

Tinnitus

ABSTRACTS

ATA., 2002. TIN-it-us or ti-NIGHT-us: Which Is Correct?

Attias J., 1994. Oral magnesium intake reduces permanent hearing loss induced by noise exposure.

Burschka MA., 2001. Effect of treatment with Ginkgo biloba extract EGb 761 (oral) on unilateral idiopathic sudden hearing loss in a prospective randomized double-blind study of 106 outpatients.

Holstein N., [Ginkgo special extract EGb 761 in tinnitus therapy. An overview of results of completed clinical trials]

Jastreboff PJ., 1997. Attenuation of salicylate-induced tinnitus by Ginkgo biloba extract in rats.

Jimenez-Cervantes Nicolas J., 1990. [Hydergine in pathology of the inner ear]

Jung HW., 1998. Effects of Ginkgo biloba extract on the cochlear damage induced by local gentamicin installation in guinea pigs.

Konopka W., 1997. [Treatment results of acoustic trauma]

MFMER., 2001. What Is Tinnitus?

Mocci F., 2001. The effect of noise on serum and urinary magnesium and catecholamines in humans.

Morgenstern C., 2002. The efficacy of Ginkgo special extract EGb 761 in patients with tinnitus.

NIH., 2001. The Noise in Your Ears.

Ochi K., 1997. [The serum zinc level in patients with tinnitus and the effect of zinc treatment]

Rosenberg SI., 1998. Effect of melatonin on tinnitus.

Shemesh Z., 1993. Vitamin B12 deficiency in patients with chronic-tinnitus and noise-induced hearing loss.

Soholm B., 1998. Clinical improvement of memory and other cognitive functions by Ginkgo biloba: review of relevant literature.

Stange G., 1975. [The influence on sound damages by an extract of ginkgo biloba]

SUGGESTED READING.

Rudin DO., 1981. The major psychoses and neuroses as omega-3 essential fatty acid deficiency syndrome: substrate pellagra.

Pilgramm M., 1986. [Need for rheologically active, vasoactive and metabolically active substances in the initial treatment of acute acoustic trauma]

Farri A., 1998. The use of Ginkgo Biloba extract associated with magnesium and arginine in patients with tinnitus of a vascular origin.

Vilholm OJ., 1998. Effect of traditional Chinese acupuncture on severe tinnitus: a double blind, placebo controlled, clinical investigation with open therapeutic control.

Enrique Gomez A., 1997. Multicenter study with standardized extract of Ginkgo-Biloba EGB 761 in the treatment of memory alteration, vertigo and tinnitus.

Roeser RJ., 1997. Physiology, pathophysiology, and anthropology/epidemiology of human ear canal secretions.

Conlon BJ., 1999. Attenuation of aminoglycoside-induced cochlear damage with the metabolic antioxidant alpha-lipoic acid.

Jacono AA., 1998. Changes in cochlear antioxidant enzyme activity after sound conditioning and noise exposure in the chinchilla.

Yamasoba T., 1998. Role of glutathione in protection against noise-induced hearing loss.

Armstrong KL., 1998. Vitamin E and lipoic acid, but not vitamin C improve blood oxygenation after high-energy IMPULSE noise (BLAST) exposure.

Konishi K., 1991. The efficacy of Lasix-vitamin therapy (L-V therapy) for sudden deafness and other sensorineural hearing loss.

Ou P., 1995. Thiocctic (lipoic) acid: a therapeutic metal-chelating antioxidant?

Kagan VE., 1992. Dihydrolipoic acid--a universal antioxidant both in the membrane and in the aqueous phase. Reduction of peroxy, ascorbyl and chromanoxyl radicals.

Bast A., 1988. Interplay between lipoic acid and glutathione in the protection against microsomal lipid peroxidation..

Anderson ME., 1985. Glutathione monoethyl ester: preparation, uptake by tissues, and conversion to

glutathione.

Garetz SL., 1994. Sulfhydryl compounds and antioxidants inhibit cytotoxicity to outer hair cells of a gentamicin metabolite in vitro.

Panigrahi M., 1996. alpha-Lipoic acid protects against reperfusion injury following cerebral ischemia in rats.

Patuzzi R., 1998. Automatic monitoring of mechano-electrical transduction in the guinea pig cochlea.

Aran JM., 1995. Uptake of amikacin by hair cells of the guinea pig cochlea and vestibule and ototoxicity: comparison with gentamicin.

Lima da Costa D., 1998. Aminoglycoside ototoxicity and the medial efferent system: II. Comparison of acute effects of different antibiotics.

Hoffmann F., 1994. [Ginkgo extract EGb 761 (tenobin)/HAES versus naftidrofuryl A randomized study of therapy of sudden deafness]

Dubreuil C., 1986. [Therapeutic trial in acute cochlear deafness. A comparative study of Ginkgo biloba extract and nicergoline]

TIN-it-us or ti-NIGHT-us: Which Is Correct? 2002.

ATA.

Portland, OR: American Tinnitus Association.

Oral magnesium intake reduces permanent hearing loss induced by noise exposure.

Attias J, Weisz G, Almog S, Shahar A, Wiener M, Joachims Z, Netzer A, Ising H, Rebentisch E, Guenther T. Institute of Noise Hazards Research, I.D.F. Medical Corps, Haifa, Israel.

Am J Otolaryngol 1994 Jan-Feb;15(1):26-32

INTRODUCTION: Following animal experiments where correlations were observed between serum magnesium level and noise-induced permanent hearing threshold shifts (NIPTS), we tested the prophylactic effect of magnesium in human subjects exposed to hazardous noise.

METHODS: Subjects were 300 young, healthy, and normal-hearing recruits who underwent 2 months of basic military training. This training necessarily included repeated exposures to high levels of impulse noises while using ear plugs. During this placebo-controlled, double-blind study, each subject received daily an additional drink containing either 6.7 mmol (167 mg) magnesium aspartate or a similar quantity of placebo (Na-aspartate).

RESULTS: NIPTS was significantly more frequent and more severe in the placebo group than in the magnesium group, especially in bilateral damages. NIPTS was negatively correlated to the magnesium content of blood red cells but especially to the magnesium mononuclear cells. Long-term additional intake of a small dose of oral magnesium was not accompanied by any notable side effect.

CONCLUSION: This study may introduce a significant natural agent for the reduction of hearing damages in noise-exposed population.

Effect of treatment with Ginkgo biloba extract EGb 761 (oral) on unilateral idiopathic sudden hearing loss in a prospective randomized double-blind study of 106 outpatients.

