

Original Article

Efficacy of methylprednisolone sodium succinate for injection (postotic injection) on the auditory threshold and speech recognition rate of sudden deafness patients

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Abstract: Objective: To investigate the effect of injecting the methylprednisolone in the ear for the sudden deafness and the improvement of speech discrimination test. Methods: 50 inpatients with a sudden hearing loss were recruited. Inject the methylprednisolone in the subperiosteal of the ear which is 0.5 cm distance to the ear ditch every three days. Methylprednisolone was placed for fifteen days. Simultaneously vasodilation, neurotrophic, thrombolysis and insulin hypoglycemia were administered in all patients. Pure tone test and speech discrimination test were conducted at Days 7 & 14 after intervention. Results: The outcome was as follows: cure (n = 8), efficacy (n = 9), effect (n = 18) and no effect (n = 15) respectively. The overall effective rate of 70%. The improvement of pure tone threshold and speech discrimination had significant statistical difference (P < 0.05). Conclusion: The therapy of postaural methylprednisolone injection can decrease pure tone threshold effectively and increased speech discrimination with a sudden hearing loss.

Keywords: Postaural injection, methylprednisolone, sudden deafness, speech discrimination test

Introduction

A sudden deafness means a sensorineural hearing loss of ≥ 20 dB at more than two adjacent frequencies out of unknown cause suddenly within several minutes, several hours or 3 d. At present, despite the yet unclear etiology and pathogenesis, such factors as viral infection, micro-circulation disorder or immune factors have been more considered as pathogenic factors, which has not yet been supported through the objective direct examination means. Therefore, the treatment method and administration route for sudden deafness have always become the clinical hot issue, and the typing treatment principle and suggested administration protocol have been determined by the Chinese Medical Association through a 3-year multi-center study on the sudden deafness. However, for sudden deafness, the administration of hormones is still in a certain dispute, and the systemic administration of

hormones is yet unacceptable by the vast patients. In 1996, Silverstein et al [1] first reported the local hormones for sudden deafness. In recent years, based on the animal experiment, some local administration routes of hormones have gradually attracted the attention of Ear-Nose-Throat Department (e.g. intratympanic injection and postotic injection). At this study, on the basis of routine treatment, Methylprednisolone Sodium Succinate for Injection (postotic subperiosteal injection) was administered in our inpatients with sudden deafness, and then its efficacy on auditory threshold of pure tone and speech recognition rate in sudden deafness was explored and analyzed.

Materials and methods

Inclusion criteria

50 inpatients with sudden deafness at our Ear-Nose-Throat Department during July 2011~

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Table 1. Difference in efficacy (number of cases)

Cured	Complete relief	Effective	Ineffective	Total effective rate
8	9	8	15	70%

Change in the auditory threshold before and after the treatment: After the treatment, the mean auditory threshold decreased and the hearing improved significantly ($t = 5.66$, $P < 0.05$).

January 2012 were randomly selected for analysis. The cases were collected and arranged according to the following inclusion criteria: ① Age 15~70 years old; ② Hearing loss of ≥ 20 dB HL at more than two adjacent frequencies within 3 d; eliminated of middle ear lesion through the special examination and imaging examination; ③ Eliminated of position-occupying lesion at the rear of cochlear through the MRI on skull (or internal auditory passage) and temporal bone CT; ④ Eliminated of hereditary factors and other pathogenic factors. All subjects were treated for two sessions (14 d), and signed the Informed Consent Form before the treatment.

Auxiliary examination

The present illness and past illness were inquired in detail. All subjects underwent the essential audiological and imaging examinations, e.g. pure tone audiometry (GSI61 dual-channel diagnostic audiometer), acoustic impedance test (via Madsen acoustic impedance device), speech recognition rate (detected via GSI-61 clinical audiometer, with the acoustic stimulus of speech signal), distortion product otoacoustic emission (DPOAE), auditory brainstem response (ABR), temporal bone CT, and MRI on the skull (or internal auditory passage). The relevant laboratory examinations were also made, e.g. blood routine examination, biochemical examination, blood coagulation examination, immunoglobulin assay and cytomegalovirus test.

Intensity of hearing loss and grading of efficacy

According to the criteria of WHO in 1997, the intensity of hearing loss is classified as follows based on the auditory threshold at the frequency of 500, 1000, 2000 and 4000 Hz: Grade 0 (normal) ≤ 25 dB HL; Grade 1 (mild) 26~40 dB HL; Grade 2 (moderate) 41~60 dB HL; Grade 3 (serious) 61~80 dB HL; and Grade 4 (extremely

serious) ≥ 81 dB HL. According to the "Guidelines on the diagnosis and treatment of sudden deafness" (Chinese Medical Association, 2005) [2], the efficacy is classified as follows: cured: the auditory threshold at an impairment frequency restores to normal state, or reaches the level of healthy ear, or reaches the level before the onset of this illness; complete relief: the mean hearing at an impairment frequency increases by > 30 dB; effective: the mean hearing at an impairment frequency increases by 15~30 dB; and ineffective: the mean hearing at an impairment frequency increases by < 15 dB.

