Newborn hearing screening by transient evoked otoacoustic emissions: analysis of response as a function of risk factors

Screening audiologico neonatale mediante otoemissioni acustiche evocate transitorie: analisi delle risposte in funzione dei fattori di rischio

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Key words

Congenital hearing loss • Diagnosis • Neonatal screening • Otoacoustic emissions

Parole chiave

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Summary

Hearing loss can be considered as the most common birth defect. Early detection of hearing loss by screening at, or shortly after, birth and appropriate intervention are critical to speech, language and cognitive development. In the present study, the characteristics of Transient Evoked Otoacoustic Emissions have been evaluated as a function of known pre- and perinatal risk factors for hearing loss. All newborns were screened for hearing loss using a physiologic test of hearing function, the Transient Evoked Otoacoustic Emissions. A total of 532 consecutive newborn infants received binaural Transient Evoked Otoacoustic Emission testing (262 males, 270 females; mean gestational age 39.2±2.1 weeks, range 26-43; birth weight: 3,240±550 g, range 910-4,780). The population examined comprised 448 control infants and 84 high-risk for hearing loss infants (Joint Committee on Infant Hearing 1994 criteria). All Transient Evoked Otoacoustic Emission recordings were performed at comparable postconceptional ages. Audiological screening by Transient Evoked Otoacoustic Emission recording showed an overall 100% sensitivity, 99.02% specificity, with negative and positive predictive values of 100% and 62.5%, respectively. As compared to controls, high-risk infants showed: 1. increased rates of Fail-1 (Transient Evoked Otoacoustic Emissions absent at first examination, 21.4% vs 9.8%, p=0.004), Fail-2 (Transient Evoked Otoacoustic Emissions absent on retesting: 8.64% vs 1.37%, p=0.0014), false positives (Transient Evoked Otoacoustic Emissions absent/V wave present: 3.7% vs 0.46%, p=0.029) and true positives (Transient Evoked Otoacoustic Emissions absent, V wave absent: 2.47% or 24.5 per 1,000 live births vs 0.22% or 2.2 per 1,000 live births, p=0.013); 2. significantly reduced Transient Evoked Otoacoustic Emission intensity in the 0.7-1 kHz (right side) and 1-2 kHz (left side) frequency ranges. Multivariate logistic regression analysis showed a significant positive correlation between congenital hearing loss and the following risk factors: assisted ventilation lasting >10 days (Odds ratio 14.8; 95% confidence interval, 4.5-48.8, p<0.000001), severe birth asphyxia (Odds ratio 5.8; 95% confidence interval; 2.1-16.1;p=0.0006) and administration of ototoxic drugs (Odds ratio 4.5; 95% confidence interval; 1.4-13.9; p=0.009). Results of this study confirm the feasibility and accuracy of universal

Riassunto

L'ipoacusia rappresenta attualmente il più frequente difetto congenito. L'identificazione precoce del deficit uditivo consente il ricorso immediato a tecniche di abilitazione sensoriale fondamentali per la prognosi definitiva. Nel presente studio sono state esaminate le caratteristiche delle emissioni otoacustiche transitorie in una popolazione di neonati in funzione della presenza/assenza dei fattori di rischio audiologico pre- e perinatale. Le emissioni otoacustiche transitorie sono state valutate bilateralmente in 532 neonati consecutivi (M:262, F:270; età gestazionale media: 39,2±2,1 settimane, range: 26-43; peso: 3.240±550 gr, range: 910-4.780). La popolazione esaminata comprendeva 448 soggetti di controllo e 84 neonati ad elevato rischio audiologico, secondo i criteri del Joint Committee on Infant Hearing 1994. Lo screening neonatale delle ipoacusie congenite mediante emissioni otoacustiche transitorie ha presentato sensibilità 100% e specificità 99,02% con potere predittivo negativo 100% e potere predittivo positivo 62,5%. Rispetto ai soggetti di controllo, ad età postconcezionali comparabili, i neonati con almeno un fattore di rischio audiologico presentavano: 1. aumentata incidenza di Fail-1 (emissioni otoacustiche transitorie assenti al 1° test: 21,4% vs 9,8%, p=0,004), Fail-2 (emissioni otoacustiche transitorie assenti al retesting: 8,64% vs 1,37%, p=0,0014), falsi-positivi (emissioni otoacustiche transitorie assenti/onda V presente: 3,7% vs 0,46%, p=0,029) e veri positivi (emissioni otoacustiche transitorie assenti/onda V assente: 2,47% o 24,7/1.000 vs 0,22% o 2,2/1.000, p=0,013); 2. riduzione significativa dell'intensità delle emissioni otoacustiche transitorie nel range di frequenza 0.7-1 kHz a destra e 1-2 kHz a sinistra. In una regressione logistica multivariata i seguenti fattori di rischio sono risultati significativamente associati con ipoacusia: ventilazione meccanica con durata >10 giorni [Odds ratio 14,8; 95% confidence interval), 4,5-48,8, p<0,000001], ipossia neonatale grave (Odds ratio 5,8; 2,1-16,1; p=0,0006) e somministrazione di farmaci ototossici (Odds ratio 4,5; 1,4-13,9; p=0,009). Il presente studio conferma l'elevato livello di accuratezza dello screening neonatale sistematico delle ipoacusie congenite mediante analisi delle emissioni otoa-

