ROSUVASTATIN AS A POSSIBLE TREATMENT FOR SUDDEN SENSORINEURAL HEARING LOSS

Syed Nadeem Ul Haq, Zeeshan Ayub Sheikh*, Ahmed Hasan Ashfaq, Azeema Ahmed*, Naeema Ahmed*****

Combined Military Hospital Quetta/National University of Medical Sciences (NUMS) Pakistan, *PAF Hospital, Sargodha Pakistan, **Holy Family Hospital, Islamabad Pakistan, ***Army Medical College/National University of Medical Sciences (NUMS) Rawalpindi Pakistan

ABSTRACT

Objective: To determine the role of Rosuvastatin as a possible treatment of sudden sensorineural hearing loss.
Study Design: Quasi-experimental study.
Place and Duration of Study: ENT Departments, Combined Military Hospital Quetta & Combined Military Hospital Lahore, from Apr 2015 to Sep 2017.
Methodology: This quasi-experimental study performed at Combined Military Hospital Quetta & Combined Military Hospital Lahore comprised of seventy-eight patients of sudden sensorineural hearing loss (SSNHL) having hyperlipidemia. Patients pre-treatment total serum cholesterol was measured, and hearing loss in speech frequencies was recorded on audiometry. The seventy-eight patients were administered tablet Rosuvastatin 10mg once daily with low fat diet for 4 months. On completion of 4 months of treatment, patients were selected by using non probability purposive sampling and divided into responder and non-responder group depending on total serum cholesterol levels. Post treatment total serum cholesterol levels and improvement in hearing levels were also recorded and graded according to siegel's criteria.
Results: Total serum cholesterol came to within normal limits in 43 (55.1%) patients (responder), while it remained high in 35 (44.9%) patients (non-responder group). Improvement in hearing scores was assessed using siegel's criteria. pearson chi square test showed statistically significant improvement (p=0.001) in hearing scores among responder group as compared to non-responder group.
Conclusion: Sudden sensorineural hearing loss, in patients having hyperlipidemia, can be managed by treating hyperlipidemia with lipidlowering agent rosuvastatin.

Keywords: Hyperlipidemias, Rosuvastatin, Sensorineural hearing loss.

INTRODUCTION

Sudden sensorineural hearing loss (SSNHL) is defined as hearing impairment of more than a 30 DB decrease, occurring over a 72 hour period, on three consecutive speech frequencies on Pure Tone Audiometry[1]. SSNHL carries a prevalence rate of 5 to 20 per 100,000 persons in United States of America[2].

Despite being not a so uncommon disease, its exact pathophysiology and causes have yet to be determined. Microcirculatory system of cochlear circulation has a pivotal rolein inner ear disease pathophysiology. Raised serum lipid and glucose levels are linked with increase in blood viscosity and a higher incidence of circulator disorders. Circulatory disorders of the stria vascularis, like atherosclerotic processes have been positively linked with hair cell damage leading to innerear diseases like vertigo and sensorineural hearing loss[3].

Metabolic disorders like altered lipid synthesis and a rise in cholesterol catabolism leadsto elevated serum cholesterol readings, further contributing to the atherosclerotic process. Trauma to vascular endothelium as a result of immune complex formation coupled with atherosclerotic process, results in increased vascular permeability, alteration in the structure of basement membrane and abnormal proliferation of endothelial cells leading to enhancement of Atherosclerosis. All the pathological processes culminate in reducing luminal patency of vessels[4]. The membranous

Correspondence: Dr Zeeshan Ayub Sheikh, Asst Prof, Classified ENT Specialist, PAF Hospital, Sargodha, Pakistan
Email: zeeshanent@yahoo.com
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labyrinth is perfused by the labyrinthine artery, whichis anend-arterial branch of the anterior inferior cerebellar artery. Labyrinthine artery is an end arteryjust like coronary vessels, thereby theoretically susceptible to a thromboembolic event like the coronary arteries. Membranous Labyrinth does not have any collateral circulation and this phenomenon coupled with atherosclerotic process negatively affects the cochlea by depriving the Labyrinth of oxygen and nutrients[5].

The fact that treatment of SSNHL involves multiple therapies, drugs and regimens, points towards the observation that pathophysiology of the disease process is not known. Among the postulated pathogenesis, vascular perfusion seems most plausible as multiple inner ear issues like early onset SSNHL[6], and tinnitus have an association with compromised blood supply[7]. Similarly, if SSNHL is managed along with lipid lowering drugs in conjunction with other treatment modalities, patients can have a better chance of recovery.

