

THERAPEUTIC EFFECTS OF CARBOGEN THERAPY IN SUDDEN SENSORINEURAL HEARING LOSSShaili Priyamvada¹, Rajeev Yande²¹Senior Resident, Department of ENT, VMMC and Safdarjung Hospital, New Delhi, India; Ex-Resident, Ruby Hall Clinic, Pune, Maharashtra, India.²Senior Consultant, Department of ENT, Jehangir Hospital, Pune, Maharashtra, India; Ex-Consultant, Ruby Hall Clinic, Pune, Maharashtra, India.**ABSTRACT****BACKGROUND**

Sudden Hearing Loss (SHL) is a rare disease accounting for 1% of all sensorineural hearing loss cases, but it is considered an otological emergency. The sooner the treatment begins, the outcome proves to be better. Different theories have been postulated with regard to determining its cause. Most accepted treatment at the present time is systemic steroid therapy.

The purpose of our study was to compare the efficacy of carbogen therapy combined with steroids, is whether or not superior to steroids alone in the treatment of sudden hearing loss.

MATERIALS AND METHODS

This prospective, non-randomised, controlled parallel trial included 60 patients with idiopathic SHL who visited our clinic within 14 days of symptom onset between August 2013 and February 2015. All patients received oral prednisolone for 10 days. Of the 60 patients, 30 received no additional treatment and 30 received additional carbogen inhalation. Hearing improvement was measured using Siegel's criteria.

RESULTS

We observed in our study that complete recovery at two months occurred in 33.33% and 26.67% subjects in Group 1 [Carbogen therapy plus steroids] and Group 2 [steroids alone] correspondingly. As for partial recovery, 53.33% and 66.67% in Group 1 and 2 correspondingly (Siegel's criteria 1 and 2). Slight improvement was noticed as follows at 10th sitting 23.33% and 13.33% and at 2 months 13.33% and 6.67% in corresponding group. Though these results show that carbogen therapy is better than steroids, the data is calculated to be statistically insignificant using Fisher's exact test (p-value 0.267 and 0.591 > 0.05). We also found that there is statistically significant [p-value 0.01] association between age of onset of sensorineural hearing loss and betterment of hearing. Younger the age at the time of onset of hearing loss, there are better chances of hearing gain towards normal hearing sensitivity.

CONCLUSION

Carbogen inhalation added to steroids was a more effective treatment than steroids alone in patients with idiopathic sudden sensorineural hearing loss.

KEY WORDS

Sudden Sensorineural Hearing Loss, Carbogen Therapy, Steroids.

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BACKGROUND

Sudden Hearing Loss (SHL) is defined as sensorineural hearing loss of 30 dB or more in three sequential frequencies occurring over 3 days or less.¹ SHL was first reported by De Kleyn² in 1944 and there have been many studies regarding SHL, but the pathogenesis remains unclear.

Idiopathic Sudden Sensorineural Hearing Loss [SSNHL] has an estimated incidence of 5 to 20 per 100,000 persons per year.³ SHL involves a variety of causative factors and therefore should be considered a syndrome rather than a single disease⁴ and it accounts for 1% of all sensorineural hearing loss cases.⁴ Males are equally affected as females.⁵ About one-third of people with SHL awaken in the morning with a hearing loss.

By definition, the aetiology of ISSNHL is unknown. Different theories have been postulated. The majority of treatment modalities are based on two common theories of aetiologies: - Circulatory disturbances and inflammatory reaction, most commonly viral infection. SSNHL is a diagnosis of exclusion. Clinical evaluation and examination are of utmost importance to rule out organic causes of sudden hearing loss.

Sudden sensorineural hearing loss is considered to be a true otologic emergency, given the observation that there is less recovery of hearing when treatment is delayed. There are no published guidelines for evaluation or management of sudden sensorineural hearing loss. The lack of a standard definition for SSNHL, lack of a standard method for audiological assessment with regard to the configuration of hearing loss and hearing recovery, low incidence rate and the fact that spontaneous recovery occurs in upto 65% of cases make any evaluation and treatment difficult for an otolaryngologist.⁶ From a therapeutic point of view the most widely accepted treatment for SHL is systemic corticosteroids,⁷ due to their ability to reduce inflammation, inhibit immune mechanisms and regulate electrolyte balance. Oral corticosteroid therapy is among the few treatment

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Corresponding Author:

Dr. Rajeev Yande,

Jeevan Sadhna Clinic,

Near Yatri Hotel, Karve Road,

Pune-411029, Maharashtra, India.

