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Effect of Intratympanic Dexamethasone on Bell's palsy: A Clinical Trial

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Abstract

Introduction:

The main objective of this study is to examine the hypothesis that intratympanic corticosteroids can benefit the treatment of Bell's palsy and shorten the period needed for recovery.

Materials and Methods:

This study was conducted prospectively using double-blind clinical trials. A total of 321 patients with acute unilateral facial paralysis were included in the survey, with 144 patients excluded due to exclusion criteria and 177 patients included. These patients were divided into an intervention group (54 patients) and a control group (123 patients). Prednisolone and acyclovir were given orally to both groups. Intratympanic dexamethasone was given to the intervention group as an additional treatment.

Results:

Patients' House-Brackmann (H.B.) scores were recorded when they were visited three days, one week, three weeks, three months, and six months after receiving intratympanic dexamethasone. It was discovered that there was no significant difference in H.B. scores between the intervention and control groups. The first day of symptom improvement in the intervention group was 1.81 days after starting treatment, while it took 2.91 days in the control group, which is a significant difference.

Conclusion:

Intratympanic dexamethasone injection, in addition to the 10-day prednisolone-acyclovir therapy regimen, did not affect patients recovering from Bell's palsy in the short term (three weeks) or long term (six months) but is significantly effective in the first day of recovery as measured by the House-Brackmann scale.

Keywords:

Clinical trial, Facial nerve palsy; Intratympanic dexamethasone, Prednisolone and acyclovir.

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Introduction

Bell's palsy, or idiopathic facial nerve paralysis, is sometimes referred to as inflammatory facial nerve paralysis (1). Dr. Charles Bell described the most common cause of facial nerve palsy. [1] Various causes have been suggested to explain the disease, such as viral infection, vascular ischemia, hereditary factors, autoimmune inflammation, etc (2-5). Herpes simplex virus type 1 is currently accepted as the most probable cause (6).

Following a viral infection, edema and bleeding inside the facial nerve may occur, putting extra pressure on the nerve inside the fallopian canal. The part of the nerve most vulnerable to pressure is the labyrinthine segment (2,6).

Combining systemic corticosteroids and antiviral medicines is currently considered the gold-standard treatment (7,8) Other therapies, including surgery, acupuncture, etc (8-10). have been performed. Due to underlying conditions such as diabetes mellitus or severe gastrointestinal problems, the administration of high-dose corticosteroids to some patients is restricted (11). In this study, some patients with Bell's palsy were treated with intratympanic corticosteroids due to the possibility of medication absorption from the middle ear **(**12).

Numerous studies have revealed that, in addition to the chorda tympani nerve dehiscence, there are multiple other dehiscences along the facial nerve in various parts of it, such as the tympanic portions of the facial nerve to the geniculate ganglion (13-15). This study looks at the concept that treating Bell's palsy with intratympanic dexamethasone is similar to treating sudden sensorineural hearing loss. This theory has been examined in a nearly identical study (11). However, this study aimed to examine this hypothesis on a larger population with a larger sample size.

Materials and Methods

From January 2018 to February 2020, Tehran's Amir-Alam Hospital investigators conducted this prospective and blinded trial (The ethical approval ID is IR. TUMS. MEDICINE. REC.1399. 089). The inclusion criteria were evaluated for patients over 18 years old diagnosed with unilateral complete Bell's palsy who came within the first 14 days of the onset of symptoms and were graded at six on the "House-Brackmann scale."(16) (Table-1).

Table 1: House-Brackman facial paralysis scale

Grade	Description	Characteristics
1	Normal	Normal
2	Mild dysfunction	Slight weakness, normal symmetry at rest.
3	Moderate dysfunction	Obvious but not disfiguring weakness with synkinesis, normal symmetry at rest, Complete eye closure with maximal effort, good forehead movement.
4	Moderately sever dysfunction	Obvious and disfiguring asymmetry, significant synkinesis, incomplete eye closure, moderate forehead movement.
5	Sever dysfunction	Barely perceptible motion, asymmetry at rest.
6	Total paralysis	No movement