METHODOLOGY

This quasi-experimental study was performed at Combined Military Hospital Quetta & Combined Military Hospital Lahore, from April 2015 to September 2017 comprised of Seventy-eight patients of SSNHL having hyperlipidemia. Sample size was determined by WHO sample size calculator, by keeping 95% confidence interval, 5% error&prevalence rate of 5 to 20 per 100, 000 persons per year[2], i.e. Seventy-eight patients of SSNHL with hyperlipidemia. Patients were selected by using non probability purposive sampling and divided into responder and non-responder group depending on total serum cholesterol levels.

The patients were selected according to their history and subsequently pure tone audiometry was done to confirm SSNHL. Any Patients who had either previous history of SSNHL, hearing loss on the contralateral ear, preexisting ipsilateral or contralateral tinnitus, diabetes mellitus, hypertension, history of vertigo, or any anatomical abnormalities on computerized tomography (CT scan) of petrous boneand patients with normal serum cholesterol were excluded from the study.

Their pre-treatment total serum cholesterols were measured using Fully Automated Chemistry Analyzer Selectra Pro M, using Cholesterol Oxidase End Pointmethod. Serum Cholesterol more than 5.1mm l/l was taken as raised serum cholesterol. The seventy-eight patients selected according to inclusion criteria were apprised of their disease and informed consent obtained. Other than pure tone audiometry, CT scan petrous bone, blood complete picture, and blood sugar fasting were done. All patients were administered tablet Rosuvastatin 10 mg once daily with low fat diet for 2 months. On completion of 2 months of treatment, patients were selected by using non probability purpose sampling and divided into responder and non-responder group depending on total serum cholesterol levels, with responder group having normal total serum cholesterol (<5.1 mmol/l). Post treatment total serum cholesterol levels were checked, and hearing was assessed using pure tone audiometry. improvement in hearing levels were assessed according to siegel's hearing recovery criteria[3]. All participating patients were also given a ten day course of prednisone (1mg/kg/day) followed by a slow tapering, also a diuretic tablet indapamide 2.5mg daily was given for 30 days. Sodium-restricted diet was advised and continued for 2 months.

Hearing loss recovery at end of two months was assessed by calculating average hearing levels in four speech frequencies i.e. 500 Hertz, 1000 Hertz, 2000 Hertz, and 4000 Hertz. Improvement in hearing levels following treatment was done by Siegel's criteria adapted as follows.

Complete recovery

Post treatment average hearing threshold of 25 Decibel (dB) or better.

Partial recovery

Post treatment recovery more than 15-dB gain and final hearing between 25–45 dB.

Slight Recovery

Post treatment recovery more than 15-dB improvement, but final hearing poorer than 45 dB.

No Recovery

Post treatment recovery less than 15-dB and final hearing worse than 75 dB. The data was entered in SPSS version 24. For purpose of statistical analysis "Complete Recovery" & "Partial Recovery" were taken as patients with "Hearing Improvement", whereas patients with "Slight Recovery" & "No Recovery" were taken as patients with "No HearingImprovement". Frequency and percentage was calculated for gender and laterality of disease. Mean and SD were calculated for quantitative variable & Pearson chi square test was used..

RESULTS

A total of 78 patients of SSNHL were included in the study with serum cholesterol levels ranging from 239–356 mg/dl. The study group comprised of 23 (29.4%) females and 55 (70.6%) males with ages ranging from 23 to 67 years. The mean age was 46.9 ± 14.8 years. Concerning laterality of disease, left ear was diseased in 31 (39.7%) patients and right ear was involved in 47 (60.3%) patients. At end of two months' therapy patients were divided using non probability purpose sampling into Responder (having normal total serum cholesterol levels) 43 (55.1%) and non-respondern 35 (44.9%) groups. Serum cholesterol levels in responsive group ranged from1 56-197 mg/dl and in the unresponsive group ranged from 241-369 mg/dl.

Post therapy outcome according to Siegels criteria[3] for both Responder 43 (55.1%) and non-responder 35 (44.9%) group are as shown in table-I (*p*-value=0.001). This result shows that Rosuvastatin has a positive outcome on hearing recovery after two months of use in cases of SSNHL.

DISCUSSION

Steroids have been used over many years for SSNHL without proper understanding the role of cochlear microcirculation in disease patho-physiology. Introduction of a lipid lowering agent along with steroids gives a better chance of recovery as elucidated by the results of this study.

Membranous labyrinth is perfused by labyrinthine artery, a branch of basilar artery. Labyrinthine artery is an end artery without any collaterals. Thus cochlea is an end organ susceptible to ischemic damage. As the labyrinthine artery enters the internal acoustic meatus it bifurcates into two terminal divisions namely the vestibular and cochlear arteries. The cochlear artery supplies the cochlea and part of vestibule whereas vestibular artery solely supplies the vestibule[8]. Therefore, there is a high probability that factors such as atherosclerosis, thrombi, emboli, arteriolar vasospasm resulting in decreased blood flow may eventually cause vascular insufficiency and thereby lead to damage of the cochlea.

