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آموزش مهارت های کاربردی در تدوین و چاپ مقاله
Hearing Impairment in Congenitally Hypothyroid Patients

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Abstract

Objective: Thyroid hormone is necessary for normal development of the auditory system. The aim of this study was to investigate the rate of hearing impairment in congenitally hypothyroid (CH) patients, and its relation with factors such as CH severity and age at starting treatment, during CH screening program in Isfahan.

Methods: Hearing acuity was assessed in two groups of children with (94 patients aged 4 months – 3 years) and without CH (450), between 2000-2006. Otoacoustic emission (OAE) was performed by a two step method. After two tests without OAE signals bilaterally, they were referred for auditory brainstem response (ABR) test. Subjects with both OAE and ABR abnormal test results were considered to have hearing problem. Obtained data was compared in case and control group and also CH patients with and without hearing impairment.

Findings: Three (3.2%) of patients and 1 of control group (0.2%) were diagnosed with sensorineural hearing loss. The rate of hearing loss was not different significantly in two studied groups (P>0.05). There was no difference between age of starting treatment and first T4 and TSH level in CH patients with and without hearing loss (P>0.05). CH neonates with hearing impairment had thyroid dyshormonogenesis according to the follow up results.

Conclusion: The rate of hearing loss was low among our studied CH patients. It may be due to proper management of CH patients. In view of the fact that all CH neonates were dyshormonogenic and considering the relation between certain gene mutations and hearing impairment in CH patients, further studies with larger sample size, with regard to different etiologies of CH should be investigated to indicate the possible gene mutations related to hearing loss in CH.

Introduction

Thyroid hormone is necessary for normal development of the auditory system [1-3] and the association between thyroid hormone and hearing development has long been recognized in patients with congenital hypothyroidism (CH), endemic cretinism and thyroid hormone resistance [4-6]. Recent genetic studies confirmed the relation between thyroid hormone and hearing system development [7,8]. So, CH, the most common endocrine disorder with an incidence rate of 1/4000-5000 live births also increase the risk of hearing impairment in children [9].
Although mental outcome of CH patients is improved if patients are treated early in infancy, during CH screening, but subtle neurological deficits such as fine motor coordination, attention deficient, speech delay, hearing impairment, and hearing problems may develop [10-12]. Many studies, both in animal models and human patients have identified auditory system dysfunction among cases with thyroid disorders [13-15]. The rate of hearing loss has been reported to be 20-36% in CH patients before Iranian national CH screening program, and reported hearing loss was bilateral and severe [16]. On the other hand, recent reports held after CH screening programs, indicate that mild hearing loss occurs in up to 20% of CH patients [17,18].

Hearing loss, specially its mild form in children may result in delayed speech and difficulties in comprehension and problems in receptive language, auditory processing and reading, which may persist, especially in those with delayed treatment [19,20]. Therefore, considering the consequences of CH and its related hearing loss and also the fact that CH was more prevalent in our community [21,22], the aim of this study was to investigate the rate of hearing impairment in CH patients, and its relation with factors such as CH severity and age at starting treatment. This was conducted during CH screening program in Isfahan.

Subjects and Methods

Hearing acuity was assessed in two groups of children with and without CH. Hearing profiles of CH patients, consisting of both transient and permanent CH patients, were studied in 94 patients aged >4 months, between 2000-2006 and diagnosed primarily during CH screening program in Isfahan [21]. The cases were all treated with thyroxin and followed up regularly at endocrine clinic of Isfahan Endocrine and Metabolism Research Center. Hearing profile of control group was studied in 450 non-CH neonates, from Sepahan hospital.

All clinical, biochemical (including TSH and T4 levels), dose of levothyroxine, and age at which treatment began, were recorded. Subjects with history of familial congenital hearing loss, VLBW (<1500), hyperbilirubinemia, craniofacial abnormalities, history of bacterial meningitis, history of neonatal mechanical ventilation, otitis media and head trauma were excluded from the study. Hearing acuity tests were performed after informed consent was obtained from the parents of both case and control groups. Hearing examination was conducted by trained audiologist. In case group (4 months – 3 years) otoacoustic emission (OAE) was performed by a two step method using Madsen-Capella (Denmark) device. After two tests without OAE signals bilaterally, the patients were referred for auditory brainstem response (ABR) test using Amplaid-MK22 (Italy) device.

In control group, hearing screening of newborns was performed before discharging from hospital on the second day in nursery by the same methods. Subjects with both OAE and ABR abnormal test results were considered to have hearing problem.

Obtained data in case and control group and in CH patients with and without hearing impairment are analyzed using SPSS version 13 software and by univariate and t-test. P-value <0.05 was considered statistically significant.