Burschka MA, Hassan HA, Reineke T, van Bebber L, Caird DM, Mosges R. Institut für Medizinische Statistik, Informatik und Epidemiologie der Medizinischen Einrichtungen der Universität Köln, Germany.

Eur Arch Otorhinolaryngol 2001 Jul;258(5):213-9

OBJECTIVE: Test of dose-response relationship for Ginkgo biloba extract EGb 761 (oral) in outpatients with acute idiopathic sudden sensorineural hearing loss (ISSHL) of at least 15 dB at one frequency within the speech range occurring less than 10 days before study inclusion.

DESIGN: Multicentre, randomized, double-blind phase III study comparing dosages of 120 mg twice daily and 12 mg twice daily over 8 weeks.

MAIN ENDPOINT: Recovery (in dB) of the auditory threshold from the initial measurement to the value on the last day of treatment, averaged over those frequencies from 0.25, 0.5, 1, 2, and 3 kHz for which the initial hearing loss amounted to 15 dB or more

compared to the level on the opposite side.

PATIENTS: 106 patients with an average age of 44+/-16 years and with hearing loss at affected frequencies 26 dB +/- 9 dB included between December 1995 and July 1997.

RESULTS: Large majorities of both treatment groups recovered completely. In exploratory analyses of the 96 patients included according to the protocol, patients given the higher dose had less risk of not recovering well (< or =10 dB residual hearing loss) (one-sided Fisher test: P = 0.0061), especially if they had no tinnitus (n = 44, P = 0.00702).

CONCLUSION: A higher dosage of EGb 761 (oral) appears to speed up and secure the recovery of ISSHL patients, with a good chance that they will recover completely, even with little treatment. This was already observed after one week of treatment. We find it justified to treat patients who have unilateral ISSHL of less than 75 dB and neither tinnitus nor vertigo with 120 mg oral EGb 761 twice daily.

[Ginkgo special extract EGb 761 in tinnitus therapy. An overview of results of completed clinical trials] [Article in German]

Holstein N. Facharzt für Hals-Nasen-Ohrenheilkunde, Allergologie, Chirotherapie, Stimm- und Sprachstörungen, Neuensteinstrasse 14, D-76227 Karlsruhe.

Fortschr Med Orig 2001 Jan 11;118(4):157-64

In a systematic search of the literature 19 clinical trials investigating the effects of tinnitus treatment with Ginkgo biloba special extract EGb 761 were identified and evaluated. The results of eight controlled studies on tinnitus due to cerebrovascular insufficiency or labyrinthine disorders of varying genesis for the most part show a statistically significant superiority of treatment with the Ginkgo biloba special extract EGb 761 as compared with placebo or reference drugs applied of periods of one to three months. Open studies, too, some involving large numbers of patients, revealed appreciable improvements under ginkgo treatment. Therapeutic success was not directly correlated with either the genesis or the duration of tinnitus. However, investigations of prognostic factors revealed that short-standing disorders have a better prognosis, so that better results can be expected from early-onset treatment. The tolerability of Ginkgo biloba special extract EGb 761 was excellent, and in this respect the controlled clinical trials revealed little difference between drug-treated and control groups.

Attenuation of salicylate-induced tinnitus by Ginkgo biloba extract in rats.

Jastreboff PJ, Zhou S, Jastreboff MM, Kwapisz U, Gryczynska U. Department of Surgery, University of Maryland School of Medicine, Baltimore 21201, USA. pjastreboff@surgery2.ab.umd.edu

Audiol Neurotol 1997 Jul-Aug;2(4):197-212

The effects of an extract from Ginkgo biloba, EGb 761, on tinnitus were tested using an animal model of tinnitus. Daily oral administration of EGb 761 in doses from 10 to 100 mg/kg/day began 2 weeks before behavioral procedures and continued until the end of the experiment. Tinnitus was induced by daily administration of 321 mg/kg sodium salicylate s.c. (corresponding to 275 mg/kg/day of salicylate acid) in fourteen groups of pigmented rats, 6 animals/group. The results from salicylate- and EGb-761-treated animals were compared to control groups receiving either salicylate, saline, or EGb 761 only in doses of 100 mg/kg. Administration of EGb 761 resulted in a statistically significant decrease of the behavioral manifestation of tinnitus for doses of 25, 50 and 100 mg/kg/day.

[Hydergine in pathology of the inner ear] [Article in Spanish]

Jimenez-Cervantes Nicolas J, Amoros Rodriguez LM.

An Otorrinolaringol Ibero Am 1990;17(1):85-98

There have been treated a total of 20 patients with troubles on the cochlear compartment and/or vestibular level which have been clinically expressed by a perceptive hypoacusia, tinnitus and rotatory vertigo. The final evaluation is referred to 17 patients, since three patients do not appear for control. All patients were treated only with Hydergine, on doses of 30 drops thrice daily, which is the equivalent to 4.5 mg/day of active substance. This treatment remained unaltered till the end of the last control. Controls have been effected after 30, 60 and 90 days of starting the treatment. In each control there was evaluated the subjective improvement of vertigo, tinnitus and hypoacusia when effecting to all patients by means of liminar- supraliminar- and automaticaudiometry, impedancimetry, T one-decay-test and electrooculonistagmography. The most meliorated symptomatology was vertigo, with a global improvement of 93.7 per cent on the treated patients. Tinnitus improve by 57.1 per cent and hypoacusia by 20 per cent. There is a total correspondence between the subjective data furnished by the patients and the objective tests carried out in the successive

controls.

Effects of Ginkgo biloba extract on the cochlear damage induced by local gentamicin installation in guinea pigs.

Jung HW; Chang SO; Kim CS; Rhee CS; Lim DH Department of Otorhinolaryngology - Head & Neck Surgery, Seoul National University College of Medicine, Korea.

J Korean Med Sci (Korea) Oct 1998, 13 (5) p525-8

Investigations evaluating the protective effect of Ginkgo biloba extract (EGb) on gentamicin (GM) ototoxicity were undertaken. Guinea pigs treated with 5 mg/kg gentamicin sulfate on the round window niche (RWN) showed acute changes on electrocochleogram and hair cell or microvilli damage on scanning electron microscopy (SEM). There was accumulation of GM in the whole cochlea, especially in the organ of Corti, stria vascularis, and type III fibrocyte on immunohistochemical study. However, the guinea pigs pretreated with local or systemic EGb revealed no significant changes by local GM installation. From these results, we concluded that EGb has a protective effect on the development of GM ototoxicity in the cochlea.

