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Evaluation of the effects of phototherapy on cochlear function in newborns

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ABSTRACT

Objective: This study aimed to evaluate any potential effects of phototherapy on cochlear function in newborns using transient evoked otoacoustic emissions (TEOAEs).
Methods and materials: Fifty-seven newborns, undergoing phototherapy for hyperbilirubinemia without any other risk factors, and a control group of 53 healthy newborns, were administered the TEOAE test prior to and following phototherapy. In the newborns undergoing phototherapy, otoacoustic emission (OAE) measurements obtained at baseline and following phototherapy were compared. Moreover, pre-phototherapy OAE measurements obtained in the newborns undergoing phototherapy were compared with the OAE measurements of the control group.
Results: In newborns undergoing phototherapy, there was no significant difference between pre- and post-phototherapy TEOAE amplitudes, nor in the reproducibility ratios. Similarly, no difference was found in the pre-treatment measurements of amplitude and reproducibility ratios between phototherapy-receiving newborns and controls ($p > 0.05$).
Conclusion: The normal TEOAE results observed in the newborns undergoing phototherapy suggest that phototherapy does not exert negative effects on the cochlea.

1. Introduction

Hearing loss affects between 1 and 4 of every 1000 live births and thus represents one of the most frequently observed congenital abnormalities in humans. In infants, auditory stimulation during the first year of life is very important for the development of language and cognitive function [1]. Newborn hearing screenings allow for the diagnosis of hearing impairments as early as 3.5 months of age. In 1999, the American Academy of Pediatrics (AAP) accepted the recommendations of the Joint Committee for Infant Hearing pertaining to screening for hearing loss within the first 3 months of life and commencing rehabilitation during the first 6 months [2].

The otoacoustic emission (OAE) test, first introduced by Kemp in 1978, currently represents the most-valuable newborn hearing screening test. OAEs constitute the low amplitude sounds produced by the outer hair cells of the cochlea and can be measured by placing a microphone within the outer ear canal. The most frequently used OAEs are transient evoked otoacoustic emissions (TEOAEs) and distortion product otoacoustic emissions (DPOAEs). TEOAEs are produced by outer hair cells following application of a wideband click stimulus at a frequency of 1–4 kHz [3]. The OAE test is a fast, simple, and non-invasive means of detecting moderate hearing loss. However, the OAE test cannot detect mild hearing loss (<35 dB) or retrocochlear pathologies [4].

Jaundice is a common neonatal condition. Severe neonatal hyperbilirubinemia is considered a paediatric emergency because it can cause kernicterus, which in turn can lead to chronic handicapping conditions, including sensorineural deafness and cerebral palsy (in those who survive). There are many treatment modalities available for newborns with hyperbilirubinemia,

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including phototherapy, exchange transfusion and the administration of various therapeutic agents. Phototherapy is the most frequently used method and is generally well tolerated. However, phototherapy also produces certain side effects, such as skin lesions, dehydration, and changes in body temperature. Despite its frequent use, no previous publications have directly assessed whether phototherapy induces side effects pertaining to cochlear function.

Various phototherapy modalities are available, including conventional phototherapy and fiberoptic light and light-emitting diode (LED)-based devices. Phototherapy induces rapid oxidative reactions and intermolecular rearrangement of bilirubin, thereby producing mutant bilirubin isomers. These isomers are polarised and thus can be separated into bile and urine without conjugation. Removal of unconjugated bilirubin from the body during phototherapy occurs according to three related mechanisms: bilirubin photo-alteration, the transport of photoproducts from the skin to circulation, and the excretion of these photoproducts by the liver and kidney [5].

Several studies have addressed the side effects of phototherapy. However, it appears that no study has investigated the possible effects of phototherapy on the cochlea. Therefore, in the present study, we aimed to evaluate the functional status of the cochlea prior to and following phototherapy.

2. Materials and methods

Following approval from the ethics committee of Fırat University, the parents of all patients were informed of the study procedure and subsequently provided their consent. In 57 otherwise healthy (in terms of their postnatal ages and weights) newborns with increased bilirubin levels, TEOAE measurements were taken prior to LED phototherapy (baby-blue, LPT240-0489). Phototherapy decisions accorded with the normograms definition provided by the AAP [6]. Phototherapy continued until the total bilirubin was decreased to a suitable level with respect to the postnatal age and weight of the patient.

