A Comparative Clinical Study on Treatment of Noise Induced Hearing Loss

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ABSTRACT

BACKGROUND

Noise-Induced Hearing Loss (NIHL) is one of the most common forms of sensorineural hearing loss. It is a major preventable problem related to hearing and is probably more widespread than revealed by conventional pure tone threshold testing. NIHL resulting from damage to the cochlea usually is associated with symmetrical mild to moderate hearing loss with associated tinnitus. But in a significant number of patients, NIHL is associated with asymmetrical thresholds and, depending on the exposure, severe to profound hearing loss as well. We wanted to evaluate audiological values and compare two oral antioxidant regimens in the treatment and prevention of NIHL.

METHODS

87 patients with noise induced hearing losses were included. They were divided into two groups A (44 patients) and group B (43 patients). Audiological examination was done with air conduction audiometry, PTA, observing notches in audiogram and DPOAE values. Both the groups were administered fixed medical regimens for a period of 6 months followed by audiological evaluation with same tests. Data was analysed using standard statistical methods.

RESULTS

In group A there were 32 males (72.72%) and 12 females (27.27%) and in group B there were 31 males (72.09%) and 12 females (27.90%) with a male to female ratio of 2.52:1. The mean ages in both groups were 47.23 ± 2.70 years and 46.25 ± 3.10 years respectively. More than 50 dB thresholds observed in 38/44 (86.36%) of group A and 35/43 (81.39%) of group B patients. PTA with above 50 dB in 27/44 (61.36%) of group A and 25/43 (58.13%) of group B patients. DPOAE values were absent in 31/44 (70.45%) of group A and 32/43 (74.41%) of group B patients. There was no significant statistical difference between the two groups and they were identical (p significant at <0.05).

CONCLUSIONS

The ideal agents for common clinical use are an oral agent with a known safety profile which is of the antioxidant category, with vasodilator properties and vitamins and steroids. There were affirmative effects of these agents improving audiological evaluation in patients with NIHL after 6 months. While there is not yet an effective medication to treat and prevent a multifactorial and complex pathological condition such as NIHL, a treatment based on the synergistic effects of natural micronutrients such as the antioxidants vitamins A, C, and E and the vasodilator magnesium all with good safety profiles, seems to be an excellent and promising efficacious therapeutic alternative for the treatment of this sensory impairment associated with NIHL.

KEYWORDS

Hearing, Noise, Cochlea, Thresholds of Hearing and Antioxidants

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BACKGROUND

Noise Induced Hearing Loss (NIHL) resulting from exposure to excessive noise is the most common preventable cause of hearing loss. The risk of the problem of NIHL among the global population is nearly 600 million people (12% or more).[1] According to WHO one third of this population hearing loss can be attributed to noise exposure.[2] NIHL has long been recognized as an occupational disease, amongst copper workers from hammering on metal, blacksmiths in the 18th century, and shipbuilders or "boilermakers" after the Industrial Revolution.[3] In United States of America among the general population the incidence of Hearing loss is 7%, Tinnitus in 5% and combined hearing loss in 2%. But in those with NIHL the incidences are 23%, 15% and 9% respectively.[4] Among the high-risk occupations resulting in NIHL, mining, mechanized wood cutting, printing and construction of buildings remain the Major industries.[5] The incidence of NIHL was observed to be more among the men than in women.

The risk of NIHL increased with increasing age. Initially for many years the NIHL was thought to be mild to moderate and symmetrical based on pure tone audiograms.[6] But the impact was found to be hidden hearing loss with or without synaptopathy- induced poor speech recognition.[7,8] Furthermore, the additional impact of noise-induced tinnitus and vestibular dysfunction is still not fully elucidated. NIHL results due to prolonged noise exposure primarily by damaging cochlear auditory outer hair cells, sometimes with concomitant inner hair cell damage with subsequent degeneration of the spiral ganglion cells.[9] High intensity sounds over a prolonged period also causes vasoconstriction in the stria vascularis and damage to the reticular lamina.[10] In the light of advancements in our understanding of oxidative stress and its role in hair cell death, a multitude of antioxidants have emerged to defend against oxidation.[11] Antioxidant agents include D-methionine, N-acetylcysteine, ebselen, aspirin, a combination of beta-carotene, vitamin C and vitamin E, Acuval, Coenzyme Q10 and molecular hydrogen.[12-16]