neonatal hearing screening based on recording Transient Evoked Otoacoustic Emissions. These data stress the importance of the risk factors for hearing loss, including prolonged assisted ventilation, ototoxic drugs, and severe birth asphyxia.

custiche transitorie. I risultati sottolineano l'importanza dei fattori di rischio audiologico, in particolare ventilazione meccanica prolungata, somministrazione di farmaci ototossici e ipossia neonatale grave.

Introduction

Hearing loss is to be seen, at present, as the most common congenital defect [1]. The prevalence of medium to severe bilateral sensorineural hearing loss (≥50 dB nHL) ranges from 1.2 per 1,000 healthy newborn infants [2] to 4-5% in high-risk newborns [3]. Over 50% of congenital sensorineural hearing loss is of genetic origin [4]. Given a rate of recessive autosomal neurosensorial hearing loss of 1 per 1,000 live births [5 6], 33-50% of congenital hearing defects cannot be detected in a selective screening based exclusively on hearing risk criteria [7]. Early detection and lowering of the age at which sensorial intervention techniques are undertaken are critical for future speech, language and cognitive development. Newborn infants with congenital hearing loss should, in fact, be identified within the first 3 months of life [8], while the average age at detection is currently 24-30 months [9]. Despite international recommendations [7 9-14], universal neonatal screening for congenital hearing loss is not yet widespread. Otoacoustic emissions (OAEs) describing the response the cochlea emits in the form of acoustic energy, are determined by the contractile activity of the external ciliate cells and the mechanical and structural features of the basilar membrane and are used as objective indicators of cochlear pathology [15 16]. OAEs may be either spontaneous (SOAEs) or induced by acoustic stimulation (EOAEs) [16]. Since the analysis is reproducible, diagnostically accurate, easy to perform and minimally invasive, the use of transient evoked otoacoustic emissions (TEOAEs) is presently the method of choice for neonatal audiological screening both in the general population [1 6 17-22] and in high-risk infants [23]. Several modifications have recently been proposed to improve the quality of current TEOAE recording methods [24-26]. The use of neonatal screening via distorsion product analysis (DPOAE) [16 27] is, instead, still limited or in the preliminary stage [28-30].

In the present study, the TEOAE characteristics of a population of newborn infants have been evaluated as a function of the presence/absence of pre- and perinatal hearing risk factors.

