotropia was reported to have decreased by 55% between 1971 and 1991 [29]. In Hong Kong, it has also been reported that the number of esotropia patients is decreasing while the number of exotropia patients is increasing. Therefore, the ratio of the number of exotropia to esotropia patients is increasing [30]. The increasing trend for this ratio has also been confirmed in the United States and Japan [31,32]. However, there have been no significant changes in the incidence when the results were limited to infantile esotropia [31,33]. Therefore, if the incidence of esotropia is decreasing, this is thought to be due to a reduction in the accommodative esotropia caused by hyperopia. The average age of onset of accommodative esotropia is 2.5 years old [34]. Even if myopia increases in school-age children, the onset of esotropia does not decrease. Thus, recent changes in the incidence of esotropia can be proof of signs of a myopic tendency beginning to appear in infancy.

Study on birth month

The purpose of studies on the relationship between birth month and disease is to investigate the influence of the environment in fetal or infantile periods by using the birth month as a proxy variable. Although many studies have been done on schizophrenia and multiple sclerosis, the relationship between refraction and the birth month has yet to be established. However, it appears that Asians born during the autumn season are more hyperopic and lesser myopic [35–37]. An inverse analysis has suggested that the relationship between the refraction of children and the birth month can be explained by a model that the deviation of day length affects the development of refraction in infancy, with a peak at 5 months of age [37]. Even in the elderly, this influence can be confirmed by the fact that the deviation of day length at around 5 months of age is an explanatory variable for the corneal curvature in a regression analysis [38]. Therefore, the influence of the natural light environment should be of concern for not only suppression of myopia in school-age children, but also on the effect it can have on the rapid infantile refractive development.

Studies on the birth month have suggested that the melatonin secretion ability of the pineal gland that occurs in infancy may be related to the onset of several diseases [39]. Myopia is one of the diseases mentioned. Vigorous secretion of melatonin requires nighttime darkness and daytime sunlight exposure. If the secretion ability during the infantile period is determined when a child is exposed to a bright environment at nighttime, the secretory ability may be lowered throughout the person's lifetime. Quinn et al. have reported that there was a difference in the incidence of myopia depending on the nighttime light environment that occurred during the first 2 years of life [40]. Although this report remains controversial, their results can be explained by assuming that there is involvement of melatonin. However, several studies have suggested that in order to elucidate the cause of myopia, it will be necessary to further investigate the relationship between melatonin and refraction [41–44].

Conclusion

Previous myopia studies have not paid adequate attention to hyperopia. Although there is tacit consent that distinguishes the development of hyperopic eyes in infancy and the onset of myopia as a boundary of emmetropia, investigations into the development of hyperopic eyes in infancy will also need to be undertaken. Our new hypothesis states that the recent increasing tendency for myopic patients is due to changes that have already occurred during the infantile period. If this hypothesis is true, we need to determine why there has been a decrease in hyperopia patients rather than focus on only why there has been an increase in myopia patients.

Declaration of Competing Interest

None.

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References

[1] Saw SM, Chua WH, Gazzard G, Koh D, Tan DT, Stone RA. Eye growth changes in myopic children in Singapore. Br J Ophthalmol. 2005;89:1489–94.
[2] Holden BA, Fricke TR, Wilson DA, et al. Global prevalence of myopia and high myopia and temporal trends from 2000 through 2050. Ophthalmology 2016;123:1036–42.
[3] Donders FC. On the anomalies of accommodation and refraction of the eye. London: The New Sydenham Society; 1864. p. 332–53.
[4] Mirshahi A, Ponto KA, Hoehn R, et al. Myopia and level of education: results from the Gutenberg Health Study. Ophthalmology 2014;121:2047–52.
[5] Schaeffel F, Glasser A, Howland HC. Accommodation, refractive error and eye growth in chickens. Vision Res 1988;28:639–57.
[6] Wu PC, Chen CT, Lin KK, et al. Myopia prevention and outdoor light intensity in a school-based cluster randomized trial. Ophthalmology 2018;125:1239–50.
[7] Cohen Y, Belkin M, Yehezkel O, Solomon AS, Polat U. Dependency between light intensity and refractive development under light-dark cycles. Exp Eye Res 2011;92:40–6.
[8] Chakraborty R, Ostrin LA, Nickla DL, Iuvone PM, Pardue MT, Stone RA. Circadian rhythms, refractive development, and myopia. Ophthalmic Physiol Opt 2018;38:217–45.
[9] Ouyang JQ, Davies S, Dominoni D. Hormonally mediated effects of artificial light at night on behavior and fitness: linking endocrine mechanisms with function. J Exp Biol 2018;221. https://doi.org/10.1242/jeb.15683.
[10] Flitcroft DI. Emmetropisation and the aetiology of refractive errors. Eye 2014;28:169–79.
[11] Mayer D, Hansen RM, Moore BD, Kim S, Fulton AB. Cycloplegic refractions in healthy children aged 1 through 48 months. Arch Ophthalmol 2001;119:1625–8.
[12] Chen YP, Hocking PM, Wang L, et al. Selective breeding for susceptibility to myopia reveals a gene-environment interaction. Invest Ophthalmol Vis Sci 2011;52:4003–11.
[13] Smith III EL, Hung LF. The role of optical defocus in regulating refractive development in infant monkeys. Vision Res 1999;39:1415–35.
[14] Czepita D, Mojsa A, Zejmo M. Prevalence of myopia and hyperopia among urban and rural schoolchildren in Poland. Ann Acad Med Stetin 2008;54:17–21.
[15] Hashemi H, Fotouhi A, Yekta A, Pakzad R, Ostadimoghaddam H, Khabazkhoob M. Global and regional estimates of prevalence of refractive errors: systematic review and meta-analysis. J Curr Ophthalmol 2017;30:3–22.
[16] Edwards MH, Lam CSY. The epidemiology of myopia in Hong Kong. Ann Acad Med Singapore 2004;33:34–8.
[17] Fan DS, Lai C, Lau HH, Cheung EY, Lam DS. Change in vision disorders among Hong Kong preschoolers in 10 years. Clin Experiment Ophthalmol 2011;39:398–403.
[18] Lan W, Zhao F, Lin L, et al. Refractive errors in 3–6 year-old Chinese children: a very low prevalence of myopia? PLoS One 2013;8:e78003https://doi.org/10.1371/journal.pone.0078003.
[19] Ingram RM, Traynar MJ, Walker C, Wilson JM. Screening for refractive errors at age 1 year: a pilot study. Br J Ophthalmol 1979;63:243–50.
[20] Mutti DO, Sinnott LT, Lynn Mitchell G, et al. Ocular component development during infancy and early childhood. Optom Vis Sci 2018;95:976–85.
[21] Yu SJ, Liu GH, Liu Y, Huang J, Han ML, Zhao BJ, et al. The evolution of refractive status in Chinese infants during the first year of life and its affected factors. Int J Ophthalmol 2017;10:1290–4.
[22] Yamashita T, Iwase A, Sakai H, Terasaki H, Sakamoto T, Araie M. Differences of body height, axial length, and refractive error at different ages in Kumejima study. Graefes Arch Clin Exp Ophthalmol 2019;257:371–8.
[23] Northstone K, Guggenheim JA, Howe LD, et al. Body stature growth trajectories during childhood and the development of myopia. Ophthalmology 2013;120:1064–73.
[24] Yokoya M, Shimizu H, Higuchi Y. Geographical distribution of adolescent body height with respect to effective day length in Japan: an ecological analysis. PLoS One 2012. https://doi.org/10.1371/journal.pone.0050994.
[25] Matsuda K, Yokoyama T. Analysis of secular trends in proportion of students with poor visual acuity and the associated factors according to government statistics [Japanese]. Nippon Ganka Gakkai Zasshi 2014;118:104–10.
[26] Garza C, Borghi E, Onyango AW, de Onis M. Parental height and child growth from birth to 2 years in the WHO Multicentre Growth Reference Study. Matern Child Nutr. 2013;9(Suppl 2):58–68.
[27] Cole TJ. Secular trends in growth. Proc Nutr Soc 2000;59:317–24.
[28] Dominoni DM, Borniger JC, Nelson RJ. Light at night, clocks and health: from