Magnesium is thought to exert its otoprotective effects partly via vasodilatation.[17] Other agents in the prevention of cellular death category include inhibitors of apoptosis such as calcineurin inhibitors, caspase inhibitors, jun-N terminal kinase inhibitors, and calcium channel blockers.[18-21] The second pharmacologic category includes Glucocorticoids, which have been widely used for otoprotection although their mechanisms remain largely unknown.[22] In 2012 Wang et al. demonstrated that one mechanism whereby dexamethasone exerts its otoprotective action involves encouraging trans-differentiation of supporting cells into outer hair cells.[23] However, systemic steroid administration presents risks such as impaired wound healing, hypokalemia, hyperglycemia, hypertension, osteoporosis, myopathy, osteonecrosis and immunosuppression.[24-31] Therefore, their use would be better suited for rescue from severe acute acoustic trauma rather than prophylaxis. For common clinical use an oral agent with a very low risk of side effects is preferable. For this reason, agents approaching clinical trials tend to be of the antioxidant category. Antioxidants such as selenium, which is found in Brazil nuts, and D-methionine, which occurs naturally in cheese and eggs, can survive the gastric system and first-pass metabolism to exert their effects. Such oral agents show promise for clinical use because of their ease of administration, safety and convenience in terms of portability and lengthy time window for administration.[31,32] In this study an attempt was made to compare two oral antioxidant and vasodilator drugs in the treatment and prevention of NIHL.

METHODS

In the present retrospective study 87 patients with Noise induced Hearing losses were included after obtaining their records from medical records section of the institute. They were divided into two groups A and B. Group A consisted of 44 patients and group B consisted of 43 patients. An institutional ethical committee clearance was obtained for the study. An ethical committee cleared consent form was used for the study.

Inclusion Criteria

1. Patients of both genders aged between 30 and 65 were included. 2. Patients involved in industries of mining, mechanized wood cutting and plywood, printing and construction of buildings. 3. Patients with hearing loss measured in terms of pure tone threshold (PTA) with 35 dB or above were included. 4. Patients who are willing to continue the medical regimens for 12 months were only included. 5. Patients who had associated with tinnitus were also included.

Exclusion Criteria

1. Patients with history of uncontrolled diabetes Mellitus were excluded. 2. Patients with history of intake of ototoxic drugs as part of treatment of co-existing diseases were excluded. 3. Patients with debilitating cardio vascular diseases were excluded. All the patients were subjected to ENT examination and audiological evaluation before and after completion of the treatment protocol. Audiological evaluation consisted of pure tone audiometry and calculation of pure tone average (PTA; mean of thresholds at 500, 1000 and 1500 KHZ) and Otoacoustic emission recording (Distortion product Otoacoustic emissions (DPOAE) are responses generated when the cochlea is stimulated simultaneously by two pure tone frequencies whose ratio is between 1.1 to 1.3). The drugs used in the regimens consisted of: In group A: 1. Tab Neuracetam 800 mg 2 times daily, 2. Vitamin B1, B6 & B12 once daily. 3. Gingko Biloba 40 mg 3 times daily were administered for 3 months. In group B: 1. Beta-carotene, vitamins C and E, magnesium (6 mint-flavoured tablets per day, taken once daily; total daily

dose label claim: micronutrient combination of 500 mg vitamin C (magnesium ascorbate), 315 mg magnesium (magnesium citrate, magnesium ascorbate, magnesium stearate), 267 mg vitamin E (d-α-tocopherol acetate), and 18 mg beta carotene. 2. Tab N-Acetyl-L Cysteine 600 mg effervescent daily once. 3. Tab Methyl Prednisolone 4 mg twice daily. Both the regimens were administered for 6 months. After 6 months the audiological evaluation was done to re assess the hearing thresholds and DPOAE values. At the end of the study available data was tabulated and analysed using standard statistical methods.

