Associations between red reflex abnormality, consanguinity and intensive care hospitalization of newborns in Turkey

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Abstract

Background: Red reflex screening is the primary but unheeded test for the detection of vision- and life-threatening eye conditions.

Aims: To evaluate the red reflex of newborns, percentage of ocular diseases resulting in red reflex abnormality, and their relation with consanguinity in Southeast Turkey.

Methods: Newborns (n = 1358) were examined with pencil light and direct ophthalmoscopy.

Results: Eight hundred of these newborns were hospitalized in a rooming-in unit. The RIU and 558 were in the neonatal intensive care service (NICS). In the RIU there were 7 (0.88%) newborns with abnormal red reflex and in the NICS there were 14 (2.51%). Sensitivity of pencil light examination was 71.4%. Studies from the Middle East have shown potential recessive genetic causes of common paediatric ocular conditions. In our study, consanguineous marriage was found to have a significant association with red reflex abnormality (P = 0.017).

Conclusions: Red reflex screening test is important in the early diagnosis of vision- and life-threatening eye disorders in Southeast Turkey where consanguinity is common.

Keywords: congenital cataract, consanguinity, intensive care, newborn screening, red reflex test

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Introduction

The red reflex test was first described by Bruckner in 1962 and has proven to be effective for detecting vision- and life-threatening ocular conditions of children and adults (1). The American Academy of Pediatrics published a policy statement in 2016 and recommended red reflex screening in infants aged 0–6 months on every visit to their general practitioner (GP) and once at age 6–12 months, 1–3 years, 4–5 years and ≥ 6 years (2). This test is simple, noninvasive and can be performed quickly by GPs and paediatricians. It depends on transmission of light through the eye, and reflection of light from the ocular fundus back to the examiner’s eye. Besides the red colour, the red reflex can also be yellow, orange or any combination (3). A normal red reflex requires transparency of the tear film, cornea, aqueous humour, crystalline lens and vitreous humour. Any transmission block at any part of the optical pathway results in reflex abnormality that includes its absence, asymmetry, leukocoria, or nonhomogeneous reflex (1,4).

Consanguineous marriage is a widely preferred custom from ancient times in the Middle East, Central and Southern Asia, and Northern Africa (5). Consanguineous marriage is also common in Turkey with an overall prevalence of 21.2%; however, the rate varies significantly according to geographical regions (6). Recent studies from the Middle East have shown potential recessive genetic causes of common paediatric ocular conditions (7). Up to one third of cataracts are inherited and they may be autosomal dominant, autosomal recessive or X linked (8–10). These data highlight the additional importance of performing red reflex screening test in Turkey. Previously, only one study about red reflex screening results was reported from Turkey; however, the associations of consanguinity, hospitalization in neonatal intensive care service (NICS) and red reflex abnormality were not reported (11). Israel is the only country in the Middle East that has reported red reflex screening results, although association with consanguinity has not been reported (3). It is important to document red reflex abnormality rates and their association with risk factors in Turkey and the Middle East to attract the attention of GPs and paediatricians. Also, indicating the association of consanguinity and ocular diseases will be helpful in informing the public about risks of intermarriages.

In this study, we evaluated the red reflex of newborns hospitalized in the NICS and in the rooming-in unit (RIU) at Dicle University, Faculty of Medicine Hospital and Diyarbakir Maternity and Child Health Hospital, Turkey. We estimated the percentage of ocular disorders that could be detected by red reflex screening test and investigated a possible relation between ocular disorders and consanguinity.
Methods

In this prospective study, between June 2013 and August 2014, we examined by the red reflex screening test results of 1358 newborns hospitalized in the RIU or NICs of Dicle University, Faculty of Medicine Hospital and Diyarbakir Maternity and Child Health Hospital. The study protocol was approved by the Institutional Review Board of the hospital and the study was conducted in accordance with the principles of the Declaration of Helsinki. Informed consent was obtained from each parent.