Exclusion criteria include ipsilateral facial paralysis or ipsilateral ear surgery, Ramsey Hunt syndrome, skin lesions concurrent with facial paralysis, acute or chronic otitis media, new hearing loss concurrent with facial paralysis, fracture of the temporal bone on the same side, or a history of acute trauma on the side of the paralysis. Systemic exclusion criteria include pregnancy, mental illness, history, or concurrent presence of head and neck cancer. Additional contraindications Receiving high-dose corticosteroids and other variables, such as a history of tuberculosis or active tuberculosis or active hepatitis B, incomplete Bell's palsy, and failure to receive complete follow-up information within six months of the start of treatment, were considered exclusion criteria in our study. A physical examination was conducted to rule out potential causes of facial paralysis. Then, the age, gender, further comorbid symptoms, and comorbidities were documented. After providing relevant explanations and receiving consent from 321 patients with acute unilateral facial paralysis,

136 patients were eliminated from the trial due to exclusion criteria, remaining 185 patients in the study. Regardless of gender, age, or underlying condition, these patients were divided into intervention and control groups. The patients were divided into two groups of six and four boxes. Two patients from a group of six received IT dexamethasone and one from a group of four (intervention group). The time between the disease's onset and the beginning of treatment was recorded. Both groups received oral prednisolone and acyclovir treatments. Intratympanic dexamethasone was administered to the intervention group in addition to the prednisolone-acyclovir regimen.

Acyclovir was given at a dose of 2000 mg in 5 daily doses for up to 10 days, and prednisolone was given at 1 ml/kg for up to 10 days (Table 2).

Table 2: Demographic and clinic data of the patients

	Intervention group	Control group	P-value
Age (year)	48.41	48.9	0.792
Gender (male) n (%) (Female) n (%)	26 (48 %) 28 (52 %)	66 (53 %) 57 (47 %)	0.499
Diabetic mellitus n (%)	7 (13 %)	18 (14.5 %)	0.769
Mean dose of prednisolone (mg per day)	73.11	71.79	0.420
Mild otalgia n (%)	13 (24%)	-	-
Mild vertigo n (%)	14 (24.9%)	-	-
Mean weight gain after 3 weeks (Kg)	0.85	0.78	0.63
Mean interval between the onset of paralysis and the starting of treatment (Days)	3.39	3.25	0.585
Mean of the first day of recovery (days)	1.81	2.91	<0.001
H.B SCORE after three weeks	3.13	2.82	0.79
H.B SCORE after six months	1.79	1.86	0.73

p-value is obtained from the chi-square test.

In the intervention group, an otolaryngologist administered intratympanic dexamethasone injections of 2 to 3 mg five times every other day (#1). For secondary blindness, a second otolaryngologist (#2) visited all patients (controls and intervention groups) three days, one week, three weeks, three months, and six months after treatment, without knowing the type of treatment the patients received, and only recorded the degree of paralysis.

Except for 16 patients who had uncontrolled diabetes mellitus and required hospitalization and supervision to control their glucose chart, all patients were treated out-patiently.

In the case of a lack of a complete response to therapy in any research groups within three weeks after starting treatment, the patient is subjected to a temporal CT scan, an MRI with and without injection, primary audiometric tests, electro-diagnostic testing, including electromyography and electro-neurography, and essential serum tests (Na, K, Ca, P, ACE inhibitor level, etc.) to rule out anatomical causes such as tumors of the facial nerve pathway and involvement with the herpes virus. Participants with reasons other than Bell's palsy are excluded from the study. The main purpose was to compare the recovery rates of Bell's palsy patients treated with intratympanic dexamethasone, prednisolone, and acyclovir after six months with those treated with prednisolone and acyclovir. As a short-term outcome, the second object was to evaluate the recovery rates of patients in the two groups after three weeks. The following object was to compare the first day of recovery on the H.B. scale between the groups registered by the otolaryngologist. (#2)

To compare the side effects of treatment in the two groups, an otolaryngologist (#1) evaluated the side effects and safety of the treatment in both groups at each visit, and the possible side effects of the intervention were recorded.

The adverse effects we expected and documented were divided into two categories:

1. Major side effects: perforations in the tympanic membrane after three weeks of dexamethasone injections, middle ear infection, and hearing loss.

