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ScienceDirect

Journal of Otology 11 (2016) 18–23

www.journals.elsevier.com/journal-of-otology/

A comparison of effects of systemic and intratympanic steroid therapies for sudden sensorineural hearing loss: A meta-analysis

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Received 5 January 2016; revised 25 February 2016; accepted 29 February 2016

Abstract

Objective: To evaluate the efficacy and safety of intratympanic and systemic steroid therapies in the initial treatment of Sudden Sensorineural Hearing Loss (SSNHL) patients.
Methods: A comprehensive search of PubMed, Wanfang database and CNKI (China National Knowledge Infrastructure) was performed covering the period from January 1990 to July 2014. A meta-analysis was conducted after filtering by the criteria of Cochrane Collaboration. Three hundred fifty six subjects in nine studies allocated to the group of intratympanic steroid therapies and 343 controls receiving systemic steroid therapies met the criteria for meta-analysis. The data were extracted and analyzed using the RevMan 5.3 meta-analysis software.
Results: The total effectiveness rate in SSNHL patients receiving intratympanic steroid therapies did not differ statistically from patients receiving systemic therapies (RR = 1.08, 95%CI = 0.99–1.99, P = 0.10), although the rate of full hearing recovery in this group differed significantly from patients receiving systemic therapies (RR = 1.29, 95%CI = 1.00–1.66, P = 0.05).
Conclusion: Local steroid therapy appears to generate higher rate of complete hearing recovery than systemic steroid treatment as an initial treatment for SSNHL, which may be especially useful for patients in whom systemic steroids are contraindicated.

Keywords: Sudden sensorineural hearing loss; Intratympanic steroids; Systemic steroid; Meta-analysis

1. Introduction

Sudden Sensorineural Hearing Loss (SSNHL), first reported by De Kleyn (Seggas et al., 2010) in 1944, is an otologic event that needs urgent intervention. SSNHL is commonly defined as hearing loss greater than 30 dB and involving at least 3 consecutive audiometric frequencies, occurring within 3 days without any identifiable cause (Seggas et al., 2010; Arastou et al., 2013). Although a number of theories regarding the cause have been suggested, the etiologies and pathogenesis of SSNHL are still unclear. The overall incidence of diagnosed SSNHL ranges from 5 to 20 per 100,000 persons per year (Seggas et al., 2010; Arslan et al., 2011; Battaglia et al., 2008). The rate of spontaneous recovery without treatment ranges 32–65% (Seggas et al., 2010; Arastou et al., 2013; Battaglia et al., 2008), and the rate of full recovery in treated patients ranges 49–79% (Arastou et al., 2013; Battaglia et al., 2008).

The cause of SSNHL has been the subject of debate for many years and has been widely studied. The suggested theories include vascular compromise, viral infection, and immune-mediated reactions (Seggas et al., 2010; Arslan et al., 2011). The condition may well have a multifactorial etiology and each

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Peer review under responsibility of PLA General Hospital Department of Otolaryngology Head and Neck Surgery.
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http://dx.doi.org/10.1016/j.joto.2016.02.002

of the above mentioned mechanisms may be responsible for a proportion of the total number of observed cases.

A number of treatments have been reported, such as vasoactive substances, hyperbaric oxygen, antivirals and vitamins (Crane et al., 2014; Koltsidopoulos et al., 2013). Each approach has, however, been debated with no standard protocol universally accepted until the introduction of steroid therapy. Administration of steroids, systemically or intratympanally, alone or in combination, is considered to be the mainstay of treatment for SSNHL (Arslan et al., 2011; Battaglia et al., 2008; Crane et al., 2014). Systemic steroid therapy, however, has serious adverse effects and contraindications and therefore local use of steroids has attracted popularity among otology centers during the last decade (Koltsidopoulos et al., 2013).

In the present study we performed a review of randomized controlled trials (RCTs) involving the use of intratympanic steroid therapy (IST) or systemic steroid therapy (SST) for initial treatment in SSNHL patients. The aim of the meta-analysis was to evaluate the efficacy and safety of IST and determine whether this treatment is more effective as a primary treatment for SSNHL than SST.

