Original Article

A Comparison of Intravenous Pulse Methylprednisolone and Intravenous Dexamethasone on Idiopathic Sudden Sensorineural Hearing Loss: A Double-Blind Randomized Controlled Trial

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Objective: To evaluate the treatment success rate and safety of intravenous pulse methylprednisolone and dexamethasone treatment in patients with idiopathic sudden sensorineural hearing loss (ISSNHL).

Materials and Methods: The present study was a double-blind randomized controlled trial. Twenty-eight patients who met the inclusion criteria were randomly divided into two groups, with 14 patients in each group. Group I patients were given intravenous pulse methylprednisolone 500 mg/day for the first three days and oral prednisolone 1 mg/kg/day for the next seven days, and Group II received intravenous dexamethasone 12 mg/day for the first three days and oral prednisolone 1 mg/kg/day for the next seven days. Pure-tone average (PTA) hearing threshold was recorded before and after treatment at third, tenth, and seventeenth day. The treatment success rate was hearing recovery level of patients whose PTA gain were 30 dB or more in each group as complete recovery and marked improvement. Audiologic improvement was classified according to the Furuhashi criteria.

Results: Treatment success rate was 64.29% with complete improvement at 35.71% and marked improvement at 28.57% in the methylprednisolone group, whereas it was 50.00% with complete improvement at 42.86% and marked improvement at 7.14% in the dexamethasone group at the seventeenth day follow-up visit. The treatment success rate was higher in the methylprednisolone group but not statistically significant. There was no significant difference of the side effect in both groups.

Conclusion: Intravenous pulse methylprednisolone is similar on treatment success rate and side effect to intravenous dexamethasone.

Trial registration: Thai Clinical Trials Registry, TCTR20211224004

Keywords: Idiopathic sudden sensorineural hearing loss; Steroid; Intravenous pulse methylprednisolone; Intravenous dexamethasone

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Idiopathic sudden sensorineural hearing loss (ISSNHL) has been defined as a sensorineural hearing loss of 30 dB or more in at least three contiguous audiometric frequencies that occur within three days and without any identifiable cause[1]. The overall incidence of ISSNHL ranges from 5 to 20 per 100,000 persons per year[2]. Different treatment modalities have been proposed for ISSNHL. However, the most effective treatment is steroid therapy[3].

Corticosteroids have different mechanisms in the inner ear such as reducing the cytotoxic immune response, increasing the microvascular blood flow in the cochlea, and decreasing the onset of endolymphatic hydrops[4]. Steroids can be administered systemically, orally, and intravenously, or locally by intratympanic (IT) injection.

Systemic steroid administration is the most common method for treating ISSNHL[5]. Pulse steroid therapy is the administration of high doses of drugs to enhance the therapeutic effect and reduce the side effects[6]. It has been used in a variety of diseases such as nephrotic syndrome, crescentic glomerulo-nephritis, systematic lupus erythematous, dermatomyositis, leukocytoclastic vasculitis, and

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rheumatoid arthritis[6,7].

Few studies are available regarding the comparison of intravenous steroid therapy in ISSNHL, especially intravenous pulse steroid. The present study was conducted to evaluate whether in ISSNHL patients pulse steroid therapy with methylprednisolone leads to better the hearing recovery level than dexamethasone with less side effect.

Materials and Methods

The present study was approved by the Ethics Committee of Burapha University on November 25, 2021 (IRB1-092/2564) and was registered at the Thai Clinical Trials Registry (TCTR20211224004).

Participants

Participants were chosen from among the patients who had unilateral ISSNHL and had been referred to the Department of Otorhinolaryngology, Faculty of Medicine, Burapha University between 2021 and 2022. The present study was performed as a double-blind randomized controlled trial. The authors enrolled 30 ISSNHL patients. Participants were all adults aged 20 to 60 years old who met the following inclusion criteria, which was unilateral ISSNHL of 30 dB or more in at least three contiguous audiometric frequencies that occurred within 14 days and had no history of disease in the affected ear and no previous treatment. The exclusion criteria were the presence of a retrocochlear lesion or a neoplasm, a history of acute or chronic otitis media or any ear infection in the affected ear, the presence of congenital cochlear malformations, a history of ear trauma in the affected ear, recent use of ototoxic medications within one month, pregnancy or breast-feeding, a history of steroid allergy, a history of steroid use within one month, and the presence of diabetic mellitus, immunocompromise, systemic infection, uncontrolled hypertension, and gastrointestinal bleeding.

Thirty patients were included according to the inclusion and exclusion criteria. At baseline, physical examinations, laboratory, and standard audiogram were performed. The laboratory examination included blood cell count, coagulation profile, blood glucose, lipid levels, blood urea nitrogen, creatinine, thyroid function test, erythrocyte sedimentation rate (ESR), venereal disease research laboratory test (VDRL), and HIV. The audiological examinations were the audiometric evaluation of the pure-tone average (PTA) and the auditory brainstem response (ABR).

