

Original Article

Effects of Glycemic Control on Hearing Outcomes in Diabetes Patients With Idiopathic Sudden Sensorineural Hearing Loss

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OBJECTIVE: This study aimed to analyze the effects of glycemic control on the hearing outcomes of type 2 diabetes patients with idiopathic sudden sensorineural hearing loss (ISSHL).

METHODS: Type 2 diabetes patients with ISSHL were enrolled. All patients were admitted for 5 days and received systemic corticosteroid treatment. Patients were divided into groups according to their degree of glycemic control pre- (glycosylated hemoglobin) and post- (mean blood glucose) onset of ISSHL. Demographic, audiometric, and hearing outcome data were analyzed. Furthermore, a multivariate analysis was performed to determine the prognostic factors affecting the hearing outcomes in these patients.

RESULTS: One hundred forty-four patients were enrolled. The hearing recovery rates were as follows: complete recovery, 19%; partial recovery, 15%; slight improvement, 22%; and no improvement, 44%. Initial hearing levels and diabetes duration were significantly higher in the pre-onset poor-controlled group (glycosylated hemoglobin $\geq 7.0\%$) than those in the well-controlled group. The hearing recovery rates did not differ significantly pre- or post-onset. In a multivariate analysis, duration from hearing loss onset to treatment, presence of vertigo, and initial hearing level were negative prognostic factors that affected hearing recovery.

CONCLUSION: The degree of pre- or post-onset glycemic control did not affect hearing outcomes in patients with ISSHL and type 2 diabetes. Therefore, the administration of systemic corticosteroid is required for diabetes patients with ISSHL within allowable blood glucose levels.

KEYWORDS: Sudden sensorineural hearing loss, diabetes mellitus, glycemic control, hearing outcomes, prognostic factor

INTRODUCTION

Sudden sensorineural hearing loss is clinically characterized by the rapid onset of unilateral sensorineural hearing loss and is generally defined as hearing loss of 30 dB or more over at least 3 contiguous audiometric frequencies occurring within 72 h.¹ Sudden sensorineural hearing loss may be caused by viral infections, vascular compromise, autoimmune processes, acoustic trauma, labyrinthine membrane ruptures, or cerebellopontine angle tumors.¹⁻³ Even during the adequate evaluation, 85-90% of patients do not present a clearly identifiable cause and are thus diagnosed with idiopathic sudden sensorineural hearing loss (ISSHL).^{4,5} The incidence of ISSHL is estimated to be 5-20 per 100 000 persons per year.⁶

Type 2 diabetes (T2D), is the most common type of diabetes, accounting for 90-95% of all diabetic cases and has shown an increase in incidence rates during recent decades.^{7,8} Microangiopathy is a common complication of diabetes,⁹ and vascular compromise in the inner ear is considered to be one of the possible causes of ISSHL.¹⁰ Therefore, some studies reported a more severe hearing loss with poor hearing outcomes in patients with ISSHL and diabetes.^{1,11,12} However, other studies reported no significant difference in hearing outcomes between patients with diabetes and those without.^{13,14}

The standard treatment for ISSHL is the administration of systemic corticosteroids.⁶ However, systemic corticosteroid administration in patients with diabetes leads to steroid-induced hyperglycemia, which is known to cause various complications and has negative effects on hearing recovery.^{15,16} Therefore, treatment of ISSHL in patients with diabetes is a challenging task for otologists and endocrinologists. We hypothesized that glycemic control may affect hearing outcomes and that there are certain

prognostic factors associated with diabetes. There have been few studies on the association between ISSHL and diabetes. Therefore, in this study, we analyzed the effects of glycemic control and prognostic factors affecting hearing outcomes in patients with ISSHL and T2D.

MATERIALS AND METHODS

Patients

We retrospectively reviewed the medical records of 929 patients with sudden sensorineural hearing loss who had been admitted to the tertiary-level referral hospital between January 2008 and January 2018. Demographic, audiometric, and hearing recovery data were extracted.