2. Minor side effects: weight gain, mild otalgia, and mild vertigo (we referred to otalgia and vertigo that resolved after 30 minutes of dexamethasone injection). Finally, 177 patients finished the entire research. During the study, variations in the rate of paralysis were graded initially using the H.B. scale.

Intervention- Intratympanic dexamethasone injection

The intervention group received 2 to 3 mg of dexamethasone intra-tympanically every other day for a maximum of 5 doses. The tympanic membrane was numbed with lidocaine-impregnated cotton with 10% lidocaine fifteen minutes before the injection. Following that, the ear canal wax and suction fluid were removed. The patient was positioned supine with the head extended on a chair, and a 25-gauge spinal needle was inserted into the middle ear space through the lower anterior portion of the eardrum. The patient was then asked to refrain from head shaking and speaking for 15 minutes.

Data analysis

SPSS version 25 was used to enter the data. Descriptions are based on frequency tables and related graphs. While frequency and percentage have been used to describe qualitative characteristics, mean and standard deviation have been used to describe quantitative characteristics. An independent t-test was used to compare quantitative variables. The Mann-Whitney test was used to compare ordinal variables. The Chi-square test was used to compare nominal variables. The significance level in all tests was considered P value <0.05.

Results

In this study, 321 patients were studied. At the first examination, 136 Patients were excluded for the reasons mentioned in the trial profile (Figure1). One hundred thirty patients were in the control group, and 55 were in the intervention group out of 85 patients included in the study. Another eight patients were excluded during the study, due to lack of follow-up (Figure 1).

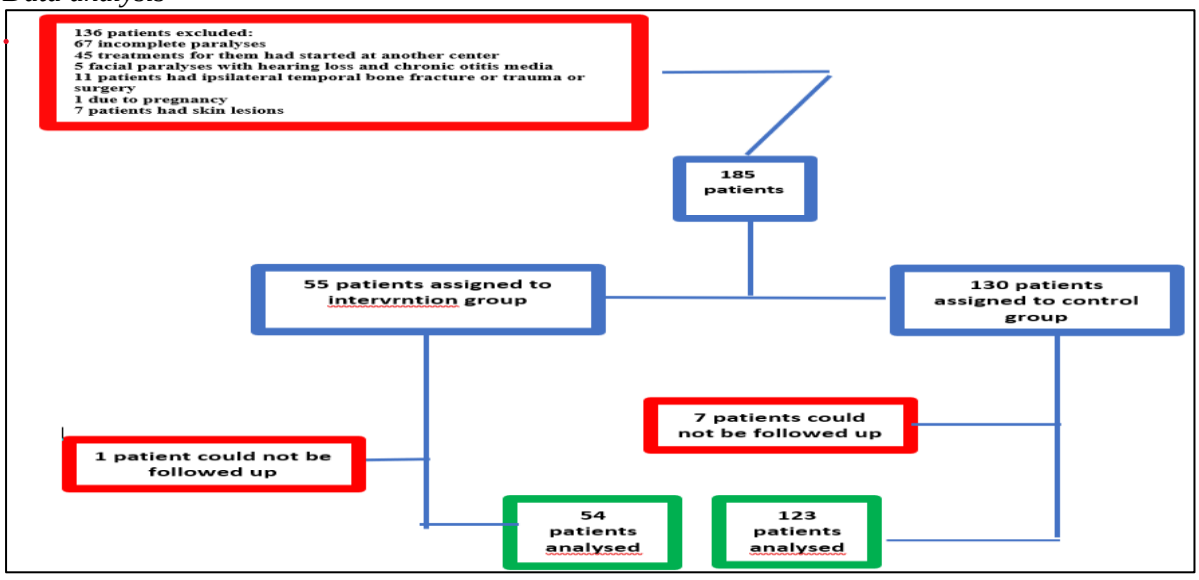

Figure 1: Trial profile

The mean age of patients was 48.7 years old. The oldest was 76, and the youngest was 23 (Std. Deviation = 12.264). The two treatment groups do not differ significantly in age (p-value: 0.792 as determined by an independent T-test) and gender (p-value: 0.499 as determined by a chi-square test), and they are nearly identical (Table 2). At baseline, both groups had the same H.B. grade. (H.B.: 6) The mean dose of prednisolone in the intervention group was 73.1 (std. deviation: 10.253) mg daily and 71.8 mg (std. deviation: 9.412) daily in the control group for up to 10 days, which was not significantly different according to the independent T-test (P-value: 0/420) (Table 2).

