Original Article

Neonatal Screening for Leukocoria

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Purpose: To incorporate distant direct ophthalmoscopy for red reflex analysis to screen neonates for leukocoria and establish its importance.

Material and Methods: A prospective study was conducted at Department of Pediatrics, Fauji Foundation Hospital, Rawalpindi, from February 2013 to September 2013. A total of 500 random neonates (newborns less than 28 days of age) were screened for leukocoria by distant direct ophthalmoscopy at 50 cm by means of a direct ophthalmoscope in dark conditions. The red reflex was compared between the two eyes and was classified into five categories: Red, orange, yellow, suspect / faint, and absent / leukocoria. The red reflex was compared to the gestational age, birth weight, oxygen therapy, phototherapy, and blood transfusion.

Results: The results were tabulated and analyzed using SPSS version 17. The red reflex was analyzed and compared with neonatal variables (weight, gestational age, use of oxygen therapy, phototherapy and blood transfusion). The red reflex was found to be normal shades of red or orange in 495 neonates (990 eyes), with orange being predominant in 786 (78.6%) eyes, red in 204 (20.4%), yellow in 4 (0.4%), suspect / faint in 4 (0.4%), and absent / leukocoria in 2 (0.2%) eyes. Statistically significant association of the red reflex was found with oxygen therapy only (p = 0.000).

Conclusion: Neonatal screening for red reflex assessment with distant direct ophthalmoscopy is essential for the early diagnosis and prompt management of ocular diseases causing leukocoria, which will subsequently prevent irreversible blindness, which is bound to occur if the diagnosis is delayed. Hence the importance of routine neonatal screening cannot be overemphasized.

Key words: Neonatal, Red reflex analysis, Leukocoria

Leukocoria is a term used for a white pupillary reflex or an altered red reflex on distant direct ophthalmoscopy,[1] and is a grave cause of visual morbidity in children. The term derives its name from the Greek[8] words, 'leukos' meaning white, and 'kore' meaning pupil. Leukocoria implies opacification of the structures lying within the visual axis and heralds danger. It is a rare and ominous finding which signifies serious ocular disease like congenital cataract, retinoblastoma, advanced retinopathy of prematurity (ROP), persistent hyperplastic primary vitreous (PHPV), Coat's disease, uveitis etc, which threaten vision permanently and some, like retinoblastoma are life threatening.[2,3]

The assessment of the red reflex or Bruckner Test by means of the direct ophthalmoscope is a very simple, useful, quick, non-invasive, and effective tool for detecting leukocoria in neonates.[4]

Childhood blindness varies in etiology according to regional and socioeconomic differences. Regarding the developing countries; 7 – 31% of childhood blindness and visual impairment can be avoided, 3 – 28% is preventable, and around 10-58% can be treated.[5] This constitutes a tremendous public health issue in such countries[6]. Hence, the need for screening for potentially blinding ocular diseases arises with enormous magnitude, to prevent blindness. According to estimates in 2000, 1.4 million children are blind[7]

globally, and the majority belongs to developing countries. In these countries, due to illiteracy, poverty, and unawareness, there is reluctance to seek medical advice, and often delayed presentation to the ophthalmologists, with resultant advanced disease or refractory amblyopia, often with no chance of salvation of vision.

The importance of neonatal screening for leukocoria is often overlooked and is not a routine in most maternity or pediatric departments in our country. This results in delay in diagnosis and seeking of medical treatment, with subsequent disastrous consequences.

Thus we decided to undertake a study to routinely screen neonates by distant direct ophthalmoscopy in order to detect those potentially vision threatening conditions which present with leukocoria, and manage them promptly. We also embarked to observe the red reflex variations in different neonates, and whether there existed an association between the reflex and the various neonatal variables; gestational age, birth weight, oxygen therapy, phototherapy, and blood transfusion. By this study, we aim to establish the importance of screening neonates for leukocoria, which should become a routine practice in all the maternity and pediatric units of the country. This will result in early detection, prompt referral, treatment and consequently good visual development of the newborns afflicted with such disease.