Ophthalmological examination was performed by an ophthalmologist (ZGO and SB) and included an external examination of the globe with pencil light and visualization of the red reflex with direct ophthalmoscopy without dilating the pupils. The eyelids of the newborns were opened gently by the examiner's fingers, and an eyelid speculum was not used. The test was performed with a direct ophthalmoscope, set at 0 lens power, held close to the newborn's eye and focused on each pupil individually at ~30 cm from the eye. Lack of a red reflex or presence of a white or dim red reflex or dark spots in the red reflex was an indication for further evaluation with pupillary dilation.

We prospectively recorded data of each newborn, including sex, number of children that the parents had, and the degree of consanguinity between the parents and concomitant systemic or genetic diseases of the newborns, if they were hospitalized in the NICs.

Statistical analysis was performed with SPSS version 15 (SPSS, Chicago, IL, USA). The statistical calculations included descriptive statistics, χ² test, Fisher's exact test and independent samples t test. Data were presented as mean (standard deviation). *P* < 0.05 was considered significant.

Results

Eight hundred (58.9%) newborns were hospitalized in the RIU and 558 (41.1%) in the NICs. We found suspicious red reflex abnormality in 30 (2.2%) patients. After further evaluation with pupillary dilation, we diagnosed ocular pathology causing red reflex abnormality in 21 (1.5%) of these newborns. Therefore, the red reflex test without pupillary dilation had a positive predictive value of 70%, which is expected to be higher with clinical experience. The pathological distribution at both locations is shown in Table 1.

Red reflex abnormality was found in seven of 800 newborns in the RIU and 14 of 558 in the NICs. The abnormal red reflex rate was 0.88% in the RIU and 2.51% in the NICs and 1.55% overall. The red reflex abnormality rate was ~3-fold higher in newborns hospitalized in the NICs compared with the RIU. Sex did not have a significant effect on red reflex abnormality (*P* = 0.58). The rate of systemic anomalies in the newborns with abnormal red reflex was 33.3%.

We analysed consanguineous marriage rates of the parents of newborns in the RIU and NICs. Overall, 27.9% of the consanguineous marriages were first-cousin and 14.3% were second-cousin marriages. There were 2 newborns for whom both maternal and paternal grandmothers and grandfathers were siblings (double-first-cousin marriages). Parental consanguineous marriage rate among the newborns with confirmed abnormal red reflex was 71.4% compared with 29.4% in newborns with normal red reflex (Table 2).

Consanguineous marriage and confirmed red reflex abnormality were significantly associated (odds ratio: 6.0, 95% confidence interval: 2.31–15.59, *P* = 0.017). We also investigated the number of children that the parents had. The mean number of children in the families with parental consanguinity was 3.5 (2.1), compared with 2.9 (1.9) in the families without parental consanguinity, which was a significant difference (*P* < 0.01).

In the external examination of the globes with pencil light illumination, no pathology was observed in six of the 21 newborns with red reflex abnormality. In 15 (71.4%) of them, suspicious abnormalities could be realized with pencil light illumination. We selected six cases of congenital cataract. In the RIU, there were two (0.25%) cases of congenital cataract and four (0.71%) in the NICs, although this difference was not significant (*P* = 0.20). Among these six cases, only two were visible with pencil light illumination.

Discussion

The red reflex screening test is an essential part of paediatric examination. It can provide early diagnosis of important treatable vision- and life-threatening conditions, such as congenital cataract and retinoblastoma (12). In several developed countries, eye-screening protocols have been applied already. In Sweden, a study conducted between 2007 and 2009 reported that, at ~90% of all paediatric and neonatal units, eye-screening protocols were used and screening with red reflex examination in maternity wards increased the detection 3-fold (19 vs 64%), which emphasizes the importance of the red reflex test (13).