[Treatment results of acoustic trauma] [Article in Polish]

Konopka W, Zalewski P, Olszewski J, Olszewska-Ziaber A, Pietkiewicz P. Kliniki Otolaryngologicznej Instytutu Chirurgii WAM w Lodzi.

Otolaryngol Pol 1997;51 Suppl 25:281-4

20 patients aged from 18 to 42 treated in the past few years because of acoustic trauma. Together the investigations concerned 24 years. Therapeutic schema comprised intravenous infusion--Sermion (Nicergoline--amp. a 4 mg) or Cavinton (Vinpocetine--amp. a 10 mg) 1 amp.--twice a day for 10 days. The treatment of 60% of the patients started in the first week after the trauma occurred, of 20% in the second week and the remaining 20% later on after 15 days when the trauma took place. The obtained results of treatment both of improvement of hearing (79.2%) and tinnitus (66.6%), support the necessity of treatment of acoustic trauma independently from the time that passed after trauma had occurred. Better results of audiometric improvement of hearing (54.2%) and tinnitus disappearance (50%) were obtained in the patients whose treatment started in the first week after trauma. The improvement of hearing and tinnitus disappearance was more observed in patients after treatment by using Sermion than Cavinton.

What Is Tinnitus?

MFMER.

2001 Apr 5. Rochester, MN:

Mayo Foundation for Medical Education and Research.

The effect of noise on serum and urinary magnesium and catecholamines in humans.

Mocci F, Canalis P, Tomasi PA, Casu F, Pettinato S. Istituto di Medicina Legale, Cattedra di Medicina del Lavoro, Universita di Sassari, Italy. mocci@ssmain.uniss.it

Occup Med (Lond) 2001 Feb;51(1):56-61

We have studied whether a short-term exposure to loud noise was able to modify urinary catecholamine excretion and serum concentration and urinary excretion of magnesium and other related electrolytes. In 25 healthy volunteers, blood and urine concentrations of magnesium, calcium, phosphorus and creatinine, and urinary catecholamines were measured before and after exposure to noise in an industrial plant. Samples were collected at 08:00 h on the day of the experiment and soon after noise exposure (at 20:00 h). Two further urine samples were collected the following day and 2 days after the experiment, always at 08:00 h in the morning. The sound energy average level was 98 dB(A), but peak levels reached 108 dB(A). Urinary catecholamines were determined by high-performance liquid chromatography. Serum magnesium and calcium were significantly increased after exposure to noise, whereas phosphorus displayed a similar but non-significant trend ($P = 0.065$). Multivariate analysis of variance (ANOVA) showed significant differences both among subjects ($P < 0.001$) and after exposure ($P < 0.001$). Adrenaline, noradrenaline and dopamine values were not significantly different after exposure to noise ($P > 0.05$). Urinary magnesium levels were significantly different across time ($P = 0.017$). Urinary calcium levels were not significantly different across time ($P = 0.36$). Urinary phosphate values were increased after exposure to noise ($P = 0.007$); urinary creatinine was not changed after exposure ($P > 0.05$). Our study shows that noise induces significant increases of serum calcium and magnesium, with a borderline increase of serum phosphorus; this in turn is reflected in a significantly increased urinary excretion of magnesium and phosphate after exposure, which lasts for the

following 2 days. Urinary calcium and creatinine were not modified by noise. The difference in catecholamine values did not reach statistical significance. Thus, we failed to substantiate a significant correlation between catecholamine secretion and magnesium metabolism, as others had suggested.

The efficacy of Ginkgo special extract EGb 761 in patients with tinnitus.

Morgenstern C, Biermann E. Allgemeines Krankenhaus St. Georg. Hamburg, Germany.

Int J Clin Pharmacol Ther 2002 May;40(5):188-97

OBJECTIVE: The objective of the present study in 60 patients with chronic tinnitus aurium was to confirm the efficacy of oral treatment with 2 x 80 mg Ginkgo special extract EGb 761 per day subsequent to 10-day EGb 761 infusion treatment.

METHODS: Patients with chronic tinnitus aurium underwent 10 days of in-patient infusion treatment with 200 mg/day EGb 761, after which they were randomized to double-blind, oral out-patient treatment with either 2 x 80 mg/day EGb 761 or placebo, given over a scheduled treatment period of 12 weeks. The primary outcome measure was the change in tinnitus volume in the more severely affected ear during randomized treatment.

RESULTS: Fifty-two of 60 patients (89.7%) completed the infusion treatment; complete sets of data were available for 40 (66.7%), 30 (50.0%) and 22 (36.7%) patients after 4, 8 and 12 weeks of randomized treatment, respectively. For the primary outcome measure, significant superiority of EGb 761 over placebo was demonstrated in the intention-to-treat analysis data set after 4, 8 and 12 weeks of out-patient treatment ($p < 0.05$, 1-tailed), although the absolute treatment group difference was moderate. The results were supported by the secondary outcome measures for efficacy (e.g. decreased hearing loss, improved self-assessment of subjective impairment). During out-patient treatment, there were no attributable adverse events under EGb 761.

CONCLUSIONS: A combination of infusion therapy followed by oral administration of Ginkgo special extract EGb 761 appears to be effective and safe in alleviating the symptoms associated with tinnitus aurium.

The Noise in Your Ears

NIH.

2001 Feb. Publ. No. 00-4896. Bethesda, MD:

National Institutes of Health/National Institute on Deafness and Other Communication Disorders.

[The serum zinc level in patients with tinnitus and the effect of zinc treatment] [Article in Japanese]

Ochi K, Ohashi T, Kinoshita H, Akagi M, Kikuchi H, Mitsui M, Kaneko T, Kato I. Department of Otorhinolaryngology, St. Marianna University School of Medicine, Kyoto-fu.