E-mail: drrdyande@gmail.com

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modalities that have gained acceptance and proved to be effective in selected studies. However, studies have shown that corticosteroid treatment is not significantly more effective than placebo and includes adverse effects.⁸

Thus, there have been continuous efforts to identify additional treatments. In case of SHL caused by viral infection, studies on antiviral therapy have shown controversial therapeutic results.⁹

Carbogen therapy is one of them which acts by inhalation, increases arterial oxygen saturation and maximises oxygen supply to the inner ear.¹⁰ Studies on the effects of carbogen therapy in SHL have shown controversial results. Shea and Kitabchi¹¹ reported that carbogen inhalation had a therapeutic effect, while Cinamon et al⁸ found no therapeutic effect. Similarly, Zhao et al¹² reported that Lipo-PGE1 had a therapeutic effect, while Ahn et al¹³ found no therapeutic effect. Despite controversial benefits, the theories remain that improving circulation may yield therapeutic results in cases where a vascular disorder underlies the SHL.

In this study, we compared two modalities of treatment options for SHL, carbogen inhalation combined with steroids to the steroids alone.

Aims and Objectives

Compare the efficacy of carbogen therapy combined with steroids, is whether or not superior to steroids alone in the treatment of sudden hearing loss.

MATERIALS AND METHODS

We have conducted the pilot survey of 10 patients for each group by considering the mean hearing loss at 10th sitting 34.15 (Group 1) and 37.41 (Group 2) with standard deviation of 13.35 and 12.47.

Sample size calculated by using 2 independent sample mean
 Total Sample size is $(N) = 4 * (M1-M2) / (SD)^2$
 Where, M1 is mean group 1, M2 is mean group 2
 SD= Standard deviation, Total Sample size is 63.

We studied 60 patients, who visited the outpatient department. It was a prospective non-randomised controlled parallel trial. Ruby Hall Clinic hospital is amongst one of the limited set-ups where carbogen therapy is administered; hence, we get referred patients of ISSNHL both from peripheries and the city itself. Patients of either sex between age group 15 - 65 years were included, who sustained sudden unilateral hearing loss in 72 hrs. or less duration and presented to us within 14 days of beginning of symptoms. Patients with similar history in past, local trauma, previous ear surgeries or having systemic illnesses were excluded. Patients were allocated in two groups, 1, 3, 5, 7.... in Group 1 and 2, 4, 6, 8...so on in Group 2. All patients underwent a thorough history and physical examination, pure tone audiometry, speech audiometry and impedance audiometry. Informed consent was obtained from all individuals and were included in the study.

Group 2 received oral prednisolone 1 mg/kg body wt. for 5 days and tapered over next 5 days (60 mg 1st 5 days, 30 mg day 6 and 7, 10 mg last three days) and Group 1 received additional inhalation of carbogen (5% CO₂ + 95% O₂ mixture). Carbogen therapy was administered to the patient for 30 minutes daily for 5 days using Magill's circuit and anatomical facemask by setting a flow of 5 litres/min of O₂ and 250

mL/min of CO₂. Patient was monitored throughout and signs and symptoms of CO₂ retention such as sweating, tachycardia or hypertension were observed.

Patients were evaluated for hearing gain by taking pure tone average at 0.5, 1 and 2 kHz pre-therapy at the time of presentation and post therapy. Patients in Group 1 underwent follow-up audiometry after 5th sitting and 10th sitting of carbogen therapy; as for Group 2 patients pre-therapy audiometry and post-therapy after 10 days. All patients were called on request at 2 months and pure tone audiometry was repeated and pure tone averages compared with previous results.

Statistical Analysis

Statistical analysis was done using Stata version 10 (StataCorp, Texas and USA). Students' test, Chi-square test and Fisher's 'exact' test was used for categorical variables.