Congenital cataract is a potential vision-threatening disease and has been reported as a priority of the Global Vision 2020 initiative of the World Health Organization (14). It is still the most common treatable cause of visual disability in infancy and childhood, accounting for nearly 10% of childhood blindness worldwide (15,16). In 2007 and 2008 Eventov-Friedman et al. screened 11 500 newborns in the Middle East with red reflex examination and reported an incidence of congenital cataract of 4.3 per 10 000 (3). In the United States of America (USA) and Europe, based on the routine notification systems for monitoring congenital anomalies, congenital or infantile cataracts were estimated to be ~1 per 10 000 births in 1996. Also, the British Congenital Cataract Interest Group reported a cumulative incidence of congenital and infantile cataract of 2.29 per 10 000 by age 1 year in 1995–1996 (17). In other studies between 2006 and 2011, the incidence was estimated between 1 and 6 per 10 000 live births (8,9). Screening of 2718 newborns between 2007 and 2010 at a hospital in Istanbul was reported. There were two (0.07%) cases of congenital cataract; however,
it was not clear whether they included newborns in the NICS (11). In our study, in the RIU, there were two (0.25%) cases of congenital cataract and 4 (0.71%) in the NICS. According to the two previous studies from Turkey, it seems that the incidence of congenital cataracts is higher in Turkey than developed countries. The high rates of consanguineous marriages may be associated with this higher incidence. We calculated consanguinity ratios among the families of the newborns. Related spouses had 3.5 (2.1) children and unrelated spouses had 2.9 (1.9), which was a significant difference (P < 0.01). This means that pencil light screening can never replace red reflex screening test, or examinations are not sensitive enough and additional training is needed. A recent study from New Zealand in 2016 suggested that development of an online resource or practical refresher sessions would help to improve current practices (22). Educational posters sent to GPs and paediatricians also increase referrals of abnormal red reflexes to ophthalmology departments (12).

Screening with pencil light illumination can be incorrectly accepted as sufficient by GPs and paediatricians. In Denmark, a study was performed with pencil light screening of 5-week-old infants between 2008 and 2012; however, the screening did not change the age at detection compared with no screening (23). In our study, six of 21 newborns with abnormal red reflex were not detectable with pencil light illumination. Among 6 cases of congenital cataract, only 2 were visible with pencil light. GPs and paediatricians should be informed that pencil light screening can never replace red reflex examination with an ophthalmoscope.

In Asia and Northern Africa, consanguinity is a widely held custom with a rate varying between 20 and 55% (3,24). Conversely, in North America and Western Europe, the rate of first-cousin marriage is 0.5% and continues to decline (25). In Turkey, consanguinity is also common, with an overall rate of 21.2%, but the rate changes according to geographical region (26,27). In our study, the rate of parental consanguineous marriage among newborns with red reflex abnormality was 70.6%, compared with 29.4% among newborns with normal red reflex. Consanguinity increases the probability of union of two identical recessive gene mutations that are both inherited from a common ancestor (28,29). A review from the Middle East shows potential recessive genetic causes of common paediatric ocular conditions (6).

Furthermore, it is known that up to one third of cataracts are inherited (7–9). Therefore, higher rates of consanguinity make the red reflex screening test even more important in Turkey, the Middle East, Asia and Africa.

First cousins marry at younger ages and they tend to have a higher mean number of pregnancies than
Associations entre anomalies du reflet rétinien, consanguinité et hospitalisation en soins intensifs des nouveau-nés en Turquie

Résumé

Contexte : Le reflet rétinien est l'examen principal permettant de détecter les affections oculaires dangereuses pour la vue et potentiellement mortelles ; pourtant, il ne reçoit pas l'attention voulue.

Objectif : Évaluer le reflet rétinien chez les nourrissons, le pourcentage de pathologies oculaires conduisant à des anomalies du reflet rétinien et leur relation avec la consanguinité dans la région du sud-est de la Turquie.

Méthodes : Des nouveau-nés (n = 1358) ont été examinés à la lampe-stylo et par ophtalmoscopie directe.