The inclusion criteria were as follows: (1) sudden unilateral sensorineural hearing loss of 30 dB or more over at least 3 contiguous audiometric frequencies occurring within 72 h; (2) normal physical examination; (3) follow-up in at least 4 weeks with hearing, evaluation, and adequate data; and (4) age over 20 years. We excluded patients with Meniere's disease, cerebellopontine angle tumors, acoustic trauma, perilymphatic fistula, and other neurologic disorders. Therefore, 739 patients were diagnosed with ISSHL. To standardize the results among the 739 patients, only patients with T2D who received systemic corticosteroid treatment were included. Thus, a final total of 144 patients were enrolled.

T2D was diagnosed by a physician and by an endocrinologist before and after admission, respectively. Data on duration from ISSHL onset to treatment, hearing level of the unaffected ear, presence of systemic disease (hypertension, chronic kidney disease), diabetes duration, glycosylated hemoglobin (HbA1c), fasting blood glucose (FBG), postprandial blood glucose (PBG), and mean blood glucose (MBG) were analyzed.

Grouping

The patients were grouped based on their HbA1c levels to determine the degree of glycemic control pre-onset of ISSHL. The HbA1c reference value was set to 7.0% as per the HbA1c target goal of the 2020 guideline from the American Diabetes Association.¹⁷ Patients with less than 7.0% HbA1c were grouped into the well-controlled

group, whereas those with more than 7.0% were grouped into the poor-controlled group.

To determine the degree of glycemic control post-onset of ISSHL, patients were grouped based on their MBG concentration. The MBG reference value was set to 200 mg/dL, which in the literature generally indicates hyperglycemia.¹⁸ Patients with an MBG concentration lower than 200 mg/dL were grouped into the well-controlled group, and those with an MBG concentration higher than 200 mg/dL were grouped into the poor-controlled group.

Treatment

All patients were admitted for 5 days and received systemic corticosteroid treatment. Oral methylprednisolone was administered in doses of 64 mg/day for 5 days and tapered for another 7 days. After admission, all patients were consulted at the department of endocrinology for strict glycemic control. As per the instruction of the endocrinologist, the oral hypoglycemic agent was discontinued, and instead, insulin was administered through multiple injections daily. During hospitalization, all patients were educated on diabetes management to control blood glucose levels after discharge and instructed to perform self-monitoring of blood glucose (SMBG) and to report the results to the physician. The MBG concentration was calculated by reflecting on the FBG and PBG results during hospitalization and the SMBG results of the patients after discharge.

Hearing Assessment

All patients underwent pure tone audiometry that averaged 250, 500, 1000, 2000, 4000, and 8000 Hz. The degree of hearing recovery at the 4-week follow-up was categorized according to Siegel's criteria as follows: complete recovery (CR; final hearing better than 25 dB), partial recovery (PR; more than 15 dB hearing gain and final hearing between 25 and 45 dB), slight improvement (SI; more than 15 dB hearing gain with final hearing between 45 and 75 dB), and no improvement (NI; less than 15 dB hearing gain and final hearing less than 75 dB).¹⁹ In this study, hearing recovery rates were determined by the sum of CR and PR rates.

Statistical Analyses

After examining variance equivalence and normal distribution, a paired t-test was applied to assess the continuous variables, whereas a chi-squared test was used to assess the categorical variables. For the multivariate analysis, logistic regression analysis was performed. All statistical processing was performed using the Statistical Package for the Social Sciences version 22.0 for Windows (International Business Machines, Armonk, NY). A *P* value < .05 was considered statistically significant.

RESULTS

Demographics and Hearing Outcomes

One hundred forty-four patients (81 male and 63 female) with a mean age of 60.8 ± 11.0 years were enrolled in this study. The initial mean hearing level of the affected ear was 80.8 ± 25.9 dB, and the final mean hearing level of the affected ear was 56.3 ± 29.7 dB. The mean hearing gain was 24.6 ± 21.2 dB. The hearing outcomes of the patients according to Siegel's criteria were 27 (18.7%) with

MAIN POINTS

- The treatment of idiopathic sudden sensorineural hearing loss (ISSHL) in patients with diabetes is a challenging task due to steroid-induced hyperglycemia.
- There have been few studies on the association between ISSHL and diabetes.
- The degree of pre-onset glycemic control seems to affect the severity of ISSHL.
- The degree of pre- and post-onset glycemic control did not affect hearing outcomes of type 2 diabetes patients with ISSHL.
- It is considered that the administration of systemic corticosteroid is required for diabetes patients with ISSHL within allowable blood glucose levels.

