A Significant Challenge During Retinopathy of Prematurity Screening: Bell's Phenomenon

Prematüre Retinopatisi Tarama Muayenesini Zorlaştıran Bir Durum: Bell Fenomeni

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ABSTRACT Objective: To evaluate the expression of Bell's phenomenon (BP) in premature infants and to discuss the effects of BP expression on retinopathy of prematurity screening examination. **Material and Methods:** Consecutive infants admitted for retinopathy of prematurity screening examination were all recruited. The expression of BP was evaluated just after the insertion of the blepharostat and during illumination of the eye by the binocular indirect ophthalmoscopic light beam. BP was recorded as grade 0 when there is no expression, grade 1 when partial response is present (the center of pupil visible) and grade 2 when full response is present (the center of pupil is not visible). **Results:** A total of 152 infants with a mean gestational age of 31.4±2.8 weeks and a mean birth weight of 1705.0±543.3 g. were enrolled in the study. Fourty-two (30.3%) grade 0, 70 (46.0%) grade 1 and 36 (23.7%) grade 2 responses were observed just after the insertion of the blepharostat. After illumination of the eye with the indirect ophthalmoscope, 31 (20.4%) grade 0, 60 (39.5%) grade 1 and 61 (40.1%) grade 2 responses were observed. No significant association was found between the gestational age and the frequency of BP just after insertion of the blepharostat. (p=0.856) However, there was a statistically significant difference of the expression frequency of BP between different age groups during illumination with the light of binocular indirect ophthalmoscope (p=0.008). **Conclusion:** BP is commonly encountered in premature infants during retinopathy of prematurity screening examination. It should be taken into consideration during screening examination and laser treatment under topical anesthesia in order to prevent conjunctival injury and anterior segment ischemia.

Key Words: Infant, premature; retinopathy of prematurity

ÖZET Amaç: Prematüre bebeklerde Bell fenomeni (BF) görülme sıklığını ve bu durumun prematüre retinopatisi tarama muayenesi sırasında neden olabileceği sonuçları tartışmak amaçlanmıştır. **Gereç ve Yöntemler:** Prematüre retinopatisi tarama muayenesi için başvuran bebeklerde blefarosta takılmasını ve indirekt oftalmoskop ışığının göze tutulmasını takiben BF varlığı değerlendirildi. Yanıt alınamayan olgular evre 0, kısmi yanıt alınan olgular (pupil merkezi görülen) evre 1 ve tam yanıt alınan olgular (pupil merkezi görülemeyen) ise evre 2 olarak kaydedildi. **Bulgular:** Ortalama gestasyonel yaşı 31,4±2,8 hafta ve doğum ağırlığı 1705,0±543,3 g olan 152 bebek çalışma kapsamına alındı. Blefarosta takılmasını takiben 42 (%30,3) bebekte evre 0, 70 (%46,0) bebekte evre 1 ve 36 (%23,7) bebekte evre 2 yanıt izlendi. İndirekt oftalmoskop ışığı ile 31 (%20,4) bebekte evre 0, 60 (%39,5) bebekte evre 1 ve 61 (%40,1) bebekte evre 2 yanıt izlendi. Gestasyonel yaş ile blefarosta takılmasını takiben ortaya çıkan BF görülme sıklığı arasında istatistiksel olarak anlamlı bir ilişki saptanmadı (p=0,856). Ancak, indirekt oftalmoskop ışığının düşürülmesi sonrası ortaya çıkan BF ile gestasyonel yaş arasında anlamlı bir ilişki saptandı (p=0,008). **Sonuç:** Prematüre retinopatisi tarama muayenesi sırasında BF ile sıklıkla karşılaşılmaktadır. Konjonktival hasarı ve ön segment iskemisini önlemek için tarama muayenesi ve özellikle de topikal anestezi altında yapılan lazer tedavisi sırasında bu durum dikkate alınmalıdır.

Anahtar Kelimeler: Bebek, prematür; prematüre retinopatisi

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Retinopathy of prematurity (ROP) is one of the major causes of preventable childhood blindness. Since early detection and treatment of threshold and high risk prethreshold ROP have shown to significantly decrease the incidence of severe vision loss, screening of high risk premature infants is critical.[1,2] ROP screening examination should be performed following pupillary dilation by using binocular indirect ophthalmoscopy with scleral indentation.[3] This technically difficult examination method requires a specialized pediatric ophthalmologist who has sufficient knowledge and experience to enable accurate diagnosis.

Strong light stimulus from the indirect ophthalmoscope, insertion of a lid speculum, and manipulation of the globe with scleral depressor may induce stress and may lead to an attempt to close the eye for the infant.[4] Bell's phenomenon (BP), which is described as an upward deviation of the eye during attempted eyelid closure of the patient, can further make the examination more difficult. BP is thought to be less prominent in premature infants when compared to term infants because of neurological immaturity.[5]

The aim of the present study was to evaluate BP on premature infants and its relationship with the degree of the prematurity and to discuss consequences of BP during ROP screening examination.