The mean interval between the onset of disease and the start of treatment in the intervention group was 3.39 days and 3.25 days

in the control group, which was not significantly different (P = 0.585) according to the independent T-test (Table 2).

Seven of the 54 patients in the intervention group had diabetes mellitus, and of them, four required hospitalization for treatment and failure of disease management. 18 of the 123 patients in the control group had diabetes mellitus, and 12 were hospitalized due to a lack of control over the disease (Table 2). In general, diagnostic testing was conducted on all patients whose Bell's palsy had not resolved fully after three weeks, and no condition other than Bell's palsy was diagnosed. At the three-week follow-up, the Mann-Whitney test (P: 0.79) revealed no significant differences regarding H.B. SCORE recovery between the intervention and control groups (Figure 2).

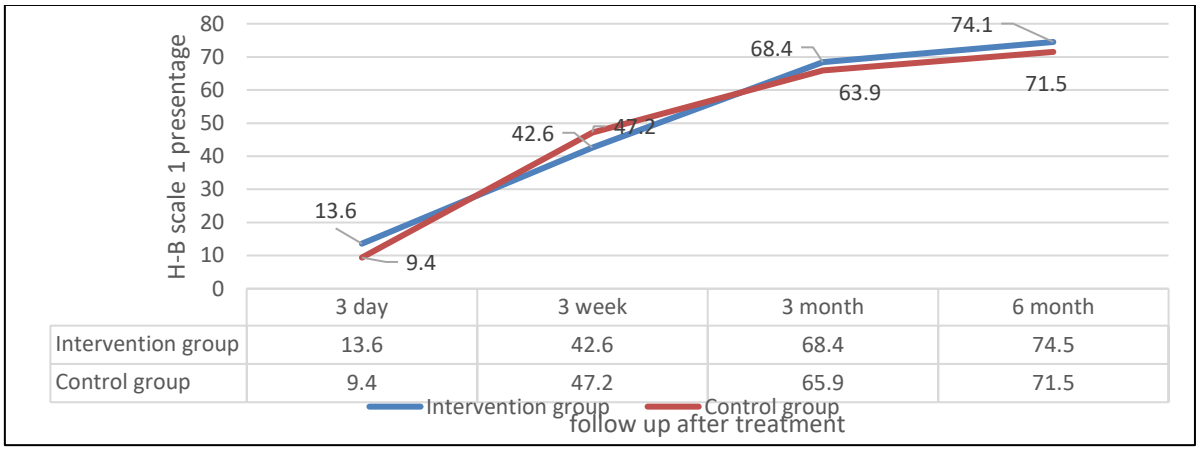

Figure 2: Percentage of treated patients (first House-Brackman (H-B) grade) in follow-up: three days, three weeks, three months, and six months after treatment.

According to the Mann-Whitney test, there was no significant difference between the intervention and control groups in H.B. Score at the 6-month follow-up for patients recovering from Bell's palsy (p-value: 0.73) (Table 3).

Table 3: The outcome of intervention and control groups treatment after 6-month follow-up of patients recovering from the House-Brackman scale.

House-Brackman scale	Intervention group		Control group	
	Frequency	percent	Frequency	percent
Grade 1	40	74.1	88	71.5
Grade 2	0	0	3	2.4
Grade 3	4	7.4	8	6.5
Grade 4	6	11.1	12	9.8
Grade 5	3	5.6	9	7.3
Grade 6	1	1.9	3	2.4

There were no severe complications (such as post-injection tympanic membrane perforations beyond three weeks) in any of the 177 participants investigated. 13 patients (24%) in the intervention group had mild otalgia, and 14 patients (24.9%) had mild vertigo. In contrast, neither condition was observed in the control group. The intervention group's mean weight gain after three weeks was 0.85 kg, while the control group's was 0.78 kg, which was not significantly different according to the independent t-test (P <0.001) (Table 2).