MATERIAL AND METHODS

This descriptive, quantitative study was carried out by the Department of Ophthalmology with cooperation of the Department of Pediatrics, Fauji Foundation Hospital, Rawalpindi, from February to September, 2013. A total of 1000 eyes of 500 random newborns in the Nursery or Neonatal Intensive care unit, which were either delivered or admitted after birth, were examined by a single observer, to assess the colour of the reflex, homogeneity, and any abnormality (Figures 1 and 2). Distant direct ophthalmoscopy of a neonate. The Heine Beta 200 direct ophthalmoscope was used at a distance of about 50 cm in dark conditions, to evaluate the red reflex, separately, and simultaneously of the two eyes. The reflex was classified into the following: red, orange, yellow, suspect / faint, or absent / leukocoria, according to the experience of the observer. The eyes were not routinely dilated except for very small pupils, in which case, dilating drops of phenylephrine 1% and cyclopentolate 0.2% were instilled thrice before the assessment. The gestational age, gender, birth weight, oxygen therapy, phototherapy, or blood transfusion (if needed) were noted for each neonate from the hospital files, as assessed by the peadiatricians and gynaecologists, to compare with the reflex, and to note any association. All these were recorded on a data sheet. Exclusion criteria included very ill newborns and those with syndromes.

Fig. 1: Distant direct ophthalmoscopy of a neonate

Fig. 2: Red reflex assessment

The data was tabulated and analyzed in the SPSS version 17 Software. Frequencies and percentages were calculated for the red reflex shades, gestational age, gender, birth weight, and the neonatal variables (oxygen therapy, phototherapy, and blood transfusion). The Chi square test was used to analyze any association between the red reflex and the above

variables. The significance level was set at 95% for each.

RESULTS

The neonates examined included 266 males, and 234 females. The red reflex was found to be normal shades of red or orange in 990 eyes, with orange being predominant in 786 (78.6%), red in 204 (20.4%), yellow in 4 (0.4%), suspect / faint in 4 (0.4%), and absent / leukocoria in 2 (0.2%) eyes (Table 1). The yellow, suspect / faint and absent reflexes were examined in detail, in the Eye Out Patient Department. One of the yellow reflexes had a normal exam, the other was lost to follow up, one suspect / faint reflex was found to be bilateral anterior uveitis, with a normal fundus, the other died before examination, and the neonate with absent reflex had bilateral leukocoria due to congenital anterior polar and nuclear cataracts, with normal posterior segments. The child was subsequently operated within 3 weeks and fitted with aphakic spectacles promptly. The reflexes were symmetrical in hue in 312 (62.4%), and asymmetrical in 188 (37.6%) neonates. Comparison of the reflex with neonatal variables resulted in a statistically significant association of the orange hue with oxygen therapy only (p = 0.000), and no association with gestational age (p = 0.559), birth weight (p = 0.204), phototherapy (p = 0.503), or blood transfusion (p = 0.476) (Table 2).

Table 1: Red Reflex shades

Red Reflex	Frequency n (%)
Orange	786 (78.6)
Red	204 (20.4)
Yellow	4 (0.4)
Suspect / Faint	4 (0.4)
Absent / Leukocoria	2 (0.2

Table 2: Significance of Neonatal variables compared to Ref reflex

	Pearson Chi Square	Significance (2 - Sided)
Oxygen therapy	27.904	0.000
Birth Weight	14.812	0.204
Gestational age	10.656	0.559
Blood transfusion	3.515	0.476
Phototherapy	3.339	0.503

DISCUSSION

Leukocoria is generally classified[1] into pre-lenticular, lenticular, retrolenticular, and mixed presentation leukocoria. Causes of leukocoria are manifold: the most devastating being the Retinoblastoma; most commonly presenting with a white pupillary reflex, with an estimated incidence of 1 in every 15000 – 20000 live births, and a worldwide mortality of 5 – 11%.[9-12] Retinopathy of prematurity (ROP), previously termed 'retrolental fibroplasia' is one major preventable cause[13]. Another major cause is congenital cataract, which represents 10% of the global preventable visual loss, with an incidence of 1 in every 2000 live births.[14-15] Other causes of leukocoria include Persistent Hyperplastic Primary Vitreous (PHPV), Coat's disease, Toxocariasis, Retinal detachment, Chorioretinal colobomas, other retinal tumors, corneal scarring, and uveitis to name a few.[2,16]