Nippon Jibiinkoka Gakkai Kaiho 1997 Sep;100(9):915-9

We measured the serum zinc level in patients with tinnitus and evaluated the effectiveness of zinc in the treatment of tinnitus. Blood zinc levels were measured in 121 patients with tinnitus. All patients were examined between 1995 and 1997 at the outpatient clinic of otorhinolaryngology St. Marianna University Toyoko Hospital. Forty-seven patients who had received any drug such as a calcium channel blocker and others or had been affected by any diseases were excluded and therefore 74 patients consisting of 46 females (62%) and 28 males (38%) were investigated. Twenty two healthy volunteers served as a control group. The mean age and standard deviations for the tinnitus group and the control group were 47.8 +/- 17.1 and 31.4 +/- 8.2 years, respectively. There was a significant decrease ($p < 0.0001$) in serum zinc levels in patients with tinnitus compared with the control group. Because there was a significant difference ($p < 0.0001$) in age distribution between tinnitus and control groups, patients were selected by their age in order to neglect the effect of aging. In this situation, a significant difference ($p < 0.01$) was noted between the tinnitus group and control group. Low blood zinc level was defined by using the mean and standard deviation for the control group (mean-1 S.D.). We treated patients with low blood zinc levels. A total dose of 34-68 mg of Zn⁺⁺ was administered daily for over 2 weeks. The degree of tinnitus was expressed on a numeric scale from 0 to 10 before and after treatment. Blood zinc levels were significantly elevated ($p < 0.05$) after treatment. We found a significant decrease ($p < 0.01$) in the numeric scale. These findings suggest that zinc is useful in at least some patients suffering from tinnitus. It is possible to classify patients with tinnitus by measuring serum zinc level and this leads to improvement of the overall treatment effect.

Effect of melatonin on tinnitus.

Laryngoscope 1998 Mar;108(3):305-10

OBJECTIVE: Evaluate melatonin as a treatment for subjective tinnitus.

STUDY DESIGN: Randomized, prospective, double-blind, placebo-controlled crossover trial. Patients were given 3.0 mg melatonin, which was taken nightly for 30 days followed or preceded by a placebo nightly for 30 days, with a 7-day washout period between medications.

SETTING: Outpatient, private, neurotology practice.

PATIENTS: Thirty patients with subjective tinnitus.

MAIN OUTCOME MEASURES: Tinnitus matching, Tinnitus Handicap Inventory (THI), patient questionnaire and interview.

RESULTS: The average pretreatment THI score was 33.91 as compared with 26.43 after the placebo and 26.09 after melatonin. The difference in the THI scores between melatonin and placebo treatment were not statistically significant. The average pretreatment THI score for patients who reported overall improvement with melatonin was statistically higher ($P = 0.02$) than the average pretreatment THI score for patients who reported no improvement with melatonin. Among subjects reporting difficulty sleeping attributable to their tinnitus, 46.7% reported an overall improvement after melatonin compared with 20.0% for placebo ($P = 0.04$). There was also a statistically significant difference in improvement with melatonin for those patients with bilateral tinnitus compared with those with unilateral tinnitus ($P = 0.02$).

CONCLUSION: Melatonin has been shown to be useful in the treatment of subjective tinnitus. Patients with high THI scores and/or difficulty sleeping are most likely to benefit from treatment with melatonin. In light of its minimal side effects, melatonin should be a part of the physician's armamentarium in the treatment of tinnitus.

Vitamin B12 deficiency in patients with chronic-tinnitus and noise-induced hearing loss.

Shemesh Z, Attias J, Ornan M, Shapira N, Shahar A. Institute of Noise Hazards Research and Evoked Potentials Laboratory, IDF, Chaim-Sheba Medical Center, Ramat-Gan, Israel.

Am J Otolaryngol 1993 Mar-Apr;14(2):94-9

INTRODUCTION: This study examines the incidence of vitamin B12 deficiency in three groups of noise-exposed subjects: patients with chronic tinnitus and noise-induced hearing loss (NIHL), patients with NIHL only, and subjects demonstrating normal hearing.

MATERIALS AND METHODS: A group of 113 army personnel exposed to military noise was studied. The mean age was 39 years. Chronic tinnitus and NIHL existed in 57 subjects. NIHL alone was observed in 29 subjects, and 27 subjects had normal audiograms. All subjects were queried about noise exposure and dietary habits. Vitamin B12 serum levels were measured.

RESULTS: Patients with tinnitus and NIHL exhibited vitamin B12 deficiency in 47% of cases (blood levels $< \text{or} = 250 \text{ pg/mL}$). This was significantly more ($P < .023$) compared with NIHL and normal subjects who exhibited vitamin B12 deficiency in 27% and 19%, respectively.

CONCLUSION: These observations suggest a relationship between vitamin B12 deficiency and dysfunction of the auditory pathway. Some improvement in tinnitus and associated complaints were observed in 12 patients following vitamin B12 replacement therapy. The authors recommend that routine vitamin B12 serum levels be determined when evaluating patients for chronic tinnitus.

Clinical improvement of memory and other cognitive functions by Ginkgo biloba: review of relevant literature.

Soholm B. Sano-Pharm A/S, Vedbaek, Denmark.

Adv Ther 1998 Jan-Feb;15(1):54-65

Ginkgo biloba is a plant extract used to alleviate symptoms associated with cognitive deficits, e.g., decreased memory performance, lack of concentration, decreased alertness, tinnitus, and dizziness. Pharmacologic studies have shown that the therapeutic effect of ginkgo is based on several active constituents with vasoactive and free radical-scavenging properties. The use of ginkgo extract in either dementias of the Alzheimer or multi-infarct type or in the case of cerebral insufficiency, a symptom

complex related to age-dependent impairment of cerebral circulation, is based mainly on positive results from good-quality placebo-controlled studies that enrolled approximately 1,200 patients with criteria established by International Classification of Diseases (9th and 10th revisions, ICD-9 and ICD-10) or the 3rd revision of the Diagnostic and Statistical Manual (DSM-III-R) (uncomplicated dementia). Effect on cognitive symptoms was within the range of a 25% reduction. Memory, concentration, and alertness were the first symptoms to be relieved, with tinnitus and dizziness improving somewhat later. A minimum of 4 to 6 weeks were needed before a pronounced effect could be expected. The pharmacologic advantage of ginkgo seems to be a very tolerable side-effect profile, with a side-effect frequency at the placebo level.

[The influence on sound damages by an extract of ginkgo biloba]

Stange G; Benning CD

Arch Otorhinolaryngol (United States) Jul 8, 1975, 209 (3) p203-15

A fraction of Ginkgo biloba, used in experiments with animals ensured significantly the diminution of sound damages caused by white noise or by a pure tone of 4.5 kHz. Higher amplitudes of the acoustic nerve potentials show the protective effect of this fraction of Ginkgo biloba at acute sound damages. It is moreover possible to hold physiologically the adaptation of excitation of the hair cells of the organ of Corti by the fraction of Ginkgo biloba before and after sound damage caused by white noise or during a pure tone of 4.5 kHz. The influence of the fraction of Ginkgo biloba can be seen by a significantly slower recovery of the noise damaged evoked potentials of the acoustic cortex. An efferent protective influence on the neurons of the acoustic cortex is discussed. The fraction of Ginkgo biloba in this form of solution has not been tested for clinical use but it seems to be rich in meaning.