Fifty-three healthy newborns, with no indirect hyperbilirubinemia or any other condition or risk factor, were selected as controls. Routine TEOAE measurements were then obtained.

TEOAE measurements were performed in both ears following an ear, nose and throat examination. Newborns with acute otitis, serious otitis or abnormal middle ear structures were excluded from the study. To ensure measurement accuracy, care was taken to place the probe in the outer ear canal correctly and to minimize environmental noise. The hearing test was conducted using Labat (Italian), Echolab TEOAE equipment. TEOAEs were produced in accordance with a nonlinear stimulus method using 80-ms rectangular pulses of 1000–5000 kHz at 80 dB SPL. TEOAE test results were compared with respect to amplitude and reproducibility ratios.

Statistical analyses were performed using the SPSS for Windows software package (SPSS, Chicago, IL, USA). Pre- and post-phototherapy OAE measurements of newborns undergoing phototherapy were compared using a paired *t*-test. The pre-phototherapy OAE measurements of the phototherapy group and the OAE measurements of the control group were compared using the Student's *t*-test. A value of $p < 0.05$ was taken to indicate statistical significance.

3. Results

A total of 220 ears from 110 newborns ($n = 53$ normal newborns, 106 ears; and $n = 57$ newborns undergoing phototherapy, 114 ears) were included in the study. There were 24 (45%) females and 29 (55%) males in the control group. Newborns undergoing phototherapy comprised 25 (43%) females and 32 (57%) males. The mean gestational age of the control group was 37.2 ± 1.06 *vs.* 36.7 ± 2.02 weeks in the group undergoing phototherapy ($p > 0.05$). During testing, the mean age of the control group was 9.96 ± 3.06 *vs.* 10.78 ± 4.48 days in the phototherapy group ($p > 0.05$). There was no group difference in gender, birth weight, gestational age or postnatal age ($p > 0.05$).

In the phototherapy group, the mean serum bilirubin level was 19.98 ± 2.85 mg/dl (range: 17–27 mg/dl), with a mean phototherapy duration of 37.85 ± 15.10 h (range: 24–72 h).

The mean bilirubin levels upon cessation of phototherapy were 8.29 ± 2.46 mg/dl (range: 7–12 mg/dl). All babies were treated effectively with phototherapy, such that exchange transfusion was not required in any case. During the study period, no newborns developed acute bilirubin encephalopathy. The TEOAE results of the newborns are delineated in Tables 1 and 2. In terms of amplitude and reproducibility ratios, no difference was found in the pre-treatment measurements between the phototherapy and control group ($p > 0.05$). Similarly, pre-treatment and post-treatment amplitude and reproducibility ratios did not differ between the two groups ($p > 0.05$).

4. Discussion

Newborns with hyperbilirubinemia are sometimes characterised by disturbed auditory brainstem responses (ABR), but hyperbilirubinemia has not been shown to affect cochlear function, as measured by TEOAs. In a study by Rhee et al. [7], neonates with sensorineural hearing loss, indexed by the ABR test, exhibited normal TEOAE responses. Thus, it was suggested that impairments in hearing dysfunction caused by hyperbilirubinemia originated from the neural structure and not from a cochlear location. Chisin et al. [8] reported the presence of cochlear microphonics in 9 of 13 hyperbilirubinemic patients not responding, or responding abnormally, to ABR. In the present study, in accordance with previous literature, bilirubin levels had no negative effect on cochlea function.

Stool water loss is increased between 2- and 3-fold during phototherapy, resulting in dehydration. Studies have indicated many morphological changes, including decreased microcirculatory blood flow and increased leukocyte adhesion, during dehydration. Dehydration also precipitates decreased plasma and blood volume, increased hematocrit and plasma osmolarity, and significantly elevated red blood cell aggregation. These hemodynamic changes become more pronounced during prolonged dehydration [9–11]. Brownell et al. [12] reported that changes in osmolarity are associated with reversible changes in the dynamic and mechanical features of outer hair cells. *In vivo*

Table 1
Comparison of the study group and the controls in terms of reproducibility ratio.

	Left ears	Right ears		Left ears	Right ears
Control group	79.69 ± 3.78	81.92 ± 3.88	Pre-phototherapy	81.02 ± 4.79	82.06 ± 4.66
Pre-phototherapy	81.02 ± 4.79	82.06 ± 4.66	Post-phototherapy	79.29 ± 3.81	80.83 ± 4.55
p Value	0.121	0.873	*p* Value	0.088	0.207