DOI: 10.18410/jebmh/2015/776

ORIGINAL ARTICLE

STUDY OF HEARING OUTCOMES IN SUDDEN SENSORINEURAL HEARING LOSS TREATED WITH TISSUE PLASMINOGEN ACTIVATOR (TPA)

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HOW TO CITE THIS ARTICLE:
Rama Krishna Tirumalabukkapatnam, Jagannatha Prasad B, Jyothi Ramakrishna, Khalsa Gurbeer Kaur, Syeda Ayesha, Devika Shere. "Study of Hearing Outcomes in Sudden Sensorineural Hearing Loss Treated With Tissue Plasminogen Activator (tPA)". Journal of Evidence based Medicine and Healthcare; Volume 2, Issue 36, September 07, 2015; Page: 5624-5629, DOI: 10.18410/jebmh/2015/776

ABSTRACT: Sudden Sensorineural Hearing Loss (SSHNL) is a clinical condition that requires immediate management. There are many treatment options, which may not always revert the hearing to normal. Not only recording the degree of hearing loss, but also establishing the concurrent dysfunction of saccule by VEMP has facilitated a new approach to treatment strategy. Recombinant tissue Plasminogen Activator ((rtPA) proved its efficacy in stroke and subsequently considered an option in the management of ISSNHL. The current study, conducted at different centres, on 15 patients utilized rtPA. The results showed a promising trend when saccular pathology is also evident by VEMP in association with Hearing loss. We recommend use of rtPA as primary modality in cases of ISSNHL with Saccular involvement.
KEYWORDS: rtPA, tPA, Idiopathic Sudden Sensorineural Hearing Loss, ISSNHL, SSNHL.

INTRODUCTION: Idiopathic sudden sensory neural hearing loss (ISSHN) is a disorder with no definitive aetiology. Hence the treatment modalities are varied as there are numerous hypotheses. The aetiology ranges from viral infections, autoimmune disorder, trauma and vascular ischemia with or without micro thrombi formation.(1) The micro thrombotic process may be due to primary or secondary to an inflammatory process. The micro thrombus formation has been associated with endolymphatic hydrops.(2) When the hydrops involves vestibular organs (saccule) there will be vertiginous attacks or unsteadiness in addition to hearing loss. The saccular pathology has been effectively and increasingly detected by vestibular evoked myogenic potentials (VEMP).(3) The role of VEMP in early detection of Meniere's disease and with glycerol testing has been well known.(4) The use of thrombolytics and fibrinolytics in the treatment of ISSHN were partially successful. Inappropriate selection of patients and dosage schedules may be a factor. A new molecule called tissue plasminogen activator (tPA) has been developed using recombinant technology (rtPA). We present our experience with rtPA in a group of patients with ISSHN.

AIM: To evaluate the efficacy of Recombinant Tissue Plasminogen activator (rtPA) in ISSNHL

OBJECTIVES:

1. To assess the involvement of saccule in cases of Idiopathic sudden sensorineural hearing loss patients by using VEMP in two age groups of patients.

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2. To assess the improvement in hearing after treating with rtPA in two groups of cochlear pathology and sacculocochlear pathology.

MATERIAL AND METHODS: In our institution, we reviewed the clinical records of Fifteen patients who presented with Sudden Sensorineural hearing Loss to the department of ENT during the period of January 2007 to December 2013. All the patients were evaluated with detailed clinical history, complete audiological profile (including BSERA and Short Increment Sensitivity Index), CT Scan Brian (with contrast wherever necessary) and Vestibular Evoked Myogenic Potentials (VEMP).

No case with head injury, intracranial lesions (CP angle tumors, Multiple Sclerosis), or Coronary artery Disease were taken. Patients with previous ear surgeries were excluded.

Out of fifteen patients, 6 patients received Transtympanic Steroid injections (Dexamethasone) for 5days before reporting to our institution as there was no improvement. Their presentation was after 3 weeks of onset of hearing impairment. They along with nine patients received Recombinant tissue Plasminogen activator (rtPA) in a single dose of 5mg on first day, and 3mg/12 hourly on second to fifth day. Pure tone audiometry (PTA), Short increment sensitivity index (SISI), Vestibular evoked potentials and Speech Discrimination scores were done daily and during follow up period at 3months, and one year.

OUTCOME MEASURE: An improvement of 20dB in the frequency range of 500Hz-4000Hz is considered "Moderate recovery" and 30dB improvement as" Good recovery".

Any improvement less than 20dB is considered failure.

Speech discrimination scores of more than 85% are considered successful.

Vestibular evoked Myogenic Potentials (VEMP) was done on all the patients at the time of admission and at the time of six month follow up.

Patient no.	Age/sex	Side	Reporting Time after the hearing loss	Associated vertigo	Loudness intolerance
1	34/M	R	24hrs	No	yes
2	65/F	L	20days	Yes	Yes
3	55/F	L	9days	Yes	Yes
4	46/F	R	48hrs	No	yes
5	70/M	L	72hrs	Yes	yes
6	56	R	48hrs	Yes	Yes
7	67	L	72hrs	Yes	No
8	35	L	7days	Yes	No
9	67	R	48hrs	yes	yes
10	44`	R	72hrs	Yes	Yes
11	75	L	25days	No	No
12	68	L	48hrs	No	Yes

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13	57	R	14days	Yes	Yes
14	74	R	18days	Yes	No
15	46	L	72hrs	Yes	yes

Table 1: Patient data with symptoms of vertigo and loudness intolerance

	Total number	**Only SISI positive (>65% score)**	**SISI & VEMP positive (Cochleo-saccular pathology)**
Less than 60 years (Group I)	5	2	3
61 years or more (Group II)	4	2	2