Table 1. Hearing recovery level by Furuhashi criteria[8]

Recovery level	Hearing recovery (PTA)
No improvement	PTA gain <10 dB
Slight improvement	10 dB ≤ PTA gain <30 dB
Marked improvement	PTA gain ≥30 dB
Complete recovery	PTA ≤25 dB or a return within 10 dB of the unaffected ear

PTA=pure-tone average

Treatment procedures

The thirty patients were randomly and equally assigned to two groups: Group I received intravenous pulse methylprednisolone, and Group II received intravenous dexamethasone. The randomization technique was a consecutive allocation by the visit sequence. Groups I and II were treated for 10 days. Group I was given intravenous pulse methylprednisolone 500 mg per day for the first three days and oral prednisolone 1 mg/kg/day for the next seven days. Group II was given intravenous dexamethasone 12 mg per day for the first three days and oral prednisolone 1 mg/kg/day for the next seven days. Two patients missed the seventeenth day follow-up visit, with one in each group as both had stopped the treatment because of a personal issue. As a result, 28 patients remained or 14 in each group.

Criteria for outcome

Pure-tone audiogram were performed before the treatment and with follow-up on the third day, tenth day, and seventeenth day. PTA was calculated as the average of the thresholds at 0.5, 1, and 2 kHz. Severity of the disease was based on PTA. PTA 25 to 40 dB loss was defined as mild, 41 to 55 dB as moderate, 56 to 70 dB as moderately severe, 71 to 90 dB as severe, and 91 dB loss and more was defined as profound hearing loss.

The primary outcome was hearing recovery level, which was compared between the two groups (Table 1)[8]. Complete recovery and marked improvement were considered successful treatment. The secondary outcome was side effect of steroid therapy, which was compared between the two groups.

Statistical analysis was performed using Stata, version 14.1 (StataCorp LP, College Station, TX, USA). The treatment effects in the two groups were compared using the chi-square test. The level of statistical significance was p-value less than 0.05.

Results

Thirty patients were randomized into two group

Table 2. Demographics and baseline audiogram of patients in the two groups

	Methylprednisolone group (n=14)	Dexamethasone group (n=14)	p-value
Age (years); mean±SD	43.71±3.74	43.36±3.47	0.945
Sex (male:female); n	5:9	6:8	0.699
Affected ear (right:left); n	7:7	6:8	0.705
Time interval to initiation of treatment (days); mean±SD	5.64±1.102	5.57±1.098	0.944
Mean initial PTA (dB); mean±SD	70.79±7.28	66.79±7.75	0.748
Severity of hearing loss; n (%)			0.908
Mild	3 (21.43)	4 (28.57)	
Moderate	2 (14.29)	1 (7.14)	
Moderately-severe	2 (14.29)	3 (21.43)	
Severe	2 (14.29)	1 (7.14)	
Profound	5 (35.71)	5 (35.71)	

PTA=pure-tone average; SD=standard deviation

Table 3. Hearing recovery level of patients in the two groups after treatment

Recovery level	Methylprednisolone group (n=14); n (%)	Dexamethasone group (n=14); n (%)	p-value
Day 3			
No improvement	3 (21.43)	6 (42.86)	0.225
Slight improvement	2 (14.29)	2 (14.29)	1.000
Marked improvement	4 (28.57)	1 (7.14)	0.139
Complete recovery	5 (35.71)	5 (35.71)	1.000
Day 10			
No improvement	2 (14.29)	4 (28.57)	0.357
Slight improvement	3 (21.43)	3 (21.43)	1.000
Marked improvement	4 (28.57)	1 (7.14)	0.139
Complete recovery	5 (35.71)	6 (42.86)	0.699
Day 17			
No improvement	2 (14.29)	4 (28.57)	0.357
Slight improvement	3 (21.43)	3 (21.43)	1.000
Marked improvement	4 (28.57)	1 (7.14)	0.139
Complete recovery	5 (35.71)	6 (42.86)	0.699

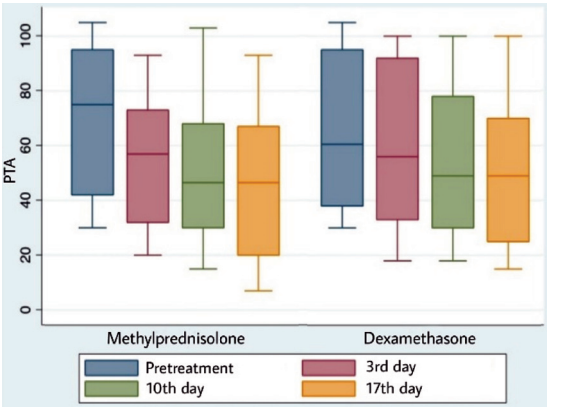

Figure 1. The distribution of PTA before treatment, in the third day, in the tenth day, and in the seventeenth day after treatment.

with 15 patients in the methylprednisolone group and 15 patients in the dexamethasone group. In both groups, one patient in each group was lost to follow-up and they missed their final audiograms. The final number of patients that met the inclusion and exclusion criteria, were followed-up for 3, 10, and 17 days after treatment and enrolled in statistical analysis, were 14 patients in each group.