Discussion

Following a review of various studies on the effects of antiviral and corticosteroid

medications, it was concluded that all of the patients in this trial had to be completely paralyzed due to a condition known as Bell's palsy. To keep the study ethical, it was preferable that patients in the control group have at least a 10-day course of prednisolone-acyclovir and that our intervention be added to this medication. The purpose of prescribing acyclovir to participants in this study was to consider a systematic review that advised that patients with severe Bell's palsy should take antiviral medications (17). Mr. Bryant's study included seven complete Bell's palsy patients treated solely with intratympanic corticosteroids. The overall recovery rate was 85%, with one patient recovering at 75%. He did not apply special grading to measure their patient's recovery progress. In addition, he did not define the level of paralysis of the patients upon their first visit (12). In this trial, the complete recovery rate in the intervention group was approximately 74.1%, while 71.5% in the control group indicated no difference.

A review of other research, as well as a comparison of the results of this study with those of previous studies, revealed that there is no significant difference in the percentage of complete recovery of paralysis when patients are given at least prednisolone and acyclovir for one week (7,12,17-23). When the study conducted by Chung et al. is compared upon this experiment, there is no significant difference in the percentage of complete paralysis recovery in the control and intervention groups after six months (11).

In contrast to previous research, which found a substantial improvement between the intervention and control groups after three weeks of treatment on the House-Beckman scale, there was no such difference in this study. Also, like the previous study, the first day of recovery after starting treatment was completely different in the two groups.

One of the contrasts between this study and earlier studies was the sensitivity of this experiment in the initial grade of paralysis; they had no limit on the scale of paralysis before starting the trial. Only patients with complete Bell's palsy were included to homogenize them before dividing them into two groups. In the study of Demir and his colleagues[24], The protocol for classifying patients and how they were intervened in this study and the percentage of patients who fully recovered was the same for all grades. The IT dexamethasone injection dose and number of doses were similar to those used in this clinical trial. In contrast to this study, the systemic dose began at 250 mg of prednisolone and reduced to 40 mg over seven days. They also did not utilize antiviral medications. Ultimately, their treatment resulted in the same outcome as this study. Furthermore, that trial did not document or provide data about the first sign of improvement on the day.In the study of Inagaki and colleagues (25), the intervention group included 35 patients who followed the same methodology described in this study, while the control group included 108. Paralysis was classified as mild to severe on the House-Beckman scale. The total systemic corticosteroids given to all patients was around 410 mg, although the average dosage was around 720 mg. Intratympanic dexamethasone was injected at an average dose of 1.65 mg for ten days. However, in this study, it was given at doses ranging from 2 to 3 mg up to 5 times every other day, and Valacyclovir was administered to patients instead of acyclovir. Notably, no substantial difference has been found between acyclovir and other medications in its family up to this point (26).

In contrast to this study, there was a substantial difference between the intervention and control groups' recovery. In the end, the authors of this manuscript are aware that issues such as randomization improve the generalizability and validity of the report. However, this was impossible for us, so we recommend that those interested in this field conduct the study with more cases and randomization.

Conclusion

Intratympanic dexamethasone injection, in addition to the ten-day prednisolone-acyclovir therapy regimen, had no effect on patients recovering from Bell's palsy in the short-term (three weeks) or long-term (six months). Still, it is significantly effective on the first day of recovery as measured by the H.B. scale.

Decelerations

Conflicts of interest: The authors declare no conflict of interest.

Financial disclosures: Tehran University of Medical Sciences is responsible for funding sources of the trial. The clinical trial registration number (IRCT) is IRCT20200314046769N1. The registration date is 2020-06-16, and registration timing is retrospective.

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Ethical approval: This study was approved by the ethics committees of the collaborating hospitals. Informed consent was obtained from all participants.

The study protocol was approved by the local Ethics Review Committee of the Tehran University of Medical Sciences. The approval ID is IR.TUMS.MEDICINE.REC.1399.089.

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