Table 2: Results of Short Increment sensitivity Index and VEMP in Two age groups, reported to hospital within 72 hours (sub group A)

	Total number	**SISI >65%**	**SISI & VEMP positive (Cochleo-saccular pathology)**
Less than 60 years (Group I)	3	2	-
61years or more (Group II)	3	-	1

Table 3: Results of Short Increment sensitivity Index and VEMP in Two age groups, reported to hospital later than 72 hours (sub group B)

	Group I A N:5	**Group II A N:4**	**Group I B N:3**	**Group II B N:3**
Good recovery 30dB or more	5 SISI:2 SISI & VEMP: 3	3 SISI:1 SISI & VEMP:2	2 SISI:2 VEMP:---	0
Moderate recovery 20db or more	0	1 SISI & VEMP:1	0	2 SISI & VEMP:1
No recovery	-	-	1	1

Table 4: Results of Hearing Improvement with relation to Age groups, SISI and VEMP

RESULTS: The data from table I indicates that vertigo and loud intolerance are predominant in 11 out of 15 patients. Three out of six in the group of patients who received dexamethasone by trans tympanic route were presented with loud intolerance and vertigo.

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Audiological evaluations with SISI scores were analysed and found to be positive in all the patients (100%) who presented with in 72hours. There were 5patients who showed saccular involvement in addition to cochlear pathology as detected on VEMP.

Only 2 out of 6 patients who received Steroid treatment earlier (sub group B) showed recruitment. However one patient showed saccular involvement. Table 4 depicted the outcome measure. Irrespective of age groups, rtPA showed improvement substantially when treatment was instituted within 72hours of onset of hearing loss. In those patients who were initially treated by dexamethasone, 4 out of 6 could regain substantial hearing. When cochleosaccular pathology (as seen by SISI and VEMP) was present, 5out of 6(83%) showed good recovery irrespective of age groups. In the group B, it was seen in only one case and showed moderate recovery.

While SISI scores (only cochlear pathology) were positive in 5 cases, all showed good recovery.

DISCUSSION: Sudden Sensorineural hearing loss is a challenging problem when it happens suddenly. Numerous theories have been put forward, with vascular ischaemia as a cause is gaining momentum. Cadoni et al. 2007,[5] observed that high levels of cholesterol and low levels of coenzyme Q are associated with SHL. This leads to speculation that micro thrombi formation may be a triggering factor in the causation of ISSHNL. Thus the role of serine protease (tPA), which catalyzes the conversion of plasminogen to plasmin, the major enzyme responsible for clot breakdown has been established. There are two different mechanisms conceived in causation of ISSNHL. The first mechanism is hyperlipidaemia that damages the endothelial lining of cochlear blood vessels. The second mechanism is hyper fibrinogenemia.[6] Both mechanisms put together cause dysfunction of outer hair cells, by causing spasm of artery of spiral modiolus and vestibulo-cochlear artery.

It is generally believed that disequilibrium when present along with ISSNHL is an indicator of poor prognosis.[7] Hypoactive caloric responses at the time of hearing loss are considered unfavourable prognostic indicator.[8] It is to be remembered that these observations were applicable to studies done with systemic steroids, low molecular dextran infusions, and trans tympanic dexamethasone injections. However, current study is not in agreement with the previous views. Whenever the ISSHNL is associated with recruitment and saccular paresis, the option of tissue Plasminogen Activator seems reasonable, as the pathology seems to be one of micro emboli formation due to vascular spasm or hyperlipidaemia. At this juncture, it is worthwhile to note the classification proposed by Iwasaki.[9] He classified the pathogenesis into three categories; C+S(cochlea and saccule), C+O(cochlea and Otolith organs) and C+O+S (cochlea, Otolith and Saccule). In a study conducted in 100 patients of SSHNL, abnormal VEMPs were observed in more than half (52%), attributed to sacculo-cochlear lesion or to brainstem hypo perfusion.[10] Profound hearing loss was observed in lesions with otolith organ and semicircular canal lesions.In patients with BPPV associated with SSNHL, Park et al.[11] found hearing loss of profound degree. Thus ISSNHL cannot be treated in isolation. If there were additional findings suggestive of saccular or otolith dysfunction, it is better treated with thrombolytics or rtPA.[12]

In our study, there were no adverse reactions or long term side effects by rtPA therapy. The advantage of rtPA even in a failed trans tympanic steroid therapy is well documented in our study

CONCLUSION: Sudden Sensorineural hearing loss (SSHNL or ISSHNL) is a challenging problem in ENT practice. Numerous mechanisms were suggested in the pathogenesis. Micro thrombi formation by hyperlipidaemia and hyper fibrinogenemia are being more often recognized in the patients with ISSNHL. Tissue Plasminogen Activator (tPA) has been attempted with varied results. We have conducted a long term study with recombinant tissue plasminogen activator (rtPA) with evidence based tests (SISI, VEMP) and found that rtPA is highly effective in ISSNHL associated with sacculo-cochlear pathologies.

ACKNOWLEDGEMENTS: We sincerely thank Dr.Ganga Vara Prasad (ENT surgeon), Miryalaguda, and Nalgonda District for constant support during the follow up of patients. Our sincere thanks to Dr. Geeta Lima Dutta, DNB (ENT) for her untiring efforts in conducting VEMP.

Our sincere gratitude to Dr. Junaid Pasha, RMO and Dr. Vasantha Prasad, Medical Superintendent, Shadan Institute of Medical Sciences, Peeramcheru, Hyderabad for constant encouragement and support during the manuscript preparation.

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Date of Submission: 24/08/2015.
Date of Peer Review: 25/08/2015.
Date of Acceptance: 29/08/2015.
Date of Publishing: 03/09/2015.