RESULTS

Totally medical records of 87 patients working in high intensity noise polluted industries presenting with loss of hearing, attending the department of ENT for medical treatment were selected from the records section of the RVM Institute of Medical sciences and research Institute were included in the study. In group A constituted of records of 44 patients and in group B records of 43 patients. There were 32 males (72.72%) and 12 females (27.27%) in group A and 31 males (72.09%) and 12 females (27.90%) in group B. Overall there were 63 males (72.41%) and 25 females (28.73%) with a male to female ratio of 2.52: 1. In group 'A' patients were aged between 31 years to 65 and in group 'B' patients were aged between 32 years and 63 years. The mean ages in both groups were 47.23 ± 2.70 years and 46.25 ± 3.10 years respectively (Table 1).

Observation	Group A- 44	Group B- 43	P Value
Age			
30 to 40 Yrs.	07 (15.90%)	09 (20.93%)	
40 to 50 Yrs.	11 (25.00%)	12 (27.90%)	0.072
50 to 60 Yrs.	19 (43.18%)	15 (34.88%)	
60 and above	07 (15.90%)	07 (16.27%)	
Gender			
Male	32 (72.72%)	31 (72.09%)	0.081
Female	12 (27.27%)	12 (27.90%)	0.063
Smoking			
Yes	20 (45.45%)	21 (48.83%)	0.091
No	24 (54.54%)	22 (51.16%)	
Profession			
Mining	09 (20.45%)	09 (20.93%)	
Printing press	10 (22.72%)	10 (23.25%)	
Wood cutting Industry	08 (18.18%)	07 (16.27%)	
Copper vessel Industry	07 (15.90%)	06 (13.95%)	
Tin Industry	05 (11.36%)	05 (11.62%)	
Traffic Police	03 (06.81%)	04 (09.30%)	0.103
Construction of Building	02 (04.54%)	02 (04.65%)	
Complaints			
Loss of Hearing	39 (88.63%)	40 (93.02%)	
Inability to discriminate	33 (75.00%)	32 (74.41%)	0.931
Tinnitus	38 (86.36%)	30 (69.76%)	
Vertigo	11 (25.00%)	10 (23.25%)	

Table 1. Demographic Data and Incidence of Symptoms in the Study Groups (Group A: n- 44 and Group B: n-43)

The incidence of smoking was similar in both the groups and there was no statistical difference with p value at 0.091 (p significant at <0.05). In group A there were 9/44 (20.45%) patients working in mining industry, 10/44 patients (22.72%) working in printing press, 8/44 patients (18.18%) in wood cutting industry, 7/44 (15.90%) in copper vessel industry, 5/44 (11.36%) patients in tin industry, 3/44 (06.81%) working as traffic police and 2/44 (04.54%) patients in construction sites. In group B there were 09/43 (20.93%) patients working in mining industry, 10/43 (23.25%) patients working in printing press, 07/43 patients (16.27%) in wood cutting industry, 06/43 (13.95%) in copper vessel industry, 05/43 (11.62%) patients in tin industry, 04/43 (09.30%) working as traffic police and 02/44 (04.65%) patients in construction sites (Table 1). Both the groups were similar in incidences of symptoms of presentation in the study with statistically insignificant p value 0.103 (p significant at <0.05).

Patients in both groups were subjected to audiological evaluation and their incidence and values were tabulated in table 2. Air conduction thresholds were above 50 dB in 38/44 (86.36%) patients in group A and in 35/43 (81.39%) patients in group B. PTA was above 50 dB in 27/44 (61.36%) patients in group A and 25/43 (58.13%) patients in group B. DPOAE values were absent in 31/44 (70.45%) patients in group A and 32/43 (74.41%) patients of group B. There was no significant statistical difference between the two groups and they were identical (p significant at <0.05), (Table 2).