SUGGESTED READING

The major psychoses and neuroses as omega-3 essential fatty acid deficiency syndrome: substrate pellagra.

Rudin DO.

Biol Psychiatry 1981 Sep;16(9):837-50

Pellagra was once a major cause of three behaviorally different mental disorders-schizophreniform, manic-depressive-like, and phobic neurotic - plus drying dermatoses, autonomic neuropathies, tinnitus, and fatigue. In this preliminary study all three of the corresponding present-day mental diseases are found to exhibit, statistically, the same pellagraform physical disorders but to ameliorate not so much with vitamins as with supplements of a newly discovered trace omega-3 essential fatty acid (w3-EFA), which provides the substrate upon which niacin and other B vitamin holoenzymes act uniquely to form the prostaglandin 3 series tissue hormones regulating neurocircuits en block. Since present-day refining and food selection patterns, as well as pure corn diets, deplete both the B vitamins and W3-EFA, the existence of therapeutically cross-reacting homologous catalyst and substrate deficiency forms of pellagra are postulated, the first contributing to the B vitamin deficiency epidemics of 50-100 years ago, the second to the more recent endemic "Diseases of Western Civilization" which express in certain genetic subgroups as the major mental illnesses of today.

[Need for rheologically active, vasoactive and metabolically active substances in the initial treatment of acute acoustic trauma] [Article in German]

Pilgramm M, Schumann K.

HNO 1986 Oct;34(10):424-8

Two rheologically active and 8 vasoactive and metabolically active substances were compared in eight independent studies, some of which were randomised and double blind, on 400 patients who had suffered acute acoustic trauma. The control group was given saline. Spontaneous recovery was excluded as far as possible. The following substances were tested: Dextran 40, hydroxyethyl starch 40/0.5, naftidrofurylhydrogenoxalate, Vinpocetin, betahistine, pentoxifylline, flunaricine, Regeneresen AU 4 and 0.9% saline. All groups showed superior results to the control group in both long-term and short-term tests with respect to hearing gain and tinnitus improvement. The rheologically effective substances showed no statistically significant variations. None of the vasoactive or metabolically active substances used as adjunctive therapy improved the results achieved with rheologically effective substances alone. These results demonstrate that acute acoustic trauma can be most effectively treated by rheologically active substances; vasoactive and metabolically active substances are unnecessary. Hyperbaric oxygenation is advantageous as an adjunctive therapy.

The use of Ginkgo Biloba extract associated with magnesium and arginine in patients with tinnitus of a vascular origin

Rivista Italiana di Otorinolaringologia Audiologia e Foniatria (Italy), 1998, 18/1 (37-39)

The Authors report the results achieved using Ginkgo Biloba associated with magnesium and arginine in patients complying of tinnitus. Case reports were previously selected considering the vascular pathology which affected patients taken into consideration. The Authors describe how they managed the treatment and the quite good results obtained in patients whose tinnitus has got a vascular origin.

Effect of traditional Chinese acupuncture on severe tinnitus: a double blind, placebo controlled, clinical investigation with open therapeutic control.

Vilholm OJ; Moller K; Jorgensen K Department of Audiology, Vejle Hospital, Denmark.

Br J Audiol (ENGLAND) Jun 1998, 32 (3) p197-204

This study aims to determine the effect of intensive acupuncture on severe tinnitus. The structure of the study was a randomized, double blind, clinical investigation with open therapeutic surveillance and included 54 patients. All were subjected to 25 treatment sessions over a period of two months, each treatment lasting 30 minutes. Fifty two patients completed the study. The variables used for self registration were based on the visual analogue scale (VAS), where annoyance, loudness and awareness of the tinnitus were assessed. These were recorded twice daily over a four month period starting one month before the first treatment and ending one month after the last treatment. Questionnaires, interviews and audiometry were carried out repeatedly. No statistically significant differences were found between the acupuncture group and the placebo group.

Multicenter study with standardized extract of Ginkgo-Biloba EGB 761 in the treatment of memory alteration, vertigo and tinnitus

Enrique Gomez A.

Investigacion Medica Internacional (Mexico) 1997, 24/2 (31-39)

Two hundred two patients with memory disturbances, vertigo and tinnitus were studied in a prospective, open and multicentric trial, to test the efficacy and safety of standardized extract of Ginkgo-biloba (EGb 761). All patients were administered 40 mg of EGb 761 tid. Observations were done at 6 and 12 weeks. Most of the patients with vertigo (73%) showed a highly significant improvement at the end of the study. Related to the memory disturbances 15% of the patients evaluated mentioned the total absence of the symptom and in 62% it was reported as mild to moderate. The drug did not show to be useful in advanced stages of the disease. In relation with tinnitus most of the patients mentioned the absent or mild degree of the symptom. Significant adverse effects were not reported and the efficacy of the drug in the assessed symptoms was confirmed. The EGb 761 showed to be well tolerated.

Physiology, pathophysiology, and anthropology/epidemiology of human ear canal secretions.

Roeser RJ; Ballachanda BB Callier Center for Communication Disorders/University of Texas at Dallas 75235, USA.

J Am Acad Audiol (CANADA) Dec 1997, 8 (6) p391-400

Two types of glands are found in the outer third of the human ear canal: sebaceous glands that produce sebum and modified apocrine glands that produce apocrine sweat. Together, these substances make up cerumen, which serves to clean, lubricate, and, to some extent, protect the ear canal from bacteria and fungus. Excessive/impacted cerumen can cause tinnitus, vertigo, itching, pain, external otitis, and hearing loss. Two populations are known to have a high incidence of excessive/impacted cerumen: individuals with mental retardation and the elderly. Anthropologists have used cerumen type to track human migratory patterns and epidemiologists have related cerumen type to breast cancer. (53 Refs.)

Attenuation of aminoglycoside-induced cochlear damage with the metabolic antioxidant alpha-lipoic acid.

Conlon BJ; Aran JM; Erre JP; Smith DW The Hearing Research Laboratories, Division of Otolaryngology-Head and Neck Surgery, Duke University Medical Center, Durham, NC 27710, USA.