Type	Hearing Recovery
I. Complete recovery	Final hearing better than 25 dB
II. Partial recovery	More than 15 dB gain, final hearing 25 - 45 dB
III. Slight improvement	More than 15 dB gain, final hearing poorer than 45 dB
IV. No improvement	Less than 15 dB gain, final hearing poorer than 75 dB

Table 1. Siegel's Criteria of Hearing Recovery

RESULTS

Patient's Characteristics

Out of 60 patients included in our study, 29 were males and 31 were females. Their mean age was 41.73 ± 16.71 for Group 1 and 38.73 ± 12.91 for Group 2 (range 15 - 65 years). The average time between onset of symptoms and presenting to clinic in two groups were 6.3 ± 3.21 and 6.93 ± 2.61 in Group 1 and 2 respectively. There was no significant difference in age, gender, mean duration of SHL, mean threshold of hearing loss, follow-up period, laterality of ear affected and disease symptoms between the two groups.

Age Group	Group		Total
	Group 1	Group 2	
≤ 20	4	3	7
21 - 30	5	6	11
31 - 40	7	8	15
41 - 50	7	9	16
51 - 60	6	3	9
> 60	1	1	2
Total	30	30	60

Table 2a. Comparison of Age (in years) in Group 1 and Group 2

	Number of Patients	Age (Years)		P-value
		Mean	SD	
Group 1	30	41.73	16.71	0.440
Group 2	30	38.73	12.91	

2b. Comparison of Age (in years) in Group 1 and Group 2

By using 2 independent sample t-test p-value > 0.05, therefore there is no significant difference between mean age (years) in Group 1 and Group 2.

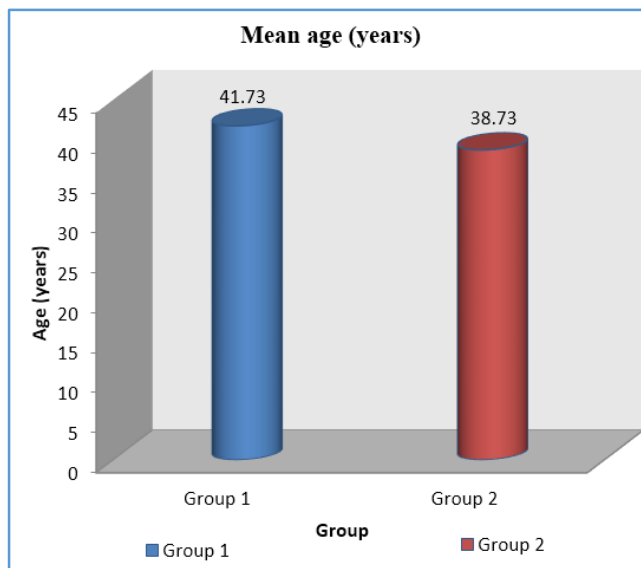


Figure 1. Comparison of Mean Age in Two Groups

HL	Group 1 (n= 30)		Group 2 (n= 30)		P-value
	Mean	SD	Mean	SD	
At baseline	61.19	15.62	59.31	10.85	0.59
At 10th sitting	34.16	13.32	37.53	12.36	0.313
At 2nd month	32.63	13.09	34.00	11.37	0.668

Table 3. Comparison of Mean HL in Group 1 and Group 2

By using 2 independent sample t-test p-value > 0.05, therefore there is no significant difference between mean HL in Group 1 and Group 2.

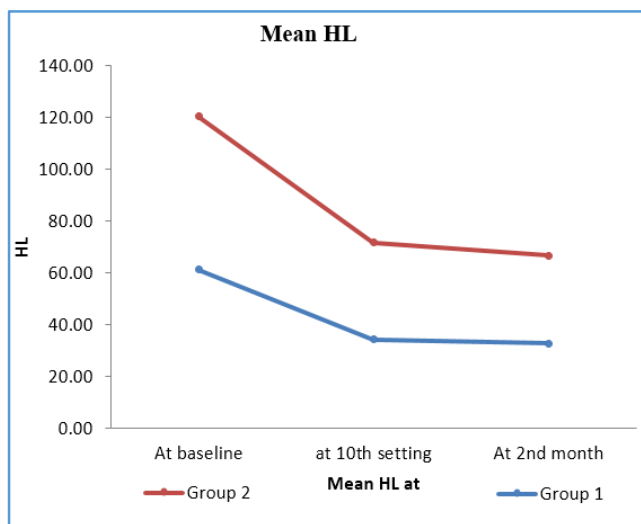


Figure 2. Comparison of Mean HL in Group 1 and Group 2

	Group 1		Group 2		P-value
	Mean	SD	Mean	SD	
RHG at 5th sitting	8.93	7.24	-	-	-
RHG at 10th sitting	27.03	11.79	21.78	11.83	0.09
RHG at 2nd month	28.56	11.45	25.31	11.58	0.279