MATERIAL AND METHODS

This prospective study was carried out between February 2013 and April 2013 in a single institution in full accord with the principles laid out in the Declaration of Helsinki, upon approval of Institutional Review Board. Consecutive infants admitted for routine ROP screening examination and who had a gestational age of less than 32 weeks or a birth weight of less than 1500 g, as well as older and heavier infants with an unstable clinical course who were believed to be at high risk for ROP by their neonatologist were recruited in the study. Verbal and written informed consent was obtained from parents. The infants with neurological disorders, intraventricular hemorrhage, periventricular leukomalacia, hydrocephalus, genetic or chromosomal disorders and those with a previous history of convulsion or labor asphyxia were all excluded. The schedule for the timing of initial screening examination was determined according to the recommendations of American Academy of Pediatrics, American Academy of Ophthalmology, and American Association for Pediatric Ophthalmology and Strabismus.[3] The rendered data included the gender, birth weight, gestational age and age at screening examination, and the degree of BP during examination.

Screening examination was performed by one of the authors (EH) and the presence and degree of BP was observed and recorded by the other (MAS). The presence of BP was evaluated after instillation of topical anesthetic proparacaine 0.5% (Alcaine®, Alcon, USA) in two steps, just after the insertion of the blepharostat (step 1) and upon illumination of the eye with the binocular indirect ophthalmoscopic light beam (step 2). The degree of BP (Bell's Phenomenon Score-BPS) was recorded as grade 0 when there is no response, grade 1 when partial response is present (the center of the pupil is visible) and grade 2 when full response is present (the center of pupil is not visible) as described elsewhere.[5,6] The blepharostat of same size and model, and the same indirect ophthalmoscope light were used for all patients (Figure 1). The data related to BP was recruited before the first ROP screening examination only from the right eye that was the first eye to be examined.

Statistical analysis was performed by using SPSS software for Windows 15.0 (Statistical Package for the Social Sciences, SPSS, Inc., Chicago, IL, USA). Median and range were given as descriptive statistics for quantitative data. Categorical data was summarized using frequency and percentages. Chi-square test and Kruskal-Wallis test were used to compare groups. Result was accepted as statistically significant when p was <0.05.

RESULTS

A total of 152 infants (85 males, 67 females) were included in the study. The gestational age ranged from 25 to 36 weeks with a mean of 31.4±2.8

weeks. The mean age during screening examination was 35.4±2.6 (31-40) weeks. Birth weight ranged from 620 to 2980 g with a mean of 1705.0±543.3 g.

Of the 152 infants, 46 (30.3%) had grade 0 response, 70 (46.0%) had grade 1 response and 36 (23.7%) had grade 2 response just after the insertion of blepharostat (step 1). After illumination of the eye with the light of indirect ophthalmoscope (step 2), 31 (20.4%) showed grade 0 response, 60 (39.5%) showed grade 1 response and 61 (40.1%) showed grade 2 response. No significant association was found between the gestational age and the frequency of BP just after insertion of the blepharostat (p=0.856) (Table 1). There was a statistically significant difference in the expression frequency of BP between different age groups upon illumination with the light of binocular indirect ophthalmoscope (p=0.08) (Table 2).

DISCUSSION

BP was first reported by Sir Charles Bell in 1823 as an upward deviation of the eye during attempted eyelid closure in a patient with a lower motor neuron defect of the seventh cranial nerve.[7] The exact mechanism of this complex phenomenon has not been clearly defined yet, but possible mechanisms related to mesencephalic reticular nucleus, and third and seventh cranial nerve nuclei have been proposed.[8,9] BP is thought as a response related to normal neurological maturation process, thus it is believed that frequency should be low in neurologically immature premature infants.[5] However, our study demonstrated that 69.7% of premature infants expressed at least a partial BP response just after insertion of the blepharostat and 79.6% after illumination of the eye with binocular indirect ophthalmoscope light during the first ROP screening examination.

Francis and Loughhead studied BP in 508 randomly selected adult patients and observed BP to be present more than 80% of healthy adults.[10] Ferrer reported a normal BP in 78% of children over 5 years of age.[11] Contrary to adults and children, Snir et al. reported a low frequency of BP in neonates with a gradual increase in the first year of the life.[5] They stated that none of the premature infants and 35.7% of the term infants exhibited BP in the first week of life. We did not evaluated BP in the first week of the life because the purpose of the present study was to evaluate the effect of BP on ROP screening examination. In the study of Snir et al.,[5] the BP increased to 29.6% at 8th week of age in premature infants and to 97.3% at 16th week of age in term infants which supports the idea that assumes BP as a consequence of longitudinal neurological maturation. BP frequency was higher in our study when compared to the study of Snir et al. This can be partly explained by the method used to evaluate BP. They used examiner's fingers to open eyelids in contrary to our study. We evaluated BP after insertion of the blepharostat and after exposure to a strong light stimulus which might be more painfull than opening the eyelids with fingers.