Patients and Methods

The TEOAEs were evaluated bilaterally in 532 consecutive newborn infants (262 males, 270 females; gestational age, 39.2±2.1 weeks (mean ± SD, range 26-43; weight at birth: 3,240±550 g, range 910-4,780). The population examined comprised 448 control infants and 84 infants at high risk for hearing loss (Joint Committee on Infant Hearing 1994 criteria) [7] (newborn infant characteristics in the two subpopulations: Table I). The Joint Committee criteria include: 1. positive family history of congenital or preverbal hearing loss; 2. infectious diseases associated with neurosensorial hearing loss (mother and child): TORCH infections (toxoplasmosis, syphillis, German measles, cytomegalovirus, herpes); 3. craniofacial malformations; 4. birth weight below 1500 g; 5. hyperbilirubinaemia requiring exchange transfusion; 6. administration of ototoxic drugs (mother and child); 7. bacterial meningitis; 8. 1-min Apgar score 0-4; 5-min Apgar score 0-6; 9. assisted ventilation for 5 days; 10. persistent pulmonary hypertension; 11. signs of a syndrome comprising sensorineural hearing loss; 12. head trauma associated with unconsciousness and basal skull fracture; 13. recurrences of OMS. Of the 84 high-risk infants, 75 (89.3%) had been in Neonatal Intensive Care (NIC) and 19 (22.62%) presented more than two risk factors. None of the infants examined had congenital craniofacial abnormalities, specific malformation patterns, TORCH complex infections, bacterial meningitis, persistent pulmonary hypertension or severe hyperbilirubinaemia requiring exchange transfusion. The TEOAEs were recorded with an ILO292 DP Echoport OAE Analyzer (Otodynamics Ltd, London, UK, software vers. 5.0) and click-induced. The screening programme comprised: 1. 1st test at median postnatal age of 4 days (interquartile age: 3-5) in infants born at term or at a postconceptional age of 37-41 weeks in premature infants in NIC; 2. retesting in cases of lack of response (Fail-1) (fail criteria: TEOAE reproducibility <50% with n<3 frequencies with intensity >3 dB SPL with respect to background noise) within 15-30 days of 1st test; 3. click Auditory Brainstem Response (ABR) testing, associated with impedence and clinical ORL evaluation, within 1 month of retesting in cases of lack of TEOAEs (Fail-2) and in all the high-risk infants. Normal hearing was defined on the basis of the presence and ABR persistence of the V wave, for acoustic stimuli ≥30 dB nHL. The infants with documented hearing defects (TEOAEs absent/V wave absent on ABR) underwent further evaluation and implementation of the sensorial activation programme [31]. All the infants with TEOAEs present and those with TEOAEs absent/V wave present were further evaluated at 6-7

Table I. Characteristics of two neonatal subpopulations (low- vs high-risk, JCIH 1994 criteria)[7] that underwent hearing screening by Transient Evoked Otoacoustic Emissions (TEOAEs).

Characteristics	Low risk	High risk	p
N	448	84	
M:F	222:226	40:44	ns
Multiple pregnancy, n (%)	5 (1.1%)	14 (16.6%)	>0.001
Caesarean section, n (%)	120 (26.8%)	37 (44.0%)	0.002
Gestational age (weeks)	39.6±1.3	36.9±3.5	<0.001
Postconceptional age (weeks), 1st TEOAE	40.43±3.1	39.8±5.2	ns
Birth weight (g)	3,338±435	2,227±807	<0.001
Apgar, 1st min.	8.8±1.4	6.7±2.8	<0.001
Apgar, 5th min.	9.8±0.5	8.9±1.4	<0.001

ns: not significant.

months of age using the Health Visitor Distraction test [32].

Results

Of the 532 infants undergoing the 1st test (postconceptional ages comparable in the two subpopulations, Table I), the TEOAEs were absent (Fail-1) in 62 (11.65%). Of the 517 newborn infants (97.2% of the initial population) who completed the re-evaluation, 13 (2.51%) were still TEOAE negative (Fail-2). Two infants (0.38% or 3.8 per 1,000 live births) were detected with monolateral neurosensorial hearing loss (medium to severe) and one infant (0.19% or 1.9 in 1,000 live births) with bilateral hearing loss with a superimposed transmission component of medium severity. The three infants presenting loss of hearing, monolateral in 2 and bilateral in 1, respectively, presented risk factors number 4,6,8,9 (monolateral cases) and 4,8,9 (bilateral case). No false negatives (TEOAEs present, V wave absent) [33 34] have, as yet, been detected. Overall, neonatal screening showed a sensitivity of 100% and a specificity of 99.02%, with negative and positive predictive values, respectively, of 100% and 62.5%. Compared with the control infants at comparable postconceptional ages, the infants with at least one audiological risk factor showed: 1. increased rates of Fail-1 (TEOAEs absent on 1st test: 21.4% vs 9.8%, p=0.004), Fail-2 (TEOAEs absent on retesting: 8.64% vs 1.37%, p=0.0014), false positives (TEOAEs absent/V wave present: 3.7% vs 0.46%, p=0.029) and true positives (TEOAEs absent/V wave absent: 2.47% or 24.7 per 1,000 live births vs 0.22% or 2.2 per 1,000 live births, p=0.013); 2. significant reduction in TEOAE intensity in the 0.7-1 kHz (right) and 1-2 kHz (left) frequency ranges (Fig. 1). Multivariate logistic re-