Hear Res (Netherlands) Feb 1999, 128 (1-2) p40-4

Free radical generation is increasingly implicated in a variety of pathological processes, including drug toxicity. Recently, a number of studies have demonstrated the ability of gentamicin to facilitate the generation of radical species both in vivo and in vitro, which

suggests that this process plays an important role in aminoglycoside-induced ototoxicity. Free radical scavengers are compounds capable of inactivating free radicals, thereby attenuating their tissue damaging capacity. In this study we have determined the ability of the powerful free radical scavenger alpha- lipoic acid (100 mg/kg/day) to attenuate the cochlear damage induced by a highly ototoxic regimen of the aminoglycoside amikacin (450 mg/kg/day, i.m.). Experiments were carried out on pigmented guinea pigs initially weighing 200-250 g. Changes in cochlear function were characterized as shifts in compound action potential (CAP) thresholds, estimated every 5 days, by use of chronic indwelling electrodes implanted at the round window, vertex, and contralateral mastoid. Results showed that animals receiving alpha- lipoic acid in combination with amikacin demonstrated a significantly less severe elevation in CAP thresholds compared with animals receiving amikacin alone ($P < 0.001$; t-test). These results provide further evidence of the recently reported intrinsic role of free radical generation in aminoglycoside ototoxicity, and highlight a potential clinical therapeutic use of alpha-lipoic acid in the management of patients undergoing aminoglycoside treatment.

Changes in cochlear antioxidant enzyme activity after sound conditioning and noise exposure in the chinchilla.

Jacono AA; Hu B; Kopke RD; Henderson D; Van De Water TR; Steinman HM Department of Otolaryngology, Albert Einstein College of Medicine, Bronx, NY 10461-1926, USA.

Hear Res (Netherlands) Mar 1998, 117 (1-2) p31-8

Exposure to low level noise prior to a high level exposure reduces noise-induced hearing loss in mammals. This phenomenon is known as sound conditioning or 'toughening'. Reactive oxygen intermediates have been implicated in noise-induced cochlear damage . To evaluate if in situ antioxidant processes may play a role in the toughening phenomenon initiated by low level noise exposure we analyzed glutathione reductase, gamma-glutamyl cysteine synthetase, and catalase in stria vascularis and organ of Corti fractions from cochleae of chinchillas exposed to a sound conditioning paradigm. Chinchillas were either (A) kept in quiet cages (control), (B) exposed to conditioning noise of a 0.5 kHz octave band (90 dB for 6 h/day for 10 days), (C) exposed to high level noise (105 dB for 4 h) or (D) exposed to conditioning noise (B) followed by exposure to the higher level noise (C). Each of the noise exposure conditions (B, C, D) induced changes in the levels of these three antioxidant enzymes. The enzyme-specific activity data for the four subject groups support the following two hypotheses. (1) Changes in glutathione reductase, gamma-glutamyl cysteine synthetase, and catalase play a role in attenuating hearing loss associated with sound conditioning followed by high level noise. (2) Hair cells in the organ of Corti are protected from noise-induced damage by increasing stria vascularis levels of catalase, a hydrogen peroxide scavenging enzyme, and of enzymes involved in maintaining glutathione in the reduced state. The model formulated by these hypotheses suggests that agents that protect or augment the glutathione system in the cochlea may be protective against noise-induced hearing loss.

Role of glutathione in protection against noise-induced hearing loss.

Yamasoba T; Nuttall AL; Harris C; Raphael Y; Miller JM Kresge Hearing Research Institute, The University of Michigan, 1301 East Ann Street, Ann Arbor, MI 48109-0506, USA.

Brain Res (Netherlands) Feb 16 1998, 784 (1-2) p82-90

A potential mechanism of hearing loss due to acoustic overstimulation is the generation of reactive oxygen species (ROS). ROS not removed by antioxidant defenses could be expected to cause significant damage to the sensory cells of the cochlea. We studied the influence of the antioxidant glutathione (GSH) on noise-induced hearing loss by using l-buthionine-[S,R]-sulfoximine (BSO), an inhibitor of GSH synthesis, and 2-oxothiazolidine-4-carboxylate (OTC), a cysteine prodrug, which promotes rapid restoration of GSH when GSH is acutely depleted. Pigmented female guinea pigs were exposed to broadband noise (102 dB SPL, 3 h/day, 5 days) while receiving daily injections of BSO, OTC, or saline. By weeks 2 and 3 after noise exposure, BSO-treated animals showed significantly greater threshold shifts above 12 kHz than saline-treated subjects, whereas OTC-treated animals showed significantly smaller threshold shifts at 12 kHz than controls. Histologically assessed noise-induced damage to the organ of Corti, predominantly basal turn row 1 outer hair cells, was most pronounced in BSO-treated animals. High performance liquid chromatographic analysis showed that OTC significantly increased cysteine levels, but not GSH levels, in the cochlea. These findings show that GSH inhibition increases the susceptibility of the cochlea to noise-induced damage and that replenishing GSH, presumably by enhancing availability of cysteine, attenuates noise-induced cochlear damage . Copyright 1997 Elsevier Science B.V.

Vitamin E and lipoic acid, but not vitamin C improve blood oxygenation after high-energy IMPULSE noise (BLAST) exposure.

Armstrong KL, Cooper MF, Williams MT, Elsayed NM Department of Respiratory Research, Walter Reed Army Institute of Research, Washington, DC 20307, USA. MAJ_KARYN_ARMSTRONG@WRSMTP-CCMAIL.ARMY.MIL

Biochem Biophys Res Commun 1998 Dec 9;253(1):114-8

Exposure to high energy impulse noise (BLAST) caused by explosions, is structural and functional damage to the hollow organs, especially to the respiratory and auditory systems. Lung damage includes alveolar wall rupture, edema and hemorrhage, and may be fatal. Previous observations at the molecular level using the rat model, suggested that secondary free radical-mediated oxidative stress occurs post exposure resulting in antioxidant depletion and hemoglobin (Hb) oxidation. This study examined whether a short period of pre-exposure supplementation with antioxidants would protect Hb from the effects of BLAST exposure. Six groups of male Sprague-Dawley rats (8/group) were gavaged with 800 IU vitamin E (VE) in 2 ml corn oil, 1000 mg vitamin C (VC) in 2 ml distilled water or 25 mg or (-lipoic acid (LA) in 2 ml corn oil for 3 days. Matched control groups were gavaged with the respective vehicles. On day 4, rats were deeply anesthetized and exposed to a simulated BLAST wave with an average peak pressure of 62 +/- 2 kPa. Rats were euthanized one hour post exposure and blood samples were obtained by cardiac puncture and analyzed using a hemoximeter. Post exposure oxygenation states (HbO₂, O₂ saturation, and O₂ content) were markedly decreased, while reduced-Hb was increased. Supplementation with VE and LA reversed the trend and increased Hb oxygenation, but VC did not. This suggests that a brief dietary loading with pharmacological doses of VE or LA, but not VC shortly before BLAST exposure may be beneficial. Moreover, measurement of blood oxygenation may function as a simple semi-invasive biomarker of BLAST-induced injury applicable to humans.