humans to wild organisms. Biol Lett 2016;12:20160015.
[29] Carney CV, Lysons DA, Tapley JV. Is the incidence of constant esotropia in childhood reducing? Eye 1995;9:40–1.
[30] Yu CBO, Fan DSP, Wong VW, Wong CY, Lam DS. Changing patterns of strabismus: a decade of experience in Hong Kong. Br J Ophthalmol 2002;86:854–6.
[31] Dabes EM, Weakley DR, Birch E. Trends in surgical correction of strabismus: a 20-year experience, 1990–2009. J AAPOS 2011;15:219–23.
[32] Matsuda K, Yokoyama T, Ra KE, Kozaki M. Long-term changes in the ratio of exotropia to esotropia patients [Japanese]. Nippon Ganka Gakkai Zasshi 2013;117:427–32.
[33] Louwagie CR, Diehl NN, Greenberg AE, Mohney BG. Is the incidence of infantile esotropia declining? Arch Ophthalmol 2009;127:200–3.
[34] Rutstein RP. Update on accommodative esotropia. Optometry 2008;79:422–31.
[35] Lee DC, Lee SY, Kim YC. An epidemiological study of the risk factors associated with myopia in young adult men in Korea. Sci Rep 2018;8:511. https://doi.org/10.1038/s41598-017-18926-2.
[36] Matsuda K, Yokoyama T, Matsuda K, Ohnaka S. Relationship between birth month and ocular refraction noted during eye disease checkups for three-and-a-half-year-old children in Japan [Japanese]. Nippon Ganka Gakkai Zasshi 2012;116:95–9.
[37] Matsuda K, Yokoyama T, Fukui M, Morita T, Kozaki M. Inverse analysis of the relationship between ocular refraction and birth month using matrix equations [Japanese]. Nippon Ganka Gakkai Zasshi 2016;120:533–9.
[38] Matsuda K, Yokoyama T, Morita T, Shiraki K. Evidence of effect of day length factor on infantile refractive development: multiple regression analysis-based examination of refractive components of cataracts [Japanese]. Nippon Ganka Gakkai Zasshi 2017;121:17–22.
[39] Matsuda K, Park K, Tatsumi H, Kitada R, Yoshiyama M. The use of electronic medical record data to analyze the association between atrial fibrillation and birth month. OJPHI 2017;9(3). https://doi.org/10.5210/ojphi.v9i3.7864.
[40] Quinn GE, Shin CH, Maguire MG, Stone RA. Myopia and ambient lighting at night. Nature 1999;399:113–4.
[41] Summers Rada JA, Wiechmann AF. Melatonin receptors in chick ocular tissues: implications for a role of melatonin in ocular growth regulation. Invest Ophthalmol Vis Sci 2006;47:25–33.
[42] Li T, Howland HC. Role of the pineal gland in ocular development of the chick in normal and constant light conditions. Invest Ophthalmol Vis Sci 2006;47:5132–6.
[43] Wiechmann AF, Summers JA. Circadian rhythms in the eye: the physiological significance of melatonin receptors in ocular tissues. Prog Retin Eye Res 2008;27:137–60.
[44] Nickla DL. Ocular diurnal rhythms and eye growth regulation:where we are 50 years after Lauber. Exp Eye Res 2013;114:25–34.