Table 4. Comparison of Mean of Relative Hearing Gain in Two Groups

By using 2 independent sample t-test p-value > 0.05, therefore there is no significant difference between mean change in HL at 10th sitting and 2nd month.

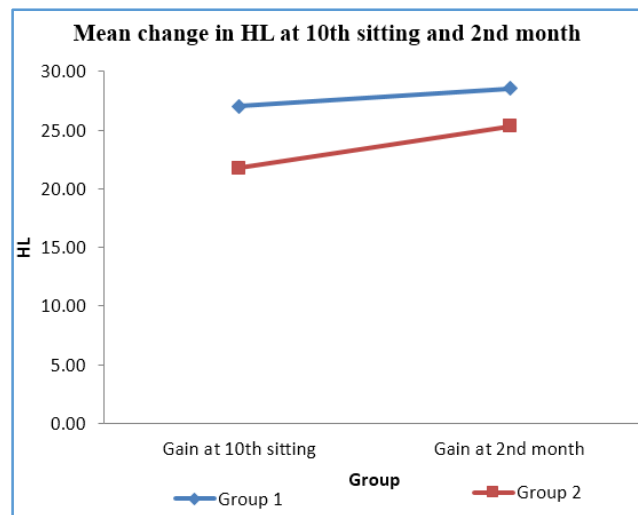


Figure 3. Comparison of Mean of Relative Hearing Gain in Two Groups

		Siegel's Criteria				Total	P-value
		Complete Recovery	Partial Recovery	Slight Improvement	No Improvement		
5th sitting	Group 1	0	11	19	0	30	-
	Group 2	0	0	0	0	0	
10th sitting	Group 1	9	14	7	0	30	0.267
	Group 2	5	20	4	1	30	
2nd month	Group 1	10	16	4	0	30	0.591
	Group 2	8	20	2	0	30	

Table 5. Comparison of Hearing Recovery based on Siegel's Criteria

By using Fisher's exact test p-value > 0.05, therefore there is no significant association between Siegel's grade with Group 1 and Group 2.

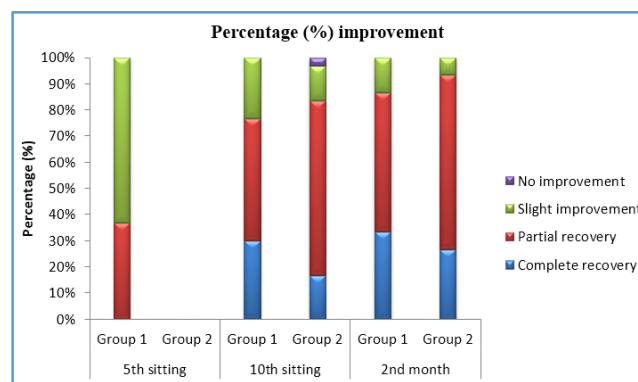


Figure 4. Comparison of % of improvement in Corresponding Group

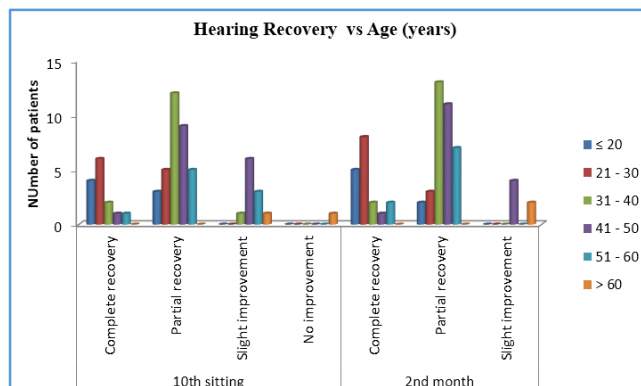


Figure 5. Comparison of Outcome based on Age of Incidence of ISSNHL

Hearing Change

We observed in our study that complete recovery at two months occurred in 33.33% and 26.67% subjects in Group 1 and 2 correspondingly.