The efficacy of Lasix-vitamin therapy (L-V therapy) for sudden deafness and other sensorineural hearing loss.

Konishi K, Nakai Y, Yamane H Department of Otolaryngology, Osaka City University Medical School, Japan.

Acta Otolaryngol Suppl (Stockh) 1991;486:78-91

The efficacy of Lasix-vitamin therapy (L-V therapy) for sudden deafness (SD) was compared with that of conventional therapeutic regimens. There was no significant difference in efficacy between the two therapies. However, in fresh cases (within 7 days from onset of SD), L-V therapy gave a cure rate of 42.3% and an effectiveness rate of 88.4%, these rates being higher than those obtained with conventional therapy; and in cases treated within 4 weeks, L-V therapy was significantly more effective than conventional therapy. Besides, in cases with severe hearing loss (more than 70 dB hearing level) or vestibular symptoms, which were important factors of prognosis, L-V therapy proved more efficient. The efficacy of L-V therapy for other sensorineural hearing loss was also evaluated. In Meniere's disease, L-V therapy proved effective in 45.9% of cases, but with only a 20-30% effectiveness rate in other cases, e.g. idiopathic hearing loss, head and neck injury, noise-induced hearing loss and chronic otitis media.

Thioctic (lipoic) acid: a therapeutic metal-chelating antioxidant?

Ou P, Tritschler HJ, Wolff SP Department of Medicine, University College London Medical School, U.K.

Biochem Pharmacol 1995 Jun 29;50(1):123-6

Thioctic (alpha-lipoic) acid (TA) is a drug used for the treatment of diabetic polyneuropathy in Germany. It has been proposed that TA acts as an antioxidant and interferes with the pathogenesis of diabetic polyneuropathy. We suggest that one component of its antioxidant activity requiring study is the direct transition metal-chelating activity of the drug. We found that TA had a profound dose-dependent inhibitory effect upon Cu(2+)-catalysed ascorbic acid oxidation (monitored by O₂ uptake and spectrophotometrically at 265 nm) and also increased the partition of Cu²⁺ into n-octanol from an aqueous solution suggesting that TA forms a lipophilic complex with Cu²⁺. TA also inhibited Cu(2+)-catalysed liposomal peroxidation. Furthermore, TA inhibited intracellular H₂O₂ production in erythrocytes challenged with ascorbate, a process thought to be mediated by loosely chelated Cu²⁺ within the erythrocyte. These data, taken together, suggest that prior intracellular reduction of TA to dihydrolipoic acid is not an obligatory mechanism for an antioxidant effect of the drug, which may also operate via Cu(2+)-chelation. The R-enantiomer and racemic mixture of the drug (alpha-TA) generally seemed more effective than the S-enantiomer in these assays of metal chelation.

Dihydrolipoic acid--a universal antioxidant both in the membrane and in the aqueous phase. Reduction of peroxy, ascorbyl and chromanoxyl radicals.

Kagan VE, Shvedova A, Serbinova E, Khan S, Swanson C, Powell R, Packer L Department of Molecular and Cell Biology, University of California, Berkeley 94720.

Biochem Pharmacol 1992 Oct 20;44(8):1637-49

Thioctic (lipoic) acid is used as a therapeutic agent in a variety of diseases in which enhanced free radical peroxidation of membrane phospholipids has been shown to be a characteristic feature. It was suggested that the antioxidant properties of thioctic acid and its reduced form, dihydrolipoic acid, are at least in part responsible for the therapeutic potential. The reported results on the antioxidant efficiency of thioctic and dihydrolipoic acids obtained in oxidation models with complex multicomponent initiation systems are controversial. In the present work we used relatively simple oxidation systems to study the antioxidant effects of dihydrolipoic and thioctic acids based on their interactions with: (1) peroxy radicals which are essential for the initiation of lipid peroxidation, (2) chromanoxyl radicals of vitamin E, and (3) ascorbyl radicals of vitamin C, the two major lipid- and water-soluble

antioxidants, respectively. We demonstrated that: (1) dihydrolipoic acid (but not thioctic acid) was an efficient direct scavenger of peroxy radicals generated in the aqueous phase by the water-soluble azoinitiator 2,2'-azobis(2-amidinopropane)-dihydrochloride, and in liposomes or in microsomal membranes by the lipid-soluble azoinitiator 2,2'-azobis(2,4-dimethylvaleronitrile); (2) both dihydrolipoic acid and thioctic acid did not interact directly with chromanoxyl radicals of vitamin E (or its synthetic homologues) generated in liposomes or in the membranes by three different ways: UV-irradiation, peroxy radicals of 2,2'-azobis(2,4-dimethylvaleronitrile), or peroxy radicals of linolenic acid formed by the lipoxygenase-catalyzed oxidation; and (3) dihydrolipoic acid (but not thioctic acid) reduced ascorbyl radicals (and dehydroascorbate) generated in the course of ascorbate oxidation by chromanoxyl radicals. This interaction resulted in ascorbate-mediated dihydrolipoic acid-dependent reduction of the vitamin E chromanoxyl radicals, i.e. vitamin E recycling. We conclude that dihydrolipoic acid may act as a strong direct chain-breaking antioxidant and may enhance the antioxidant potency of other antioxidants (ascorbate and vitamin E) in both the aqueous and the hydrophobic membraneous phases.

Interplay between lipoic acid and glutathione in the protection against microsomal lipid peroxidation.

Bast A, Haenen GR Department of Pharmacochemistry, Faculty of Chemistry, Vrije Universiteit, Amsterdam, The Netherlands.

Biochim Biophys Acta 1988 Dec 16;963(3):558-61

Reduced glutathione (GSH) delays microsomal lipid peroxidation via the reduction of vitamin E radicals, which is catalyzed by a free radical reductase (Haenen, G.R.M.M. et al. (1987) Arch. Biochem. Biophys. 259, 449-456). Lipoic acid exerts its therapeutic effect in pathologies in which free radicals are involved. We investigated the interplay between lipoic acid and glutathione in microsomal Fe²⁺ (10 microM)/ascorbate (0.2 mM)-induced lipid peroxidation. Neither reduced nor oxidized lipoic acid (0.5 mM) displayed protection against microsomal lipid peroxidation, measured as thiobarbituric acid-reactive material. Reduced lipoic acid even had a pro-oxidant activity, which is probably due to reduction of Fe³⁺. Notably, protection against lipid peroxidation was afforded by the combination of oxidized glutathione (GSSG) and reduced lipoic acid. It is shown that this effect can be ascribed completely to reduction of GSSG to GSH by reduced lipoic acid. This may provide a rationale for the therapeutic effectiveness of lipoic acid.