Table 1. Demographics and Hearing Outcomes of Type 2 Diabetes Patients With Idiopathic Sudden Sensorineural Hearing Loss (n = 144)

Parameters	T2D (n = 144)
Demographics	
Age (years)	60.8 ± 11.0
Sex (male:female)	81:63
Initial hearing level of affected ear (dB)	80.8 ± 25.9
Final hearing level of affected ear (dB)	56.3 ± 29.7
Hearing gain of affected ear (dB)	24.6 ± 21.2
Hearing outcomes	
Complete recovery (n)	27 (18.7)
Partial recovery (n)	21 (14.6)
Slight improvement (n)	32 (22.2)
No improvement (n)	64 (44.4)
Recovery in this study (CR+PR) (n)	48 (33.3)

Data are means ± S.D., or subject number (percent).

Recovery means complete recovery + partial recovery according to Siegel's criteria.
T2D, type 2 diabetes.

CR, 21 (14.6%) with PR, 32 (22.2%) with SI, and 64 (44.4%) with NI. The recovery rate (CR + PR) of the T2D patients with ISSHL was 33.3% (Table 1).

Hearing Outcomes According to the Pre-onset Glycemic Control State

Of the 144 patients, 72 were assigned in the well-controlled group (HbA1c < 7.0%), and 72 were assigned in the poor-controlled group (HbA1c ≥ 7.0%). In the degree comparison of pre-onset glycemic

control, the initial hearing level of the affected ear (76.5 ± 26.5 dB vs. 85.1 ± 24.7 dB) and diabetes duration (6.6 ± 5.8 years vs. 11.1 ± 7.1 years) were significantly higher in the poor-controlled group than those in the well-controlled group. However, the hearing recovery rate (CR + PR) showed no statistical significance between the 2 groups (Table 2).

Hearing Outcomes According to the Post-onset Glycemic Control State

Of the 144 patients, 76 were assigned to the well-controlled group (MBG < 200 mg/dL), and 68 were assigned to the poor-controlled group (MBG ≥ 200 mg/dL). In the degree comparison of post-onset glycemic control, all variables except blood glucose levels were not significantly different for the 2 groups. The hearing recovery rate was not statistically significant (Table 3).

Prognostic Factors

In the multivariate analysis, the duration from ISSHL onset to treatment, the presence of vertigo, and the initial hearing level were all negative prognostic factors affecting the hearing recovery of T2D patients with ISSHL (Table 4). Age, sex, side of the affected ear, hearing level of unaffected ear, hypertension, chronic kidney disease, FBG, PBG, HbA1c, and diabetes duration were not significant.

DISCUSSION

Hyperglycemia caused by systemic corticosteroid administration in patients with diabetes is a challenging complication for physicians. To the best of our knowledge, the association between glycemic control and hearing recovery in diabetes patients with ISSHL has not been studied. This study is the first to demonstrate how the degree of glycemic control pre- and post-ISSHL onset may affect hearing

Table 2. Comparison of the Demographic and Audiologic Data According to the Pre-onset Glycemic Control State: Well-Controlled and Poor-Controlled Groups Among the Type 2 Diabetes Patients With Idiopathic Sudden Sensorineural Hearing Loss

Parameter	Well-Controlled (HbA1C < 7.0 %) (n = 72)	Poor-Controlled (HbA1C ≥ 7.0 %) (n = 72)	P
Age (years)	61.6 ± 10.5	60.0 ± 11.5	.374
Gender (male:female)	45:27	36:36	.131
Affected ear (right:left)	34:38	36:36	.739
Duration from onset to treatment (days)	4.2 ± 4.0	4.4 ± 4.6	.819
Initial hearing level of affected ear (dB)	76.5 ± 26.5	85.1 ± 24.7	.046*
Final hearing level of affected ear (dB)	53.7 ± 30.3	59.0 ± 29.1	.274
Hearing gain of affected ear (dB)	23.0 ± 23.2	26.1 ± 19.0	.371
Hearing level of unaffected ear (dB)	30.6 ± 25.6	29.2 ± 18.8	.705
Vertigo (n)	26 (36.1)	30 (41.7)	.494
Hypertension (n)	49 (68.1)	40 (55.6)	.123
Chronic kidney disease (n)	8 (11.1)	8 (11.1)	1.000
Diabetes status			
Diabetes duration (years)	6.6 ± 5.8	11.1 ± 7.1	<.001**
HbA1C (%)	6.4 ± 0.4	8.6 ± 1.5	<.001**
FBG (mg/dL)	172.0 ± 36.7	173.2 ± 45.6	.864
PBG (mg/dL)	228.9 ± 49.8	214.7 ± 60.0	.123
Recovery (n)	25 (34.7)	23 (31.9)	.724