Like myocardial infarction, a sudden ischemic event of the cochlear structures may be the cause of SSNHL. This hypothesis gives weight to a vascular etiology for SSNHL[9]. Presence of distortion product otoacoustic emissions have

Table: Hearing recovery.

Patients (n=78)	Post Therapy Outcome				*p*-value
	Complete Recovery (Hearing Improvement)	Partial Recovery (Hearing Improvement)	Slight Improvement (No Hearing Improvement)	No Improvement (No Hearing Improvement)	
Responder Group 43 (55.1%)	18 (23.1%)	13 (16.7%)	9 (11.5%)	3 (3.8%)	0.001
Non-Responder Group, 35 (44.9%)	4 (5.1%)	3 (3.8%)	16 (20.5%)	12 (15.4%)	

also been seen in patients suffering from high cholesterol levels and diabetes mellitus[10]. Poor perfusion adversely effects performance of the antioxidant enzymes resulting in free radical accumulation. Inner haircells of the cochlea are less resilient as compared to outer hair cells and peroxidative damage is more likely in inner hair cells[11].

Animal model studies have shown that anti hyperlipidemics like simvastatin have a protective effect on cells by inducing enzymatic degradation of HMG-Co A into mevalonate,an initial and rate limiting part of cholesterol synthesis cycle[12].

Lin *et al* conducted an experiment comprising of study cohort and a comparison cohort group, comprising of more than 7000 patients. They tried to estimate the risk of stroke development in patients of SSNHL by following these patients over a five-year period. The authors concluded in their study that an episode of SSNHL can be used an early warning sign of impending stroke in susceptible patients, as patients who had a history of SSNHL had a 1.63% more chance of developing an ischemic stroke in the next 5 years. The authors further suggested that every case of SSNHL should undergo a comprehensive neurological examination to avert a potentially life threatening stroke from developing in the near future[13].

Park in a retrospective study of 85 patients suffering with SSNHL found that patients who along with systemic steroids and antiviral were given Low molecular weight heparin 10,000 Units daily for 10 days had a greater chance of hearing recovery than those individuals treated with only systemic steroids. The author concluded that use of heparin corrects the impairments in microcirculation of the inner ear. Thromboembolic events lead to vasospasm and was proposed as a vascular theory by the authors[14]. The same observations were made by Yue *et al*[15], that heparin has a positive outcome on hearing restoration in cases of SSNHL.

A case-controlled study with a longitudinal design of 324 patients of SSNHL and 972 subjects with normal hearing were studied to determine whether raised serum lipid readings in over weight obesity patients had a negative impact on the outcomeof SSNHL. The results of the study reveal that altered serum lipid profile and raised BMI are associated with a higher prevalence of SSNHL. There by giving weight to the theory that vascular compromise has a central role in the pathophysiology of SSNHL[16].

Increased arterial stiffness is positively related to development of SSNHL, as postulated by Chung *et al* by demonstrating increased arterial wall rigidity in patients of SSNHL. The authors studied in a cross sectional manner, 54 cases of idiopathic SSNHL gender matched & 54 age controls between Jan 2014 and May 2015. Arterial stiffness in both groups was assessed by measuring brachial ankle pulse wave velocity Bapwv, along withother cardiovascular markers like blood pressure, body mass index, and serum lipid levels. The study revealed that a higher Bapwv (increased arterial wall stiffness) was associated with progression and grade of SSNHL, but arterial stiffness according to the study had no role in predicting the prognosis of SSNHL[17].

Weng in a case control study of 250 patients of SSNHL age and gender matched with 250 patients undergoing nasal surgery found that Serum Lipid levels were significantly raised in the SSNHL patients as compared to the other group[18].

Although hearing loss is the only symptom in the case of cochlear artery obstructions, vestibular symptoms like vertigo and tinnitus are also present in labyrinthine artery obstructions along with hearing loss[19]. Sutbas in a prospective study comprising of 120 patients of noise induced hearing loss found that tinnitus and hearing loss co-existing with hyperlipidemias showed marked improvement when treated with antihyperlipidemics and low cholesterol diet[20].

CONCLUSION

Sudden Sensorineural Hearing Loss (SSNHL) an enigma of ENT world, can be effectively managed by overcoming vascular pathology by Rosuvastatin therapy.

CONFLICT OF INTEREST

This study has no conflict of interest to declare by any author.

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