Observation	Group A- 44	Group B- 43	P Value
Air conduction Thresholds			
40 to 45 dB	06 (13.63%)	08 (18.60%)	
45 to 50 dB	11 (25.00%)	10 (23.25%)	
50 to 60 dB	09 (20.45%)	08 (18.60%)	0.706
60 to 65 dB	08 (18.18%)	06 (13.95%)	
65 to 70 dB	06 (13.63%)	06 (13.95%)	
70 to 75 dB	04 (09.09%)	05 (11.62%)	
Pure tone Average			
35 to 40 dB	07 (15.90%)	09 (20.93%)	
45 to 50 dB	09 (20.45%)	08 (18.60%)	
50 to 55 dB	08 (18.18%)	09 (20.93%)	0.642
55 to 60 dB	09 (20.45%)	07 (16.27%)	
60 to 65 dB	07 (15.90%)	06 (13.95%)	
65 to 70 dB	04 (09.09%)	04 (09.30%)	
Air conduction notches at			
3 KHz	14 (31.81%)	12 (27.90%)	
4 KHz	15 (34.09%)	13 (30.23%)	0.715
6 KHz	10 (22.72%)	11 (25.58%)	
8 KHz	05 (11.36%)	07 (16.27%)	
DPOAE values			
Absent	31	32	
Clearly present and Normal	06	09	0.610
Present but not normal	07	04	

Table 2. Audiological Evaluation Tests and Their Results before Treatment (Group A: n- 44 and Group B: n-43)

Observation	Group A- 44	Group B- 43	P Value
Air conduction Thresholds			
40 to 45 dB	19 (43.18%)	15 (34.88%)	
45 to 50 dB	09 (20.45%)	12 (27.90%)	
50 to 60 dB	06 (13.63%)	07 (16.27%)	0.041
60 to 65 db	04 (09.09%)	04 (09.30%)	
65 to 70 dB	03 (06.81%)	03 (06.97%)	
70 to 75 db	03 (06.81%)	02 (04.65%)	
Pure tone Average			
35 to 40 dB	16 (36.36%)	14 (32.55%)	
45 to 50 dB	11 (25.00%)	11 (25.58%)	
50 to 55 dB	05 (11.36%)	06 (13.95%)	0.031
55 to 60 dB	05 (11.36%)	05 (11.62%)	
60 to 65 dB	04 (09.09%)	04 (09.30%)	
65 to 70 db	03 (06.81%)	03 (06.97%)	
Air conduction notches at			
3 KHz	14 (31.81%)	12 (27.90%)	
4 KHz	15 (34.09%)	13 (30.23%)	0.715
6 KHz	10 (22.72%)	11 (25.58%)	
8 KHz	05 (11.36%)	07 (16.27%)	
DPOAE values			
Absent	09 (20.45%)	10 (23.25%)	
Clearly present and Normal	25 (56.81%)	21 (48.83%)	0.028
Present but not normal	10 (22.72%)	12 (27.90%)	

Table 3. Audiological Evaluation Tests and Their Results 6 Months after Treatment (Group A: n- 44 and Group B: n-43)

Audiological evaluation of patients in both the groups was performed after 6 months and it was observed that Air conduction thresholds were above 50 dB in 16/44 (36.36%)

patients in group A and in 16/43 (37.20%) patients in group B. PTA was above 50 dB in 17/44 (38.63%) patients in group A and 17/43 (39.53%) patients in group B. DPOAE values were absent in 09/44 (20.45%) patients in group A and 10/43 (23.25%) patients of group B. DPOAE was normal in 25/44 (56.81%) in group A and 21/43 (48.83%) patients in group B. There was significant statistical difference between the two groups after 6 months of treatment in their audiological values and they were identical (p significant at <0.05), (Table 3). However, there was no change in the notches in their audiograms before and after treatment (Table 3).