2. Materials and methods

2.1. Strategy and criteria

Literature search was performed using a combination of the keywords "sudden hearing loss", "hearing loss", ''steroid'', "transtympanic" and ''intratympanic''. PubMed, Wanfang database and CNKI were searched to yield all possible relevant results. Articles limited to human subjects and published in the English or Chinese languages between January 1990 and July 2014 were included. All RCTs based on the use of steroids and the efficacies of intratympanic and systemic steroid treatments in patients with SSNHL were assessed. Two authors collected and extracted the data independently. Disagreements were solved through discussion. RCTs fulfilling the following criteria were included: (1) the RCT was designed to study the efficacy and safety of SST and IST as initial treatment of SSNHL; (2) SSNHL was reliably diagnosed, excluding other causes, and the RCT presented with a control arm (systemic steroid treatment) and a treatment arm (intratympanic steroids), as well as a clear description of the steroid treatment regimen; (3) the age and sex in the treatment and control groups were not limited, but with no significant difference at baseline.

Data fulfilling the following criteria were excluded: (i) articles that were reviews, expert commentaries, case reports or other non-clinical research literature, (ii) trials that had incomplete reporting of pre- and post-treatment PTA results, (iii) trials that did not evaluate steroids as a primary treatment of SSNHL, and did not evaluate systemic steroids alone or intratympanic steroids alone as the primary treatment.

Nine studies met the criteria and were included for analysis (Table 1). The following information was extracted from each article: sample size of each study arm, type and dose of steroids, methods of steroid administration, duration of therapy, outcomes, major complications and follow-up time.

After identifying the reports, the abstract and full text were carefully read and the publication's quality was screened and evaluated according to the Handbook of System Quality Evaluation of Cochrane criteria. Pre- and post-treatment pure-tone audiometry (PTA) results were noted. Treatment efficacy was determined in accordance to the sudden deafness diagnosis and treatment standards by the Chinese Medical Association Otolaryngology Head and Neck Surgery Branch, Ji'nan, 2005. A change of hearing thresholds within the 250–4000 Hz frequency range back to within normal range, or to the level of the healthy ear, or back to the level before SSNHL was considered to represent a full recovery (cured); and a threshold recovery of 15 dB or greater was considered to indicate significant improvement (Spear and Schwartz, 2011). The rates of full recovery and significant improvements were calculated.

2.2. Statistical analysis

Data analysis was performed with the RevMan5.3 software. Tests of heterogeneity were conducted with the chi-square test, as an x^2 variate. Between-study heterogeneity was assessed using the I^2, as the percentage of variability among effect estimates beyond that expected by chance (Ng et al., 2014). As a reference, I^2 values of 25% were considered low, 50% as moderate, and 75% as high (Ng et al., 2014). If the result did not show heterogeneity (i.e. $I^2 < 50\%$, $P > 0.10$), the fixed-

Table 1
Characteristics of the included research.

Included literature (author, published time)	Intratympanic therapy			Systemic therapy			Follow-up time
	Drug	Usage and dosage	Time	Drug	Usage and dosage	Time	
Lim et al. (2013)	Dexamethasone	Intratympanic injection, 1.5–2 mg	2w	Prednisone	Oral, 60 mg/d	10d	3w
Rauch et al. (2011)	Methylprednisolone	Intratympanic injection, 40 mg	2w	Prednisone	Oral, 60 mg/d	19d	6m
Dispenza et al. (2011)	Dexamethasone	Intratympanic injection, 4 mg	4w	Prednisone	Oral, 6 mg/d	14d	6m
Zhou et al. (2006)	Dexamethasone	Intratympanic injection, 2.5 mg	8d	Prednisone	Oral, 30 mg/d	8d	20d
Peng et al. (2008)	Dexamethasone	Intratympanic injection, 5 mg	10d	Dexamethasone	Intravenous, 10 mg	10d	20d
Deng (2011)	Dexamethasone	Intratympanic injection, 1 mg	10d	Dexamethasone	Intravenous, 10 mg	10d	30d
Yi et al. (2011)	Dexamethasone	Auditory tube injection, 5 mg	10d	Dexamethasone	Intravenous,10 mg	7d	30d
You et al. (2008)	Dexamethasone	Intratympanic injection, 1–1.5 mg	10d	Dexamethasone	Intravenous, 10 mg	10d	15d
Mao et al. (2005)	Methylprednisolone	Auditory tube injection, 5 mg	10d	Methylprednisolone	Intravenous, 40 mg	7d	20d