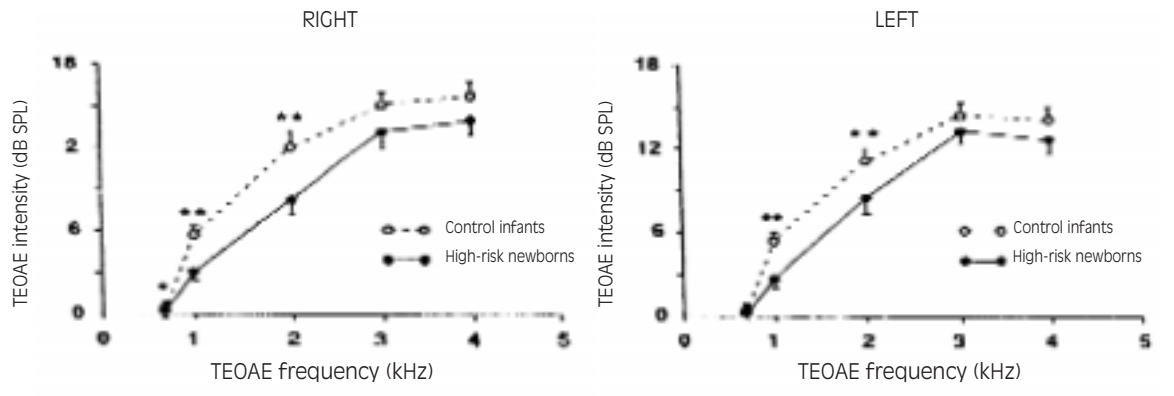

Fig. 1. Abnormal TEOAEs (Transient Evoked Otoacoustic Emissions) on 1st test in high-risk newborn infants (JCIH 1994 criteria)[7]. (Data calculated from responses of first test; dots are mean values and vertical bars represent standard median error (SME).

gression analysis showed that the following risk factors were significantly associated with loss of hearing: assisted ventilation lasting >10 days [Odds ratio (OR) 14.8; 95% confidence interval (CI), 4.5-48.8, p<0.000001], severe birth asphyxia (OR 5.8; 95% CI; 2.1-16.1; p=0.0006) and administration of ototoxic drugs (OR 4.5; 95% CI, 1.4-13.9; p=0.009).

Discussion

The present study confirms the great accuracy of neonatal screening for congenital hearing loss by means of TEOAE analysis, despite the fact that the possibility of false negatives (hearing neuropathy) [14 33] must always be considered. The low frequency of TEOAEs detectable in the high-risk subpopulation confirms data in the literature [35]. Possible explanations include cochlear immaturity in premature infants [36 37] and middle ear with effusion secondary to prolonged naso-tracheal intubation [38]. The results stress the importance of audiological risk factors, in particular of prolonged assisted ventilation, the administration of ototoxic drugs and severe birth asphyxia. The prevalence of congenital loss of hearing was 11.2 times higher in the high-risk subpopulation compared to the control group (24.7 per 1,000 live births vs 2.2 per 1,000 live births). Data in the literature have reported a prevalence of neurosensorial hearing defects from 4.4-7.1 up to 50 times greater in premature infants in NIC [32 39]. The high rate of sensorineural hearing damage in these risk categories has been attributed to a combination of 1. cochlear immaturity [36 37], 2. hypoxia-acidosis [40], 3. prolonged exposure to acoustic trauma [41] and 4. ototoxic drugs [42]. Results of the study further demonstrate, in the recordable responses of the high-risk population, a reduced range of TEOAE response. It is unknown whether the abnormalities indicated, hypothetically connected with damage to the cochlear site (0.7/1.0-2 kHz), are caused by a temporary or permanent lesion. Overall, the data confirm the feasibility of universal screening for congenital hearing loss ≥30 dB nHL and demonstrate the importance of the data that may be obtained via TEOAEs in high-risk infants.