As for partial recovery, 53.33% and 66.67% in Group 1 and 2 correspondingly (Siegel's criteria 1 and 2).

Slight improvement was noticed as follows- at 10th sitting 23.33% and 13.33% and at 2 months 13.33% and 6.67% in corresponding group.

We also found that after initiating carbogen post 5th sitting of therapy, there was hearing improvement of 33.67% (Partial recovery) and 66.33% (Slight improvement) in the carbogen group (Table 5).

Though these results show that carbogen therapy is better than steroids, the data is calculated to be statistically insignificant using Fisher's exact test (p-value 0.267 and 0.591 > 0.05).

In regard to the average relative hearing gain, i.e. RHG (hearing difference between pre- and post-pure tone threshold) was 27.03 ± 11.79 on 10th day and 28.56 ± 11.45 at 2 months in Group 1, correspondingly it was 21.78 ± 11.83 and 25.31 ± 11.58 in Group 2.

By comparing this data, carbogen group has higher RHG as compared to steroid only group both at 10 days and 2 months follow-up. But there was no statistically significant difference found using independent sample student t-test between RHG at 10th sitting and 2nd month in Group 1 and Group 2 (p-values 0.09 and 0.279 > 0.05).

Outcome based on Age

We also observed that the patients who had ISSNHL at older age showed poorer hearing improved as compared to younger age group of patients, both at 10th day and 2nd month of follow-up. This data by using Fisher's exact test is calculated to be significant statistically and hence there is association between hearing outcome with increasing age (p value= 0.01 i.e. < 0.05).

Complications

There were no major complications during our treatment. Vitals were monitored for all the patients throughout carbogen sittings and were stable. We did not observe tachycardia, hypertension or sweating for any of our patients. Few of the patients complained of feeling of suffocation on starting of CO₂ gas, which weaned off in 5 - 10 seconds of discontinuation.

DISCUSSION

Although, the underlying mechanism of SHL is unknown, the most common causes are thought to be vascular disorders and inflammatory reactions due to viral insult of the inner ear. Antivirals have been proposed to treat SHL caused by a viral infection, although Stokroos et al⁹ found no significant difference in recovery between patients receiving acyclovir (68% of 22 patients) and those in the control group (43% of 21 patients). Furthermore, Westerlaken et al¹⁴ reported that antiviral treatment had no effect on hearing gain.

Lee HJ et al¹⁵ in 2012 retrospectively reviewed 202 patients with idiopathic SHL. In their study, it was concluded that Carbogen inhalation added to steroid was a more effective treatment than Lipo-PGE1 added to steroid or steroid alone in patients with SHL. Chaturvedi et al¹⁶ in 1990 studied therapeutic role of carbogen therapy evaluated in subjects with sensorineural hearing loss and significant improvement was observed both in air and bone conduction threshold levels on seventh day of carbogen administration. They concluded that improvement in hearing may be due to action of CO₂ as an otic vasodilator coupled with supplementation of the O₂ requirement of degenerating hair cells.

Carbogen inhalation therapy (inhalation of a mixture of 5% CO₂ and 95% O₂) is based on the theory that carbon dioxide causes vasodilation, increasing blood flow and oxygen to the injured hair cells of cochlear and inner ear structures. According to a study on therapeutic gas proportions, arterial CO₂ tension affects oxygen saturation more than does arterial O₂ tension. The authors reported that inhalation of 100% O₂ gas decreased perilymphic oxygen saturation, while inhalation of a mixture of 95% O₂ with 5% CO₂ increased perilymphic oxygen saturation.¹⁰

Likewise, Fisch et al¹⁷ reported that carbogen inhalation increases inner ear oxygen saturation as measured by perilymphic oxygen saturation. Furthermore, Kallinen et al¹⁸ reported that carbogen inhalation is an effective treatment for high frequency hearing loss, although there was no significant difference in RHG in frequencies between patients receiving carbogen and those receiving Lipo-PGE1 in this study.