DISCUSSION

There were 32 males (72.72%) and 12 females (27.27%) in group A and 31 males (72.09%) and 12 females (27.90%) in group B. Overall there were 63 males (72.41%) and 25 females (28.73%) with a male to female ratio of 2.52: 1. In group 'A' patients were aged between 31 years to 65 and in group 'B' patients were aged between 32 years and 63 years. The mean ages in both groups were 47.23 ± 2.70 years and 46.25 ± 3.10 years respectively (Table 1). The incidence of smoking was similar in both the groups and there was no statistical difference with p value at 0.091 (p significant at <0.05). In group A there were 9/44 (20.45%) patients working in mining industry, 10/44 patients (22.72%) working in printing press, 8/44 patients (18.18%) 9n wood cutting industry, 7/44 (15.90%) in copper vessel industry, 5/44 (11.36%) patients in tin industry, 3/44 (06.81%) working as traffic police and 2/44 (04.54%) patients in construction sites. In group B there were 09/43 (20.93%) patients working in mining industry, 10/43 (23.25%) patients working in printing press, 07/43 patients (16.27%) in wood cutting industry, 06/43 (13.95%) in copper vessel industry, 05/43 (11.62%) patients in tin industry, 04/43 (09.30%) working as traffic police and 02/44 (04.65%) patients in construction sites (Table 1). NIHL results in decrease in hearing thresholds depending on the intensity and duration of the exposure.

NIHL causes temporary threshold shift' (TTS) or transient attenuation of hearing acuity and permanent threshold shift (PTS) or permanent change in the hair cells and the acuity of hearing.[33] In PTS, the audiogram characteristically shows a sharp dip between 3 kHz and 6 kHz. NIHL with mild hearing loss (HL), (15 to 20 dB), but might not be noticed in everyday life in one-on-one conversations. But in more severe NIHL the speech perception is certainly affected with auditory damage up to complete deafness.[34] Inner hair cells are mainly the primary transducers and are innervated by more than 90% of the auditory afferent nerve fibers. In this study air conduction thresholds were above 50 dB in 38/44 (86.36%) patients in group A and in 35/43 (81.39%) patients in group B. PTA was above 50 dB in 27/44 (61.36%) patients in group A and 25/43 (58.13%) patients in group B. DPOAE values were absent in 31/44 (70.45%) patients in group A and 32/43 (74.41%) patients of group B. There was no significant statistical difference between the two groups and they were identical (p significant at <0.05). Outer hair cells mostly receive efferent innervations and serve to enhance the sensitivity to sound stimulation. Several types of supporting cells and auxiliary structures such as the stria vascularis and spiral ligament are critical in maintaining the structural organization and homeostasis of cochlea.[35] Outer hair cells damage increases hearing thresholds to 40 to 60 dB. An additional loss of inner hair cells will result in even higher threshold shifts up to complete deafness. Associated degeneration of the auditory nerve corresponded with loss of outer hair cells. Intense noise can damage the cochlea mechanically by vibrating the organ of Corti beyond its structural limits.[36]

NIHL causes metabolic stress by forming reactive oxygen species (free radicals, ROS) in the hair cells which triggers its death. ROS emerge immediately after noise exposure and persist for 7–10 days thereafter, spreading apically from the basal end of the organ of Corti, thus widening the area of damage. Free radicals in the form of reactive nitrogen species (RNS) derived from nitric oxide (NO) are also present. Peroxynitrite (ONOO-), generated by the combination of NO and ROS, has been found in the cochlea several days after noise exposure, underscoring the case for oxidant stress contributing hair cell death.[37,38] Another effect on High intensity noise on cochlea is decreased cochlear blood flow caused by vasoactive lipid peroxidation products such as isoprostanes.[36] Exposure to high intensity noise causes a decrease in serum total antioxidant capacity and an increase in nitric oxide in guinea pigs.[37] Increased nitric oxide causes formation of peroxynitrite, which is very damaging to hair cells. Formation of free radicals following exposure to impulse noise has been reported in some animal studies.[38-39] The levels of nitric oxide, peroxynitrite, oxidative stress, nuclear factor kappa-beta (NF-kappa), glutamate receptor (N-methyl-D-aspartate), and calcium are elevated in patients with NHIL and tinnitus.[40,41]