The demographics and baseline audiogram of the patients are summarized in Table 2, which showed no significant difference between the two groups.

Table 3 shows comparison of hearing recovery level on the third, tenth, and seventeenth day after treatment in the two groups. The hearing recovery level improvement had no statistically significant difference between the two groups.

According to the Furuhashi criteria, the treatment success rate was 64.29% with a complete improvement in 35.71% and marked improvement in 28.57% in the methylprednisolone group, whereas 50.00% with a complete improvement 42.86% and marked improvement in 7.14% in the dexamethasone group. The treatment success rate was higher in the methylprednisolone group but not statistically significant.

The distributions of PTA performed before treatment, in the third day, in the tenth day, and in the seventeenth day after treatment are demonstrated again in boxplots (Figure 1).

No serious complications were observed in the patients after both treatments. There was no significant difference of the side effect in both groups. Dyspepsia was higher in the dexamethasone group but not statistically significant (Table 4).

Table 4. Side effect in the two groups after treatment

Side effect	Methylprednisolone group (n=14); n (%)	Dexamethasone group (n=14); n (%)	p-value
Dyspepsia	0 (0.0)	3 (21.43)	0.067
Hematemesis	0 (0.0)	0 (0.0)	-
Fever	0 (0.0)	0 (0.0)	-

Discussion

The most effective treatment for ISSNHL is steroids, which is commonly used to improve hearing. Steroids can be administered systemically, orally, and intravenously, or locally by IT injection[9,10].

Oral steroid has the adverse effects such as dyspepsia, or gastritis due to the direct gastrointestinal irritation[11]. The complications of IT steroid injection have otalgia, vertigo, tympanic membrane perforation, and acute otitis media[12], all of which are less common in intravenous steroid injection. Furthermore, intravenous administration is easier to control blood sugar than oral steroid when the patients take medication at home.

Pulse therapy is the administration of high doses of drugs to enhance the therapeutic effect and reduce the side effects[6].

There are few reports of pulse therapy in ISSNHL especially a comparison of intravenous steroid injection, however, there are reports of pulse therapy compared with oral prednisolone. In those reports, the intravenous pulse therapy had significantly better hearing recovery levels than oral prednisolone. Narozny et al[12], reported their study group received 1,000 mg of intravenous methylprednisolone injection for three days, prednisolone 60 mg per day in decreasing doses, plus hyperbaric oxygen therapy. Their control group received 30 mg of oral prednisolone per day in decreasing dose for up to 14 days. The study group had significantly better hearing recovery levels. Eftekharian et al[13], reported their study group received 500 mg of intravenous methylprednisolone for three consecutive days, followed by 1 mg/kg oral prednisolone for 11 days. The control group received 1 mg/kg oral prednisolone for 14 days. Pulse therapy with methylprednisolone and oral prednisolone therapy resulted in similar hearing recovery levels. Westerlaken et al[14], reported their patients received 300 mg of dexamethasone for three consecutive days as pulse therapy, followed by four days of placebo. The control group received 70 mg of prednisone per day, tapered in steps of 10 mg per day to 0 mg. The hearing recovery levels was not significantly different between the two groups.

The different results obtained from these studies can be explained by the different dosage of drugs, and route of administration.

According to the Clinical Practice Guideline (CPG): Sudden Hearing Loss (Update) Executive Summary 2019, the prognosis for recovery is dependent on a number of factors including patient age, presence of vertigo at onset, degree of hearing loss, initial audiogram shape, and time between onset of hearing loss and treatment[15]. The present study showed that there was no presence of vertigo at onset in both groups. In no recovery group, mean age of patient, degree of hearing loss, and time between onset of hearing loss and the treatment in both groups were 49.17±5.53 years old, 81.50±8.27 dB, and 8.17±2.06 days, respectively, and the initial audiogram shape was flat or down-sloping shape in both groups which were negative prognostic indicators. All of these are consistent with the poor prognosis for recovery in CPG that affect the outcome of the present study.

There are limitations in the present study. The small sample sizes presented due to the low incidence of the disease, especially when inclusion and exclusion criteria are applied. A the multicenter study may get better outcome on this problem.

Future studies are recommended with a larger sample size and different dosages of steroids to improve hearing recovery level.

Conclusion

This double-blind randomized controlled trial showed the intravenous pulse methylprednisolone has similar treatment success rate and side effect to the intravenous dexamethasone in patients with ISSNHL.

What is already known on this topic?

Treatment of ISSNHL.

What this study adds?

The treatment success rate of intravenous steroid injection of ISSNHL and adverse side effects.

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Conflicts of interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

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