In conclusion, SHL has a variety of causes and is currently treated with combination modalities. Our findings suggest that efficacy of carbogen inhalation treatment is positive and it can be beneficial and additive to relative hearing gain and hence better hearing outcome.

We also found that there is significant association between age of onset of sensorineural hearing loss and betterment of hearing. Younger the age at the time of onset of hearing loss, there are better chances of hearing gain towards normal hearing sensitivity.

CONCLUSION

There is no definite treatment protocol available at present for ISSNHL, most accepted treatment modality being systemic steroids. In our study, we conclude that carbogen therapy is a beneficial addition to steroids in the treatment of sudden sensorineural hearing loss.

REFERENCES

- [1] Arts HA. Sensorineural hearing loss in adults. In: Flint PW, edr. Cummings Otolaryngology: head & neck surgery. 5th edn. Philadelphia: Mosby 2010: p. 2117-30.
- [2] De Kleyn A. Sudden complete or partial loss of function of the octavus-system in apparently normal persons. *Acta Otolaryngol* 1944;32(5-6):407-29.
- [3] Byl FM Jr. Sudden hearing loss: eight years' experience and suggested prognostic table. *Laryngoscope* 1984;94(5 Pt 1):647-61.
- [4] Hughes GB, Freedman MA, Haberkamp TJ, et al. Sudden sensorineural hearing loss. *Otolaryngologic Clinics of North America* 1996;29(3):393-405.
- [5] Fetterman BL, Luxford WM, Saunders JE. Sudden bilateral sensorineural hearing loss. *Laryngoscope* 1996;106(11):1347-50.
- [6] Mattox DE, Simmons FB. Natural history of sudden sensorineural hearing loss. *Ann Otol Rhinol Laryngol* 1977;86(4 Pt 1):463-80.
- [7] Wilson WR, Byl FM, Laird N. The efficacy of steroids in the treatment of idiopathic sudden hearing loss. A double-blind clinical study. *Arch Otolaryngol* 1980;106(12):772-6.
- [8] Cinamon U, Bendet E, Kronenberg J. Steroids, carbogen or placebo for sudden hearing loss: a prospective double-blind study. *Eur Arch Otorhinolaryngol* 2001;258(9):477-80.
- [9] Stokroos RJ, Albers FW, Tenvergert EM. Antiviral treatment of idiopathic sudden sensorineural hearing loss: a prospective, randomized, double-blind clinical trial. *Acta Otolaryngol* 1998;118(4):488-95.
- [10] Kallinen J, Didier A, Miller JM, et al. The effect of CO₂- and O₂-gas mixtures on laser Doppler measured cochlear and skin blood flow in guinea pigs. *Hear Res* 1991;55(2):255-62.
- [11] Shea JJ, Kitabchi AE. Management of fluctuant hearing loss. *Arch Otolaryngol* 1973;97(2):118-24.
- [12] Ni Y, Zhao X. Carbogen combined with drugs in the treatment of sudden deafness. *Lin Chuang Er Bi Yan Hou Ke Za Zhi* 2004;18(7):414-5.
- [13] Ahn JH, Kim MR, Kim HC. Therapeutic effect of lipoprostaglandin E1 on sudden hearing loss. *Am J Otolaryngol* 2005;26(4):245-8.
- [14] Westerlaken BO, de Kleine E, van der Laan B, et al. The treatment of idiopathic sudden sensorineural hearing loss using pulse therapy: a prospective, randomized, double-blind clinical trial. *The Laryngoscope* 2007;117(4):684-90.
- [15] Lee HJ, Park CY, Lee JH, et al. Therapeutic effects of carbogen inhalation and lipo prostaglandin E1 in sudden hearing loss. *Yonsei Med J* 2012;53(5):999-1004.
- [16] Chaturvedi RC, Rai RM, Sharma RK. Therapeutic role of carbogen in impaired hearing. *Indian J Med Res* 1990;92:420-3.
- [17] Fisch U, Murata K, Hossli G. Measurement of oxygen tension in human perilymph. *Acta Otolaryngol* 1976;81(3-4):278-82.
- [18] Kallinen J, Laurikainen E, Laippala P, et al. Sudden deafness: a comparison of anticoagulant therapy and carbogen inhalation therapy. *Ann Otol Rhinol Laryngol* 1997;106(1):22-6.