Résultats : Parmi eux, 800 étaient hospitalisés en pouponnière et 558 se trouvaient en unité de soins intensifs néonatals. Sept (0,88 %) nouveau-nés en pouponnière avaient une anomalie du reflet rétinien contre 14 (2,51 %) à l'unité de soins intensifs néonatals. La sensibilité à l'examen par lampe-stylo était de 71,4 %. Des études issues du Moyen-Orient ont démontré l'existence potentielle de causes génétiques récessives à l'origine de pathologies oculaires pédiatriques courantes. Notre étude a révélé que le mariage consanguin était associé de façon significative à des anomalies du reflet rétinien (p = 0,017).

Conclusion : L'examen du reflet rétinien est important dans le cadre du diagnostic précoce de troubles oculaires dangereux pour la vue et potentiellement mortels dans le sud-est de la Turquie, où la consanguinité est courante.

الرابط بين المتعكس الأحمر غير الطبيعي وزواج الأقارب وإدخال حديثي الولادة في الرعاية المركزة في منطقة جنوب شرق تركيا

الخلاصة

إن التحري عن المنعكس الأحمر هو الاختبار الأولي المكشوف عن حالات بالعين قد تهدد سلامة الرؤية وتهدد الحياة، ولكنه اختبار لا يلقى الاهتمام.

هدف: تقييم المتعكس الأحمر لدى حديثي الولادة، والنسبة المئوية لأمراض العين التي تؤدي إلى المتعكس الأحمر غير الطبيعي، وعلاقة ذلك بزواج الأقارب في جنوب شرق تركيا.

البحث: حديث الولادة 1358 حديث الولادة باستخدام الضوء المكشوف من مصابي أصبغة ونتج الأنسوجة إدخال 800 حديث الولادة إلى وحدة المشاكة (إيقاف حديث الولادة مع الأم) في المستشفى 558 حديث الولادة وحدهم 78% لحيجدهم الأطفال غير طبيعي، وفي وحدة الرعاية المركزية لحديثي الولادة، وفي وحدة الخدمة كانت هناك 7 حديث الولادة (58% ) على المتعكس الأحمر غير طبيعي، وفي وحدة الرعاية المركزية لحديثي الولادة كان هناك 14 حديث الولادة (2%) كانت حساسية لحيده مصاصي الأصبغة 4/71 و 4/71. وقد أظهرت الدراسات من الشرق الأوسط الأسباب الوراثية المنحدرة حالات بالعين شائعة لدى الأطفال. وفي هذه الدراسة اقتضى وجود أعراض يُعتَدُّ بها إحصائيًا بين زواج الأقارب وويلك المتعكس الأحمر غير طبيعي وكان ( p = 0.017).

الاستنتاج: اختبار فحص المتعكس الأحمر مهم في التشخيص المكشوف لاضطرابات العين التي تهدأ البصر والحياة في جنوب شرق تركيا حيث يشيع زواج الأقارب.

unrelated spouses have (30). In our study, related spouses had a significantly higher mean number of children than unrelated spouses had, which carries an extra risk of ocular genetic diseases. Such cultural features in Turkey contribute to the added importance of the red reflex screening test.

The main limitation of our study was the small number of newborns examined for calculating the incidence of common ocular disorders resulting in red reflex abnormality. In Turkey, consanguinity rate changes widely according to geographical region, so screening newborns in only 1 region of the country limits the generalization of our results to the rest of the country.

Conclusion

In conclusion, the red reflex screening test is important in the early diagnosis of vision- and life-threatening eye disorders. Congenital cataracts and retinoblastomas are not detected by GPs and paediatricians. The high rates of consanguineous marriages and the demand of related spouses to have more offspring make this screening test even more important in Southeast Turkey. We suggest that the Ministry of Health should make red reflex screening test a legal requirement and GPs and paediatricians should be educated about its importance.

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References