Before the treatment, all subjects underwent the pure tone audiometry, acoustic impedance measurement and speech recognition rate detection; and after the treatment, the pure tone audiometry and speech recognition rate were detected once every 3 d continuously for 2 sessions (7 d a session). Under the acoustic stimulus of 30 dB higher than the auditory threshold, 25 Chinese vocabularies were tested, and then the correct percentage was calculated to obtain the speech recognition rate (normal range: 80%~100%).

Treatment method

During the hospitalization, all subjects received the same basic treatment protocol, i.e. Ginkgo Biloba Leaf Extract Injection (for improving the blood circulation), Batroxobin (for reducing the blood fibrinogen level) and Mecobalamin + mouse nerve growth factor (neurotrophyl). Methylprednisolone Sodium Succinate for Injection (postotic injection) was administered through the following procedures: draw 40 mg of Methylprednisolone Sodium Succinate for Injection with 1 ml syringe, make the postotic subperiosteal injection by sticking the syringe needle onto the surface of mastoid bone at the postotic position 0.5 cm from postotic groove, compress for a short while after the completion of postotic injection, and inject continuously for 5 times (once every 3 d).

Statistical processing

The test data was analyzed through the SPSS 18.0 software, and mainly underwent the t test and χ^2 tests. $P < 0.05$ indicated a significant difference.

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Table 2. Change in the mean auditory threshold of pure tone before and after the treatment ($\bar{x} \pm s$, dB)

Group	n	Mean auditory threshold ($\bar{x} \pm s$, dB)	Difference before and after the treatment (paired t test, $\bar{d} \pm s$, dB)	t value	P value
Before the treatment	50	70.9 \pm 26.25	14.0667 \pm 17.57	5.66	< 0.01
After the treatment	50	56.83 \pm 27.46			

P < 0.05. Change in the speech recognition rate before and after the treatment: After the treatment, the speech recognition rate increased significantly (t = 4.97, P < 0.05).

Table 3. Change in the speech recognition rate before and after the treatment ($\bar{x} \pm s$, dB)

Group	n	Speech recognition rate ($\bar{x} \pm s$, dB)	Difference before and after the treatment (paired t test, $\bar{d} \pm s$, dB)	t value	P value
Before the treatment	50	37.96 \pm 35.31	14.36 \pm 20.45	4.97	< 0.01
After the treatment	50	52.32 \pm 34.97			

P < 0.05. Correlation between speech recognition rate and efficacy before and after the treatment.

Table 4. Correlation between speech recognition rate and efficacy before and after the treatment

Efficacy	n	Improvement cases of speech recognition rate
Cured	8	8
Complete relief	9	8
Effective	15	14
Ineffective	18	7

Results

Difference in the efficacy: Difference of curative effect in 50 cases. As shown in **Table 1**. The total effective rate was 70%.

Change in the auditory threshold before and after the treatment: After the treatment, the mean auditory threshold decreased and the hearing improved significantly (t = 5.66, P < 0.05). As shown in **Table 2**.

Change in the speech recognition rate before and after the treatment: After the treatment, the speech recognition rate increased significantly (t = 4.97, P < 0.05). As shown in **Table 3**.

Correlation between speech recognition rate and efficacy before and after the treatment. As shown in **Table 4**.

Discussion

Up to now, the sudden deafness is yet of unclear pathogenesis, with the following main etiological hypothesis: vascular factors, auto-

immune factors, viral infection and structural rupture of cochlear endomembrane [3]. The sudden deafness is mainly treated through the following comprehensive methods: improvement of internal ear micro-circulation, promotion of oxygen supply, neurotrophs and improvement of immunity. In a retrospective analysis of 67 sudden deafness patients [4], the hormone treatment was recommended. The systemic hormones caused more adverse reactions, which was far more than those of local hormones. The receptors of steroid hormones were widely distributed in the internal ear (more in cochlea than in vestibule) [6]. In the study of Rarey et al on one dead people of Parkinson's disease [6, 7], the receptors of steroid hormones were widely distributed in the internal ear (more in cochlea than in vestibule), and primarily in spiral ligament of cochlea and secondarily in the Corti organ and vascular stria (which was similar to that in the cochlea of rats). Since the systemic hormones caused more adverse reactions (which was far more than those of local hormones), the local hormones were administered at the postotic subperiosteal site at this study.