The red reflex seen by illuminating the fundus by means of a direct ophthalmoscope is caused by light passing through the pupil onto the retina, and resultant partial reflecting back of the light from the retina, through the pupil to give a reddish – brown homogenous reflex indicating the colour of retina and choroid. The test should be performed with the ophthalmoscope at 50 cm away, with the dial preferably set at '0', in a dark room to allow mydriasis and for better contrast. In presence of normal transparent ocular media the reflex is reddish-orange. Any abnormality or opacification of the cornea, aqueous humor, lens, vitreous, or retina can result in a suspect or absent red reflex. Hence, this test is very useful and any absence of the red reflex, abnormal size, shape, position, non-homogeneity, presence of dark spots, significant asymmetry, or milky white spots, need immediate ophthalmologist referral. Variations in colour exist with race due to difference in fundus pigmentation.[17-22]

In our study, we found the red reflex to be of varying shades of red and orange predominantly, with yellow, suspect or absent reflex in only 5 neonates. We found bilateral anterior uveitis and congenital cataract in one child each. Studies carried out on red reflex screening on neonates and children are many fold.

A study[18] carried out in Brazil on 190 neonates found a suspect reflex in 3 newborns. Five infants were identified with congenital cataract on routine testing, in a study carried out in Israel in 2007-2008[19]. The sensitivity of this test in detecting ocular pathology is 82.6%, as depicted by a study from Nepal in 2012.[22]

In our study, a significant association of the red reflex was found, with oxygen therapy only. Out of the 125 neonates who received oxygen therapy after birth, predominantly orange reflex was observed in 84 (67.2%) cases, followed by red in 39 (31.2%) cases. Although, we consider red and orange reflexes to be normal, larger scale studies are needed to establish a definitive relation of oxygen therapy if any. We did not include duration of oxygen therapy in our study. A colour gradient instrument was used in a study carried out in Brazil[18] in 2011 to classify the red reflex and significant associations were found between the instrument and neonatal variables including weight, gestational age, and oxygen therapy. Here too, orange reflex was predominant in 52.6% of neonates receiving oxygen; however, no relationship was seen with duration of exposure. The importance[18-28] of red reflex screening of neonates and children has been established in various countries around the world like America, Canada, Britain, Israel, and India, to name a few. Studies carried out by Abramson[29] et al and Canzano[30] et al recommend pupillary dilatation for detection of retinoblastoma as a dilated pupil increases the sensitivity of the red reflex test. We avoided dilating all the patients, for fear of the known adverse effects of the topical agents, and only dilated those neonates with very small pupils in which the red reflex was difficult to discern. This could be a limitation of our study.

The importance of red reflex testing needs to be realized by ophthalmologists, and measures to create awareness of this noninvasive and useful test need to be undertaken in the nurseries and pediatric units of all hospitals, to train their doctors; with appropriate urgent referral to the ophthalmologist if any abnormality is detected on routine testing.

The early detection of such diseases which cause leukocoria would result in saving vision or lives of children, which would have immense long-term benefits for those unfortunately afflicted with the disease. Prevention of visual loss is also our responsibility and we should play our role as much as we can for this cause. Identification of risk factors such as low birth weight and a positive family history for certain diseases like Retinoblastoma and congenital cataract would result in meticulous screening at birth and at frequent follow ups.

Childhood blindness and visual impairment is a considerable public health issue. Prevention of visual impairment and blindness in children is an international concern of foremost priority. Screening for ocular diseases by doctors will play a key role in early detection, intervention and subsequent management.

CONCLUSION

Screening of neonates for red reflex assessment with distant direct ophthalmoscopy, for diagnosing leukocoria is an extremely easy, noninvasive and useful test for early detection and management of, vision or life threatening diseases, and needs to become a routine in all hospitals of our country. This will have a long term effect on the lives of neonates affected by ocular disease.

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