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Review Article

Hearing loss in type 1 diabetes: Are we facing another microvascular disease? A meta-analysis

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ABSTRACT

Objective: Evidence shows type 1 diabetes(T1D) leads to vascular damage and neuropathy. The purpose of this study was to perform a systematic review and a meta-analysis to assess the evidence of the effects of T1D on hearing function.

Methods: Three electronic databases were used. The articles were independently reviewed by two authors using predefined inclusion criteria to identify eligible studies. They were then classified as high or low methodological quality. Meta-analysis was performed on pooled data of hearing loss(HL) prevalence, pure tone audiometry (PTA), otoacoustic emissions(OAE) and auditory brainstem response(ABR).

Results: Twenty-one articles fulfilled the inclusion criteria. In all studies, HL was defined as pure tone greater than 20 dB in at least one frequency. The prevalence of HL ranged between 5.17% and 48% for diabetics, which was higher than in controls which ranged between 0% à 40% (OR = 7.7, 95% CI 3.32–17.98, $p < 0.05$ and $I^2 = 40\%$). The tendency of mean thresholds of PTA was higher in diabetics than in controls, with results being statistically significant at 250, 500 and 1000 Hz. OAE were significantly lower in diabetic patients. ABR latencies were longer in T1D group compared to controls and were statistical significant.

Conclusions: Patients with T1D have a significantly greater prevalence of HL compared to the control group. These damages could be compared to other microvascular diseases. Further studies are needed to assess whether hearing testing should be considered as a part of the screening process in T1D patients and therefore, secondary preventive treatment may be warranted as well.

1. Introduction

Diabetes mellitus is characterized by a metabolic disorder in which there is a state of hyperglycemia in the organism. While type 2 diabetes is a result of insulin resistance, type 1 diabetes (T1D) is mainly due to a lack of insulin caused by the destruction of beta cells in the pancreas by an autoimmune process [1]. The late vascular complications found in type 2 diabetes are due to long standing hyperglycemia. Since this pathology is more frequent in adults the hearing loss seen in these patients may be partially caused by normal aging. This latter factor is probably absent or minimal in young patients with T1D. Thus, the complications seen in children and young adults with diabetes otherwise healthy could reflect purely the consequences of a hyperglycemic state in the hearing organ.

T1D is one of the most common autoimmune disorders found amongst children and adolescent [2]. In 2015, over a half of million children were diagnosed with T1D and the rate of incidence among patients under the age of 14 is estimated to increase by 3% annually worldwide with North America being the most affected area [3]' [4].

It is well established that T1D differs from type 2 in its etiology, pathogenesis, clinical features, and predisposition to complications T1D manifests at earlier ages than type 2 DM and therefore its complications tend to present at young adulthood. Furthermore, statistics in 2010 stated that 85% of the type 1 diabetics were adults. Eventually, an endocrinologist or a primary care physician will investigate these patients for subclinical microvascular complications. Therefore, improvement in health care practices leading to early detection is needed for these patients.

The chronic state of hyperglycemia commonly leads to microvascular damage as demonstrated by clinical and animal research proving its deleterious effects on retinal and renal tissues [5–8]. Furthermore, some studies suggest that it can cause damages to the capillaries of the stria vascularis within the Organ of Corti. This damage is extensive to neurons of the cochlea [9–11].

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Hence, clinical studies have tried to find out a link between diabetes mellitus and hearing loss (HL). In a recent review, Horikawa et al. showed an association between diabetes (type 1 and type 2 combined), and hearing loss [12]. Another latest review on type 2 diabetics by Akinpelu et al. demonstrated a higher incidence of hearing loss in type 2 diabetic patients when compared with controls subjects [13]. While performing this research, another group published a meta-analysis that found an association between TD1 and hearing loss [14]. Besides the lack of analysis in OAE and the absence of sensitivity analysis according to methodological quality, the authors did not make a link between their findings and their potential practice change implications. Our recent meta-analyse will hence cover these discrepancies.

Currently, the International Guidelines for Pediatric and Adolescent Diabetes recommend starting screening type 1 diabetics for retinopathy and nephropathy at the age of 11 years old and/or after 5 years of diagnosis [15]. Nevertheless, there is no consensus of opinion on an initial screening age for hearing loss.

The objective of this study is to perform a systematic review and meta-analysis to assess the relation between T1D and hearing loss. We compared the prevalence of HL and thresholds between type 1 diabetics and control subjects evaluated by pure tone audiometry (PTA), auditory brainstem-evoked responses (ABR) or otoacoustic emissions (OAE).

2. Methodology

2.1. Search strategy

Articles published until 28th March 2017 were identified through a comprehensive search of the following electronic databases: PubMed, Ovid Embase and EBM Reviews. A search of the reference lists from relevant studies was also performed. The search strategy included medical subject headings, subheadings, and text words such as: “Type 1 Diabetes Mellitus,” “IDDM OR Type 1 Diabetes OR IDDM OR DM type 1” “Hearing,” “auditory system”, “hearing loss”, “hearing disorder”, “deaf”, “hypoacusis.” Since Wolfram syndrome is known to present with sensorineural hearing loss and insulin-dependent diabetes, the terms “wolfram” and “wolfram syndrome” were used as exclusion criteria in our search strategy. Search words and keywords used in the search strategies are shown in Table 1.