In the study of Jing Yuanyuan and Yu Lisheng et al. [8], the pharmacokinetic characteristics in the plasma of guinea-pig were explored after the administration of Compound Betamethasone Injection (postotic injection). In order to explore the pharmacokinetic characteristics in the plasma of sigmoid sinus and systemic circulation after the postotic and systemic administration of Compound Betamethasone Injection, the guinea-pigs were randomly divided

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into two groups: postotic injection group and intramuscular injection group. The blood of sigmoid sinus at both sides and systemic circulation was collected at 0.5 h, 1 h, 1.5 h, 2 h, 3 h, 5 h, 7 h, 1 wk, 2 wk and 4 wk after the postotic and systemic administration respectively. Then, the blood medicine concentration was determined through HPLC respectively. The pharmacokinetic characteristics in the blood of sigmoid sinus were explored after the postotic injection. In the animal experiment (with the medicine tracer of Compound Betamethasone Injection), the medicine after the postotic injection reached a higher concentration (HPLC) in the sigmoid sinus (especially in that at the same side), and acted for a longer time at a large total medicine absorption, possibly because the venous reflux rate was slow. The area under curve (AUC) of medicine-time curve is an objective evaluation index for in vivo medicine concentration. The peak AUC the blood of sigmoid sinus at the same side after the postotic injection was 2.41 times of that at the opposite side, and 2.93 times of that after the intramuscular injection, indicating that the medicine after the postotic injection aggregated in the blood of sigmoid sinus (especially at the same side). Therefore, compared with that after the intramuscular injection at the same dose, the medicine after the postotic injection reached a higher peak concentration and acted for a longer time. After the postotic injection, the medicine concentration in the blood of systemic circulation always kept at a lower level. The peak medicine concentration (C_{max}) and AUC in the blood of systemic circulation were 1/10 and 1/3 of those after the intramuscular injection respectively. Compared with that after the intramuscular injection at the same dose, the medicine after the postotic injection reached a higher peak concentration in the blood of systemic circulation, with a lower total medicine absorption. Therefore, the medicine after the postotic injection always maintained a lower concentration in the blood of systemic circulation, so as to reduce the possibility of systemic adverse reactions after the administration of large-dose glucocorticosteroids.

The postotic injection achieved a good efficacy, but through an unclear action route and mechanism. In terms of anatomic characteristics of venous reflux in the external ear, the blood in the postotic area first reflowed to the postotic vein, then some blood converged from external

jugular vein into systemic circulation, and the other blood converged from mastoid emissary vein into sigmoid sinus [9, 10].

The speech recognition rate is an important index for evaluating the effect of speech rehabilitation in the patients with hearing disorder, and a closer and closer attention of audiologists is attracted to the speech ability and its influencing factors. The speech audiometry is a subjective test method, and the speech recognition is overall influenced by the physical, physiological and psychological factors. Under the following conditions of subjects, the speech recognition rate is generally lower: more serious hearing loss, higher position of deafness-related lesion, feigned deafness, and less tests [11]. The speech recognition threshold is tested for three purposes. Firstly, it can verify the results of pure tone audiometry: if the audiogram of subjects is flat, the mean value of thresholds at the speech frequency of 500, 1000 and 2000 Hz approximates to speech recognition threshold at a deviation of ± 6 dB; and if the audiogram of subjects is a steep rise or steep fall, the mean value of two better thresholds at above three speech frequencies approximates to speech recognition threshold. Secondly, it can indicate the sensitivity of speech hearing according to the following criteria for older children and adults: normal (≤ 20 dB HL), mild abnormality (> 25 dB HL), moderate abnormality (> 40 dB HL), serious abnormality (> 60 dB HL), and extremely serious abnormality (> 90 dB HL). Thirdly, it can indicate the intensity of acoustic stimulus at the supra-threshold speech test.

At this study, in the sudden deafness patients, Methylprednisolone Sodium Succinate for Injection (postotic subperiosteal injection) could not only reduce the auditory threshold, but also improve the speech recognition rate; and in some cases, the auditory threshold did not change significantly, but the speech recognition rate increased. In the study of Hou Zhiqiang and Wang Qiuju et al. [12], the speech recognition was recovered better in the sudden deafness patients of effective treatment than those of ineffective treatment, which consisted with the results of this study. Therefore, the prognostic conditions of sudden deafness patients can be predicted by detecting the speech recognition rate. The speech recognition is an important respect of human auditory function, and the speech recognition ability can

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not only reflect the hearing level, but also indicate the conduction path of auditory nerve and the functional state of auditory center. The hearing loss caused by post-cochlear and central lesion can significantly separate the speech hearing from pure tone hearing [13]. Therefore, the detection of speech recognition rate can eliminate the sudden hearing loss caused by the post-cochlear and central lesion.

Disclosure of conflict of interest

None.

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