*P < .05; **P < .01.

Data are means ± S.D., or subject number (percent).

HbA1C, glycosylated hemoglobin; FBG, fasting blood glucose; PBG, postprandial blood glucose.

Table 3. Comparison of the Demographic and Audiologic Data According to the Post-Onset Glycemic Control State: Well-Controlled and Poor-Controlled Groups Among the Type 2 Diabetes Patients With Idiopathic Sudden Sensorineural Hearing Loss

Parameter	Well-Controlled (MBG < 200 mg/dL) (n = 76)	Poor-Controlled (MBG ≥ 200 mg/dL) (n = 68)	P
Age (years)	60.4 ± 10.4	61.4 ± 11.8	.584
Gender (male:female)	43:33	38:30	.933
Affected ear (right:left)	35:41	35:33	.516
Duration from onset to treatment (days)	4.3 ± 4.4	4.3 ± 4.3	.947
Initial hearing level of affected ear (dB)	81.2 ± 26.0	80.5 ± 25.9	.871
Final hearing level of affected ear (dB)	57.8 ± 27.7	54.6 ± 31.9	.526
Hearing gain of affected ear (dB)	23.4 ± 18.7	25.6 ± 23.7	.494
Hearing level of unaffected ear (dB)	28.1 ± 19.7	31.9 ± 25.0	.317
Vertigo (n)	33 (43.4)	23 (33.8)	.238
Hypertension (n)	46 (60.5)	43 (63.2)	.738
Chronic kidney disease (n)	7 (9.2)	9 (13.2)	.443
Diabetes status			
Diabetes duration (years)	9.0 ± 6.9	8.9 ± 6.9	.921
HbA1C (%)	7.6 ± 1.6	7.3 ± 1.5	.201
FBG (mg/dL)	150.3 ± 29.3	197.6 ± 38.4	<.001**
PBG (mg/dL)	184.5 ± 36.5	263.4 ± 41.5	<.001**
Recovery (n)	23 (30.3)	25 (36.8)	.409

P* < .05; *P* < .01.

Data are means ± S.D., or subject number (percent).

HbA1C, glycosylated hemoglobin; FBG, fasting blood glucose; PBG, postprandial blood glucose.

outcomes. Our results showed that the degree of glycemic control pre- or post-onset had no effect on hearing outcomes.

Corticosteroid administration in ISSHL is currently the most widely accepted and practiced treatment.²⁰ Several studies have been conducted to determine which method of corticosteroid administration, systemic or intratympanic, is more effective.²⁰⁻²³ There are numerous studies showing that intratympanic injection has a similar effect to systemic administration. However, studies have reported that a combination of both systemic and intratympanic administration has a better effect than a single administration.²⁴ Therefore, systemic corticosteroid administration will continue to play an important role in the treatment of ISSHL.

There have been several studies on the association between diabetes and ISSHL. Weng et al. reported that diabetes causes severe hearing loss in patients with ISSHL and a poorer prognosis compared to patients without diabetes.¹ In the above study, PBG was reported to be associated with the hearing level of the unaffected ear; however, our study did not show any correlation between glycemic

control pre- or post-onset with the hearing level of the unaffected ear. Wen et al. studied the prognostic factors in 576 patients with profound ISSHL and reported that systemic diseases such as diabetes were not associated with hearing recovery.¹⁴ However, there were limitations as only patients with profound hearing loss were enrolled and the treatment methods were not standardized. Fukui et al. reported in a study of 148 patients with ISSHL associated with T2D displayed a more severe hearing loss.¹²