2.2. Inclusion and exclusion criteria

For our initial screening, studies describing hearing assessment in type 1 diabetic patients using either PTA, OAE or ABR were included.

Table 1
Search terms and keywords used in the search strategy.

Pubmed
(((Diabet*[tiab] OR IDDM[tiab] OR T1DM[tiab] OR T1D[tiab] OR Diabet*[ot] OR IDDM[ot] OR T1DM[ot] OR T1D[ot] OR ″Diabetes Mellitus, Type 1"[Mesh:NoExp]) NOT (wolfram*[tiab] OR wolfram*[ot] OR Wolfram Syndrome [mh])) AND (Hearing loss[mh] OR Hearing loss[tiab] OR Hearing Impairment*[tiab] OR hearing disorder*[tiab] OR Hypoacus*[tiab] OR Deaf*[tiab] OR Hearing loss[ot] OR Hearing Impairment*[ot] OR Deaf*[ot] OR hearing disorder*[ot] OR Hypoacus*[ot]))
Embase
1 insulin dependent diabetes mellitus/or (diabet* OR IDDM OR T1DM OR T1D).tw,kw
2 exp hearing impairment/or (Hearing loss OR Hearing Impairment* OR hearing disorder* OR Hypoacus* OR Deaf*).tw,kw
3 wolfram syndrome/or wolfram*.tw,kw
4 (1 and 2) not 3
EBM Reviews
1 Diabetes Mellitus, Type 1/or (diabet* OR IDDM OR T1DM OR T1D).ti,ab
2 - exp hearing loss/or (Hearing loss OR Hearing Impairment* OR hearing disorder* OR Hypoacus* OR Deaf*).ti,ab
3 wolfram syndrome/or wolfram*.ti,ab
4 (1 and 2) not 3

Only controlled studies were eligible. Letters, commentaries, conference abstracts, surveys and case reports were not eligible for evaluation. Studies evaluating veterans and/or presbycusis as well as syndromes presenting with both hearing loss and insulin-dependent diabetes (such as Wolfram's syndrome) were excluded. Articles involving patients below the age of 14 were excluded. The reason is that the average age of T1D diagnosis peaks around the age of 6 years [16,17] and it takes a minimum of 7.8 years to measure a deleterious effect on the hearing system in type 2 diabetes [13]. Moreover, it was decided to exclude articles before 1977, which was the year that Wolfram Syndrome was extensively reviewed. Studies in language other than English, French and Spanish were excluded.

2.3. Study selection

The first two authors (MMM and NP) preset the criteria for study eligibility and independently screened the titles and abstracts retrieved by the electronic search as performed by a librarian. A first-stage list of relevant articles was generated by a joint-review between authors.

For second-stage review, full texts were independently reviewed to justify inclusion or exclusion to generate a second and final list. Studies were then excluded if the type of DM was not defined or when the diagnosis was based on patient self-report. Also, studies were excluded if there was no control group. If data was repeated in two articles, only one article fitting the criteria of this review was included. Articles not available through the National Institutes of Health-National Library of Medicine and North American university libraries were also excluded. At last, articles whose data was not precisely reported were excluded (i.e. no standard deviation available or graphical information available only).

2.4. Quality assessment

Eligible articles were rated independently for quality assessment using the modified Downs and Black scale with a maximum of 21 points [18]. Articles with a score of less than 14, those with no age-sex matched controls or with no information concerning the exclusion of risk factors (chronic noise exposure, iatrogenic ototoxicity, previous ear surgery/trauma and conductive hearing loss) of hearing loss were considered as low quality studies. Scores were compared using the Pearson correlation coefficient to determine the inter-rater reliability. Correlation coefficient greater than 0.8 was considered acceptable for a significance level of $p < 0.05$.

2.5. Hearing assessment among studies

Audiogram is performed and PTA represents thresholds at frequencies of 250–8000 Hz, which are the normal range of frequencies of hearing that are tested usually for the human being [19]. The normal hearing threshold is considered less than 21 dB in all frequencies as established by Jerger and Jerger in 1980 [20].

The otoacoustic emissions (OAE) detect the pressure variations in the cochlear fluids after an acoustic stimulus is sent to the inner ear through a probe placed in the external auditory canal and reflected by the hair cells of the inner ear [19]. These emissions can be evaluated by transient evoked (TEOAE) or distortion product otoacoustic emissions (DPOAE) giving a result of ¨Pass or Fail¨ according to the intensity of the reflection received by the probe at different frequencies. The former uses a wide band stimulus at one intensity. The latter uses two continuous sounds of near frequencies and at different intensities [21]. While the results of these tools are taken over a mean of frequencies in clinical settings, some studies report their results for each frequency giving further insight on which part of the cochlea could be involved.

Finally, ABR measures the electrical response to sounds, when the latter is converted in electrical impulses from the eighth cranial nerve through the brainstem, which are represented as waves I to V in a