References

1 Sorenson P. *Universal hearing screening in the NICU: the Loma Linda University Children's Hospital experience*. Neonatal Netw 1998;17:43-8.

2 Davis A, Wood S. *The epidemiology of childhood hearing impairment: factors relevant to planning of services*. Br J Audiol 1992;26:77-90.

3 Hall JW. *Handbook of auditory evoked responses*. III. Needman Heights, MA: Allyn & Bacon; 1992.

4 Dallapiccola B, Mingarelli R, Gennarelli M, Novelli G. *Aspetti genetici della sordità*. Acta Otorhinolaryngol Ital 1996;16:79-90.

5 Mehl AL, Thomson V. *Newborn hearing screening: the great omission*. Pediatrics 1998;101:1:E4.

6 Bantock HM, Croxson S. *Universal hearing screening using transient otoacoustic emissions in a community health clinic*. Arch Dis Child 1998;78:249-52.

7 Joint Committee on Infant Hearing. *Joint Committee on Infant Hearing 1994 position statement*. ASHA 1994;36:38-41.

8 National Institutes of Health. Early identification of hearing impairment in infants and young Children. *Consensus Development Conference on Early Identification of hear Loss in Infants and Young Children*. Bethesda, MD. NIH Consensus Statement 1993:11:1-24.

9 Mauk GW, Behrens TR. *Historical, political, and technological context associated with early identification of hearing loss*. Semin Hearing 1993;14:1-17.

10 Stevens JC, Hall DMB, Davis A, Davies CM, Dixon S. *The costs of early screening in England and Wales*. Arch Dis Child 1998;78:14-9.

11 Bamford J, Davis A, Stevens J. *Screening for congenital hearing impairment: time for a change*. Arch Dis Child 1998;79:F73-6.

12 Finitzo T, Albright K, O'Neal J. *The newborn with hearing loss: detection in the nursery*. Pediatrics 1998;102:1452-60.

13 Lutman ME, Grandori F. *Screening for neonatal hearing defects. European consensus statement*. Eur J Pediatr 1999;158:95-6.

14 Stein LK. *Factors influencing the efficacy of universal newborn hearing screening*. In: *Hearing loss in children*. Pediatr Clin North Am 1999;46:95-105.

15 Kemp DT. *Stimulated acoustic emissions from within the human auditory system*. J Acoust Soc Am 1978;64:1386-91.

16 Probst R, Lonsbury-Martin BL, Martin GK. *A review of otoacoustic emissions*. J Acoust Soc Am 1991;89:2027-67.

17 White KR, Behrens TR. *The Rhode Island hearing assessment project: implications for universal newborn hearing screening*. Semin Hear 1993;14:1-119.

18 Bonfils P, François M, Aidan D, Avan P, Parat S, Boissinot C, et al. *La surdité en période néonatale: les bases du dépistage*. Arch Pédiatr 1995;2:685-91.

19 Huynh MT, Pollack RA, Cunningham RA. *Universal newborn hearing screening – feasibility in a community hospital*. J Fam Pract 1996;42:487-90.

20 Salamy A, Eldredge L, Sweetow R. *Transient evoked otoacoustic emissions: feasibility in the nursery*. Ear Hear 1996;17:42-8.

21 Luppari R, Arslan E. *Screening neonatale: fattori di rischio e risultati su 4400 bambini*. Acta Otorhinolaryngol Ital 1996;16:501-7.

22 Pelosi G, Hatzopoulos S, Chierici R, Vigi V, Martini A. *Valutazione di un protocollo TEOAE lineare nello screening audiologico neonatale: studio di fattibilità*. Acta Othorhinolaryngol Ital 1998;18:213-7.

[23] Gill AW, Gosling D, Kelly C, Walker P, Wooderson S. *Predischarge screening in very low birth weight infants by click evoked ototacoustic emissions*. J Paediatr Child Health 1998;34:456-9.