Findings

In this study 94 CH patients aged 4 months - 3 years (mean 19.5±7.2 months) were studied. Mean T4 and TSH level in the first estimation was 6.3±3.85 μg/dL and 117.1±91.5 MIU/L respectively. Three (3.2%) cases were diagnosed as sensorineural hearing loss. In control group 450 healthy neonates with mean age 2.3±1.1 days were screened for hearing loss and one (0.2%) had sensorineural hearing loss. Mean value of T4 and TSH in the first estimation was 10.52±2.5 μg/dL and 3.12±2.94 mIU/L, respectively.

The rate of hearing loss was not different significantly in the two studied groups, using univariate test (3.2% vs. 0.2%, P>0.05). Characteristics of CH patients with and without hearing impairment are presented in Table 1.

During follow up, it had been determined that the etiology of CH among those who had
sensorineural hearing loss was dyshormogenesis.

**Discussion**

The findings of our study indicate that 3.2% of studied CH patients diagnosed in newborn screening and treated early and followed up regularly had sensorineural hearing loss, whereas 0.2% of healthy neonates had this problem. The difference was not significant.

The prevalence of hearing loss in control group was similar to that reported by other studies for the general population [23-25], but the prevalence of hearing loss among CH patients was lower than in many other studies in this field [11,26,27], though there were also studies with lower [28] or similar prevalence [28]. Chou et al in Taiwan, during 1996-98, have reported that 25% of CH patients aged 3-5 years, who received early treatment, had hearing impairment diagnosed by auditory brainstem evoked potentials [26]. Rovet et al in their study in Canada have indicated that hearing impairment was presented in up to 20% of children with CH diagnosed by newborn screening and treated early [27].

Vanderschueren-Lodeweyckx et al have found that in 45 children with sporadic CH with adequate long-term treatment, 9 (20%) had sensorineural hearing loss, particularly in higher frequencies [11]. On the other hand, Francois et al in France have reported that none of their 49 CH patients had a sensorineural hearing loss that required prosthesis [28], and similar to our study, according to the results of Bellman et al, 5% of their CH patients with early treatment had hearing problem [29].

Parazzini and colleagues indicated that there was not any significant difference in the prevalence of hearing impairment among untreated CH patients within the first month after birth and control group [30]. The differences between mentioned studies may be due to different hearing acuity screening tests, age of hearing examination or genetic factors.

All CH patients with hearing impairment had sensorineural hearing loss, which support the previous reports regarding the histological findings in congenital hypothyroid animals. According to these reports, immature development of the organ of Corti including hair cells and tectorial membrane was observed among cases with hypothyroidism [13]. Our studied population consists of CH patients younger than 3 years old, so they are younger than most studied patients in mentioned studies (3-16 years old). Moreover, we studied all CH patients preliminary diagnosed and treated during CH screening program. They consisted of both transient and permanent CH patients, as permanency of hypothyroidism can be determined after 3 years follow up [31]. The lower rate of hearing loss in our study could be explained by proper management of CH regarding the mean age in which treatment began or administration of appropriate levothyroxine dosage [31]. However, it seems that for more accurate conclusion this study should be continued with longer sample size.

There are different reports about hearing impairment and time of starting treatment. In some studies, there was association between hearing loss and delay in initiating therapy [27], whereas in others, there was no relation found between mentioned factors [28,32]. Wasniewska and colleagues have reported that sensorineural
hearing loss may be found in CH patients when the substitutive treatment starts many years after its presentation [33].

In current study, there was no difference between age of starting treatment in CH patients with and without hearing loss. Our results were in agreement with those of De Laca et al [32] and Francois et al [28], but Rovet et al have reported that hearing impaired children, differed from children with normal hearing in age of treatment onset (22 vs. 14 days) [27].

Our findings indicate that there was no difference between mean screening T4 and TSH level and hearing impairment, which is in accordance with the results of Rovet et al [27]. In their study, TSH level at diagnosis was not different in CH patients.

CH neonates with hearing impairment had thyroid dyshormonogenesis according to follow up results, which was in line with the results of Crifo et al. They indicated that dyshormonogenesis was associated with a higher risk of hearing loss among CH patients [16].

Unlike Crifo et al Vanderschueren-Ladeweyckx found hearing loss in some patients with an ectopic thyroid gland, too [11]. However, recent studies reported the relation between hearing impairment and certain gene mutations such as TP0 and DUOX2 among CH patients [34,35]. So, regarding the fact that the most common etiology of CH in Isfahan was dyshormonogenesis [36], it seems that further studies in this field including genetic studies should be done.

Considering that there were only 3 CH patients with hearing loss, our results would be more conclusive with larger sample size.

**Conclusion**

In spite of lower rate of hearing loss among our studied CH patients, regarding the importance of early treatment of hearing loss in order to prevent speech and language development problems, it seems that physicians should look for hearing loss in any patient with CH and in addition, further studies with larger sample size, with regard to different etiologies of CH should be investigated to indicate the possible gene mutations related to hearing loss in CH.

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**Conflict of Interest:** None

**References**

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