Antioxidants are known to reduce oxidative stress and inflammation; therefore, supplementation with antioxidants appears to be one of the most rational approaches to prevent and improve hearing disorders in combination with standard therapy. Several animal and some human studies show that supplementation with antioxidants produces beneficial effects and improves hearing disorders, including: 1. in a prospective, double-blind study, supplementation of vitamin E alone provided better recovery than the standard therapy in patients with idiopathic sudden hearing loss.[42] 2. In a prospective double-blind study, vitamin E alone administered orally improved the efficacy of standard therapy.[43] 3. In a prospective randomized study, intravenous administration of magnesium sulfate improved hearing recovery in patients with idiopathic sudden sensorineural hearing loss.[44] 4. The use of glutamate antagonists, steroids, and antioxidants may also be useful in the management of hearing loss and tinnitus.[45] Several studies have also looked at the use of antioxidants in the prevention of noise-induced hearing loss, including: 1. Vitamin E, when administered

intraperitoneal route 3 days before and 3 days after noise exposure, reduced noise-induced cochlear damage and hearing loss in guinea pigs.[40,43] 2. It also protected against noise-induced damage to the inner ear in cyprinid fish.[46] 3. Alpha-lipoic acid protects against noise-induced hearing loss in guinea pigs. 4. An intraperitoneal injection of n-acetylcysteine (NAC) significantly reduced hair cell loss in cochlear cells of rats.[47] 5. NAC attenuated noise-induced hearing disorders in guinea pigs.[48] 6. Acetyl-L-carnitine and NAC administered twice a day for 2 days and 1 hour before and 1 hour after noise exposure for an additional 2 days provided protection against hearing loss.[49] Among the steroids specifically Intratympanic dexamethasone, may have a therapeutic beneficial effect on NIHL when given before[50] or after[51] acoustic trauma in animals. Although an effect is shown in a wide range of dosages, higher dosages appear to be associated with better hearing preservation.[50] In animal studies even though the routes of administration either intratympanic, intraperitoneal and direct administration into the scala tympani, and all have demonstrated protective effects as evidenced by preserved hearing (15–20 dB lower hearing thresholds on auditory brainstem response (ABR) measurement and preserved cochlear architecture,[51,52] there appears to be a synergistic benefit from the administration by both routes when treating NIHL.[53]

In human studies, it has been shown that after acoustic trauma, the administration of systemic with intratympanic steroid treatment results in better hearing outcomes than with systemic steroids alone.[53,54] Although there is some evidence for a protective effect of steroids in acute acoustic trauma, clearly it is not a long-term option for chronic occupational noise exposure considering the negative side effects of systemic long-term steroid usage. Antioxidants may be a safer alternative to steroids given a more favourable side effect profile. Free oxygen radicals and oxidative stress are important in the pathogenesis of the NIHL, and therefore antioxidants could theoretically constitute an effective treatment. N-acetylcysteine (NAC) has been reported to reduce the ototoxic effects of noise exposure in animal models.[55,56] In humans, however, the data is limited.[57,58] Doosti et al[57] evaluated TTS in 48 textile workers and showed that daily oral administration of NAC (1200 mg/day) during continuous noise exposure prevented the occurrence of a TTS after 14 days of treatment, whereas the untreated group showed a TTS of approximately 1.5–3 dB.[57] Lin et al.[59] also found a significant improvement in TTS after NAC (1200 mg/day for 14 days).