Various studies have reported on the relationship between diabetes duration and severity of ISSHL. Weng et al. reported that there was no correlation between the diabetes duration and the level of hearing loss, but Tay et al. reported the correlation between the diabetes duration and hearing loss.^{1,25} In this study, the poor-controlled group had a longer duration of diabetes (11.1 ± 7.1 years vs 6.6 ± 5.8 years, *P* < .001) and a severe hearing loss (85.1 ± 24.7 dB vs 76.5 ± 26.5 dB, *P* = .046) than the well-controlled group. The authors speculate that the risk of ischemic injury to the inner ear increases as the diabetes duration increases, and this may affect the severity of ISSHL.

Table 4. Prognostic Factors of Hearing Recovery in Type 2 Diabetes Patients With Idiopathic Sudden Sensorineural Hearing Loss: Results of Multivariate Analysis

Parameter	B	SE	Exp (B)	P
Duration from onset to treatment	−0.116	0.055	0.890	.034
Vertigo	−0.943	0.430	0.389	.028
Initial hearing level of affected ear (>70 dB)	− 1.090	0.434	0.336	.012

B, regression coefficient; SE, standard error.

Age, sex, side of the affected ear, hearing level of unaffected ear, hypertension, chronic kidney disease, FBG, PBG, HbA1c, underlying or new-onset, and diabetes duration were not significant.

It is well known that glycemic control acts as a prognostic factor for several diseases and surgical outcomes²⁶⁻²⁸ and that strict glycemic control in patients with diabetes is essential for treatment. However, it has been reported that in some diseases, glycemic control is not associated with prognosis. Loh et al. reported that the prognosis of malignant otitis externa was not associated with glycemic control,²⁹ and Riga et al. reported that glycemic control was associated with the severity of Bell's palsy, but not the prognosis.³⁰ Similarly, in this study, patients with poor glycemic control pre-onset tended to have a more severe hearing loss; however, this was not related to prognosis.

Recently, intratympanic corticosteroid injection has been attracting attention as a treatment for ISSHL. As intratympanic corticosteroid injection does not induce hyperglycemia, it may be suitable for the treatment of ISSHL in patients with diabetes. In a prospective study of patients with ISSHL and diabetes, it was further found that treatment with intratympanic steroid injection alone showed a treatment effect comparable to systemic corticosteroid treatment.³¹ However, intratympanic corticosteroid injection has more several disadvantages compared to systemic administration. First is "delivery failure." It has been reported that 5- 29% of drugs injected into the intratympanic space are not delivered into the inner ear for several reasons, such as false round window membrane, dissipation through the Eustachian tube, poor penetration due to intrinsic reasons of the round window membrane, and air trapped in the round window niche.^{32,33} Second is an inevitable concentration gradient between the cochlear base and apex, limiting the pharmacological effect in the low-frequency range.^{34,35} Considering the above reasons, the authors suggest that systemic corticosteroid administration should be sustained, even in patients with diabetes, until the effectiveness of intratympanic corticosteroid injection is demonstrated in a large-scale randomized controlled study.

This study enrolled patients with ISSHL who had T2D; thus, there was a limitation of a relatively small study population. However, among previous studies of ISSHL and diabetes, this study has the largest number of patients. Additionally, HbA1c levels of all patients were assessed, blood glucose was recorded during treatment, and long-term results were confirmed (4 weeks later), which had the advantage of standardizing treatment methods within a single center.

CONCLUSION

The degree of pre-onset glycemic control seems to affect the severity of ISSHL. However, the degree of pre- and post-onset glycemic control did not affect hearing outcomes of T2D patients with ISSHL. Therefore, it is considered that the administration of systemic corticosteroid is required for diabetes patients with ISSHL within allowable blood glucose levels. Long duration from ISSHL onset to treatment, presence of vertigo, and an initial hearing level over 70 dB were negative prognostic factors affecting the hearing recovery of patients with ISSHL and T2D.

Ethics Committee Approval: Approval for the study was obtained from the Institutional Review Board of the Medical Center (2015AN0225).

Informed Consent: Written informed consent is obtained from the Institutional Review Board (IRB) for all study participants.

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