Lee et al. reported the frequency of BP after the blepharostat insertion and the illumination as 77% and 92% in infants with a gestational age of 32 weeks or younger, and 16% and 57% in infants with a gestational age of 42 weeks or older.[6] In conradiction with the previous reports, the frequency of BP decreased as infants become more mature in

TABLE 1: Bell's Phenomenon Scores (BPS) in different age groups during Step 1.

		BPS		
		Grade 0	Grade 1	Grade 2
Gestational age (week)	≤28 weeks	5 (16.7%)	12 (40.0%)	13 (43.3%)
	29-32 weeks	26 (44.8%)	31 (53.4%)	1 (1.7%)
	>32 weeks	15 (23.4%)	27 (42.2%)	22 (34.4)

Results are shown as number (% within age groups), p=0.856

TABLE 2: Bell's Phenomenon Scores (BPS) in different age groups during Step 2.

		BPS		
		Grade 0	Grade 1	Grade 2
Gestational age (week)	≤28 weeks	1 (3.4%)	4 (13.3%)	25 (83.3%)
	29-32 weeks	16 (27.6%)	32 (55.2%)	10 (17.2%)
	>32 weeks	14 (21.9%)	24 (37.5%)	26 (40.6%)

Results are shown as number (% within age groups), p=0.008

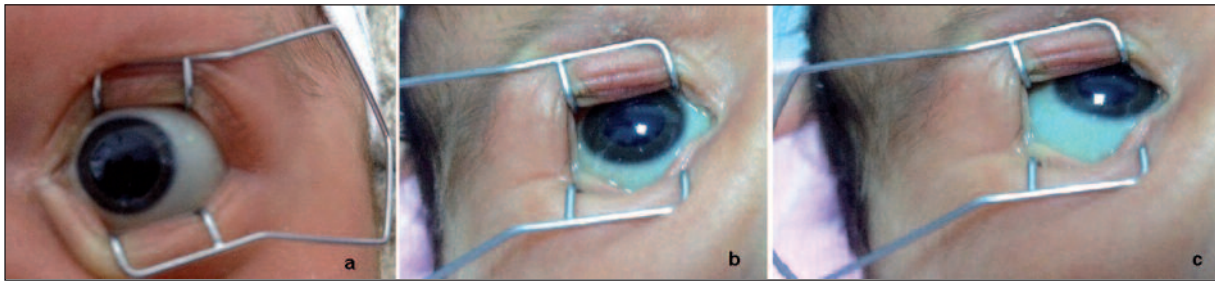

FIGURE1: Bell's Phenomenon Score a.Grade 0, b.Grade 1, c.Grade 2.
(See color figure at http://www.turkiyeklinikleri.com/journal/oftalmoloji-ozel-dergisi/1308-111X/)

their study. Our study differs from the study of Lee et al. in which the topical anesthesia is not used before assessing BP. We used topical proparacaine for anesthesia to simulate the scene of ROP screening examination. Many studies found a decreased ''Premature Infant Pain Profile'' scores after instillation of topical anesthetic proparacaine 0.5% eye drops and supported the use of it during eye examinations of premature babies, which marginally decreases pain without any adverse effects.[12] The frequency of BP was still high after instillation of topical anesthetic in the current study.

Strong light stimulus from the indirect ophthalmoscope, insertion of a lid speculum, and manipulation of the globe with scleral depressor are all painfull procedures, furthermore they have the potential to induce stress which may be the cause of systemic instability of the neonate.[13] Increased manifestation of BP due to pain can cause subconjunctival hemorrhage and conjunctival laceration especially during ROP examination of the lower quadrants. Additionally, laser treatment for ROP has been started to be practised under topical anesthesia.[14,15] Presence of BP makes it more difficult when treating the lower quadrants.[16] BP and unwanted ocular movements may increase the risk of accidental ablation of the posterior retina. Prolonged depression of the globe during laser treatment of lower quadrants may also rarely cause anterior segment ischemia.[17]

In spite of neurological immaturity, the frequency of BP was higher in premature infants with a gestational age of 28 weeks or smaller when compared to older babies in the present study. This can be partly related to a well known concept; ROP screening examination is more stressfull for extremely small premature infants. The size of blepharostat may be another factor; because blepharostat of the same size which were relatively large for extremely premature babies were used for all babies, which in turn may cause more pain.

The present study should be viewed in context of some limitations. First of all, the method used for the evaluation of BP is a subjective method which classifies the response in three grades. Secondly, there was no control group such as term babies which may limit extrapolation of the results. Thirdly, we did not observed the longitudinal course of BP with time, such as the response of same babies one month after the first examination. Despite all these limitations of the current study, there are important implications regarding the frequency of BP in premature infants in different gestational age groups. It introduces a critical knowledge regarding the possible consequences of BP during ROP screening.

CONCLUSION

BP is a frequently encountered response in premature infants during ROP screening examination in spite of neurological immaturity. Upward rotation of the globe makes the visualisation of the retina challenging. BP should be taken into consideration during screening examination and laser treatment of ROP under topical anesthesia in order to prevent conjunctival injury, accidental ablation of the posterior retina and anterior segment ischemia due to prolonged and forcefull indentation of the globe.

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