Kramer et al. did not find a significant protective effect of NAC when using a single lower dose (900 mg PO) administered before noise exposure.[60] A more recent randomized, double-blinded, placebo-controlled trial among a larger military group (n = 566), found a 6–7% reduction in hearing threshold shift rate, with a total daily dose of 2700 mg of NAC after noise exposure for 16 days during weapon training, but this was only statistically significant when handedness was taken into account (i.e. evaluating the effect on the right ear only in right handed participants). In summary, there is potentially a small benefit of NAC in reducing the rate of threshold shift in a noise-exposed population.[61] Glucocorticoids (GC) are widely used for the treatment of inner ear disease; they exert their effects by binding to its Glucocorticoid receptor, GR[62] Therefore, the expression of GR mediates the effects of GC.[63] GRs are highly expressed throughout the inner ear, including the stria vascularis, inner hair cells, OHCs, and spiral ligament of the cochlea and cochlear nerve.[64,65] The GR mRNA expression level was reported to be significantly decreased following acoustic trauma in the cochlea[66] as well as in the organ of Corti.[67]

Terunuma et al. reported that GR mRNA expression was significantly decreased following acoustic trauma.[66] Mori et al. reported that compound action potentials (CAPs) at a threshold of 5–8 kHz were significantly elevated when the GR antagonist, mifepristone, was administered following exposure to noise with a sound pressure level (SPL) of 120 dB.[68] The ABR threshold shift was found to be significantly decreased by pre-treatment with the corticosteroid, methylprednisolone.[69] Other antioxidants that can potentially play a protective role against noise-induced cochlear trauma include ginseng,[57] as well as several vitamins, such as vitamin A,[70] vitamin C,[71,72] vitamin E,[73,74] and vitamin B12.[70] Studies animals showed a protective benefit from combination antioxidant treatment, such as magnesium and vitamin A, C, and E,[71] possibly due to synergistic effects,[72,73] These studies were mainly performed in animals or in small groups of humans and the results should be considered preliminary. The efficacy of combining treatments in humans is still unknown. Vitamin B_{12} is another nutrient that might influence auditory performance and sensitivity to noise. Army personnel with vitamin B_{12} deficiency showed a greater incidence of noise-induced tinnitus and hearing loss than subjects with normal levels.[75]

Conversely, the administration of high doses of vitamin B_{12}, reduced noise-induced TTS in a double-blind clinical study. Another trial testing NAC against noise-induced TTS studied workers employed at a steel manufacturing company.[76] NAC or placebo was orally administered at 1200 mg a day, for 14 days, in a 2 × 2 crossover design with 14-day wash-out periods between treatments. The result not only underlined the importance of endogenous antioxidant defences but also points to genetics as an important modulator of noise trauma. Magnesium had been explored as an interceptive agent against permanent NIHL even before its evaluation for TTS, based on early demonstrations of magnesium- mediated modulation of NIHL in experimental animals and humans.[77,78] Audiological evaluation of patients in both the groups was performed after 6 months and it was observed that Air conduction thresholds were above 50 dB in 16/44 (36.36%) patients in group A and in 16/43 (37.20%) patients in group B. PTA was above 50 dB in 17/44 (38.63%) patients in group A and 17/43 (39.53%) patients in group B. DPOAE values were absent in 09/44 (20.45%) patients in group A and 10/43 (23.25%) patients of group B. DPOAE was normal in 25/44 (56.81%) in group A and 21/43 (48.83%) patients in group

B. There was significant statistical difference between the two groups after 6 months of treatment in their audiological values and they were identical (p significant at <0.05), (Table 3). However there was no change in the notches in their audiograms before and after treatment.

CONCLUSIONS

Noise Induced Hearing Loss (NIHL) affects millions of Indians working in industries like mining, wood cutting, tin, copper printing press, and construction works. Presently there is no approved agent or regimen for treatment and prevention of NIHL in India. Pharmacologic agents exert their otoprotective effects by either preventing or minimizing hair cell death. The ideal agents for common clinical use are an oral agent with a known safety profile which is of the antioxidant category, with vasodilator properties and vitamins and steroids. There were affirmative effects of these agents improving audiological evaluation in patients with NIHL after 6 months. While there is not yet an effective medication to treat and prevent a multifactorial and complex pathological condition such as NIHL, a treatment based on the synergistic effects of natural micronutrients such as the antioxidants vitamins A, C, and E and the vasodilator magnesium all with good safety profiles, seems to be an excellent and promising efficacious therapeutic alternative for the treatment of this sensory impairment associated with NIHL.

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