[24] Rasmussen AN, Osterhammel PA, Johannesen PT, Borgkvist B. *Neonatal hearing screening using otoacoustic emissions elicited by maximum length sequences*. Br J Audiol 1998;32:355-66.

[25] Vinck BM, Van Cauwenberge PB, Corthals P, De Vel E. *Multi-variant analysis of otoacoustic emissions and estimation of hearing thresholds: transient evoked otoacoustic emissions*. Audiology 1998;37:315-34.

[26] Hatzopoulos S, Petruccelli J, Pelosi G, Martini A. *A TEOAE screening protocol based on linear click stimuli: performance and scoring criteria*. Acta Otolaryngol (Stock) 1999;119:135-9.

[27] Kakigi A, Hirakawa H, Hare N, Mount RJ, Harrison RV. *Comparison of distortion - product and transient evoked otoacoustic emissions with ABR threshold shift in chinchillas with ototoxic damage*. Auris Nasus Larynx 1998;25:223-32.

[28] Ochi A, Yasuhara A, Kobayashi Y. *Comparison of distortion product otoacoustic emissions with auditory brainstem response for clinical use in neonatal intensive care unit*. Electroencephalogr Clin Neuropathol 1998;108:577-83.

[29] Luppari R, Orzan E, Arslan E. *L'impiego delle DPOAE negli screenings neonatali*. Acta Otorhinolaryngol Ital 1999;19:57-63.

[30] Rhodes MC, Margolis RH, Hirsch JE, Napp AP. *Hearing screening in the newborn intensive care nursery: comparison of methods*. Otolaryngol Head Neck Surg 1999;120:799-808.

[31] Joint Committee of ASHA and Council on Education of the Deaf. *Service provision under the Individual with Disabilities Education Act - Part H, as amended (IDEA - part H) for children who are deaf and hard of hearing aged birth to 36 months*. ASHA 1994;36:117-21.

[32] Davis A, Bamford JM, Wilson I, Ramkalawan T, Forshaw M, Wright S. *A critical review of the role of neonatal screening in the detection of congenital screening impairment*. Health Technol Assess 1997;1:1-176.

[33] Starr A, Picton TW, Sininger Y, Hood LJ, Berlin CI. *Auditory neuropathy*. Brain 1996;119:741-53.

[34] Psarommatis IM, Tsakanikos MD, Kontorgianni AD, Ntouniadakis DE, Apostolopoulos NK. *Profound hearing loss and presence of click-evoked otoacoustic emissions in the neonate: a report of two cases*. Int J Pediatr Otorhinolaryngol 1997;39:237-43.

[35] Brienesse P, Maertzdorf WJ, Anteunis LJC, Manni JJ, Blanco CE. *Click-evoked otoacoustic emission measurement in preterm infants*. Eur J Pediatr 1998;157:999-1003.

[36] Bredberg G. *The human cochlea during development and ageing*. J Lar Otol 1967;81:739-58.

[37] Brienesse P, Anteunis LJC, Wit HP, Gavilanes AWD, Maertzdorf WJ. *Otoacoustic emissions in preterm infants: indications for cochlear maturation?* Audiology 1996;35:296-306.

[38] Sutton GJ, Gleadle P, Rowe SJ. *Tympanometry and otoacoustic emissions in a cohort of special care neonates*. Br J Audiol 1996;30:9-17.

[39] Eavey RD, Bertero MDC, Thornton AR, Herrmann BS, Joseph JM, Gliklich RE, et al. *Failure to clinically predict NICU hearing loss*. Clin Pediatr 1995;34:138-45.

[40] Eichwald J, Mahoney T. *Apgar scores in the identification of sensorincural hearing loss*. J Am Acad Audiol 1993;4:133-8.

[41] Magnavita V, Arslan E, Benini F. *Esposizione a rumore nelle Terapie Neonatali Intensive*. Acta Otorhinolaryngol Ital 1994;14:489-501.

[42] Hotz MA, Harris FP, Probst R. *Otoacoustic emissions: an approach for monitoring aminoglycoside-induced ototoxicity*. Laryngoscope 1994;104:1130-4.

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