Glutathione monoethyl ester: preparation, uptake by tissues, and conversion to glutathione.

Anderson ME, Powrie F, Puri RN, Meister A

Arch Biochem Biophys 1985 Jun;239(2):538-48

Glutathione monoethyl ester (L-gamma-glutamyl-L-cysteinylglycyl ethyl ester), in contrast to glutathione itself, is effectively transported into many types of cells. The ester is converted intracellularly into glutathione. Intraperitoneal injection of ³⁵S-labeled ester into mice was followed by rapid appearance of isotope in the glutathione of liver, kidney, spleen, pancreas, and heart; the glutathione levels of these tissues also increased. Oral administration of the ester to mice also increased cellular glutathione levels. Relatively little extracellular deesterification was found. Transport of glutathione ester into human erythrocytes and intracellular conversion to glutathione was observed. The findings suggest that the glutathione ester will be useful as a radioprotecting agent and in the prevention and treatment of toxicity due to certain foreign compounds and oxygen. The ester may be useful in experimental work on glutathione transport, metabolism, and function, and in related studies on oxygen toxicity, radiation, mutagenesis, and ageing. Methods for the preparation of glutathione monoethyl ester and several related compounds are given.

Sulfhydryl compounds and antioxidants inhibit cytotoxicity to outer hair cells of a gentamicin metabolite in vitro.

Garetz SL, Rhee DJ, Schacht J Kresge Hearing Research Institute, Department of Otolaryngology, University of Michigan, Ann Arbor 48109-0506.

Hear Res 1994 Jun 15;77(1-2):75-80

Aminoglycoside antibiotics such as gentamicin have long been known to destroy cochlear and vestibular hair cells in vivo. In the cochlea outer hair cells are preferentially affected. In contrast, gentamicin will not damage outer hair cells in vitro unless it has been enzymatically converted to a cytotoxic metabolite. Several potential inhibitors of this enzymatic reaction were tested in an in vitro assay against outer hair cells isolated from the guinea pig cochlea. Viability of hair cells (viable cells as per cent of total number of cells observed) averaged about 70% under control conditions. Addition of metabolized gentamicin significantly reduced viability to less than 50% in one hour. Sulfhydryl compounds (glutathione, dithioerythritol) and antioxidants (vitamin C, phenylene diamine, trolox) prevented the cytotoxic actions of the gentamicin metabolite. Inhibitors of amine oxidases and compounds reportedly protective against renal and acute lethal toxicity of aminoglycosides (poly-L-aspartate and pyridoxal phosphate, respectively) were ineffective as protectants. The results reinforce the hypothesis that gentamicin is enzymatically converted to a cytotoxin and imply the participation of sulfhydryl-sensitive groups or free radicals in this reaction. Alternatively or additionally, sulfhydryl compounds or antioxidants may participate in detoxification reactions.

alpha-Lipoic acid protects against reperfusion injury following cerebral ischemia in rats.

Panigrahi M, Sadguna Y, Shivakumar BR, Kolluri SV, Roy S, Packer L, Ravindranath V Department of Neurochemistry, National Institute of Mental Health and Neurosciences, Bangalore, India.

Brain Res 1996 Apr 22;717(1-2):184-8

Ischemic-reperfusion injury in humans occurs in conditions such as stroke, cardiac arrest, subarachnoid hemorrhage or head trauma. Maximal tissue damage is observed during reperfusion, which is primarily attributed to oxidative injury resulting from production of oxygen free radicals. One of the major consequences of such damage is the depletion of the cellular antioxidant, glutathione (GSH) leading to oxidation of protein thiols to disulfides and the loss of activity of critical enzymes having active thiol group(s). Thus, the maintenance of thiol homeostasis is an important factor in cell survival. The effect of thiol antioxidants like alpha-lipoic acid and the isopropyl ester of GSH was examined on the morbidity and mortality of rats subjected to reperfusion following cerebral ischemia induced by bilateral carotid artery occlusion and hypotension. While the GSH isopropyl ester had no significant protective effect; after pretreatment of rats, alpha-lipoic acid was detected in the rat brain and it dramatically reduced the mortality rate from 78% to 26% during 24 h of reperfusion. The natural thiol antioxidant, alpha-lipoic acid is effective in improving survival and protecting the rat brain against reperfusion injury following cerebral ischemia.

Automatic monitoring of mechano-electrical transduction in the guinea pig cochlea.

Patuzzi R, Moleirinho A Physiology Department, University of Western Australia, Nedlands, Australia.
rpatuzzi@cyllene.uwa.edu.au

Hear Res 1998 Nov;125(1-2):1-16

We have estimated the transfer curve relating instantaneous sound pressure in the ear canal to instantaneous receptor current through the outer hair cells (OHCs) in the basal turn of the guinea pig cochlea using the cochlear microphonic (CM) elicited by continuous 200 Hz tones. The transfer curve is well approximated by a Boltzmann activation curve which has been automatically analysed using a custom-built electronic circuit which continuously derives the three parameters defining the curve with a time resolution of seconds. This technique offers a convenient method of monitoring changes in OHC mechano-electrical transduction due to cochlear disturbances, and allows the investigation of cochlear homeostasis over the course of hours. We present here details of the technique, evidence that the recordings are minimally contaminated by neural responses, and normative data on the changes in the parameters with sound level. As the level of the 200 Hz tone increases, the equivalent operating point on the transfer curve migrates in a way consistent with a movement of the organ of Corti towards scala tympani or a contraction of the outer hair cells. Surprisingly, the effective slope of the curve which represents the mechanical sensitivity of the transduction process decreases over an 8 to 1 range as the level of the 200 Hz tone is increased. The effect of this variation is that the amplitude of the equivalent mechanical displacement input to the mechano-electrical transduction process appears to increase by a mere 2 to 1 while the sound level increases by a factor of 20 to 1. These changes are not neurally mediated, since they also occur in the presence of tetrodotoxin and the blocker of afferent neurotransmission, kainate.

Uptake of amikacin by hair cells of the guinea pig cochlea and vestibule and ototoxicity: comparison with gentamicin.

Aran JM, Chappert C, Dulon D, Erre JP, Arousseau C Laboratoire d'Audiologie Experimentale, Inserm U 229, Hopital Pellegrin, Bordeaux, France.

Hear Res 1995 Feb;82(2):179-83

The distribution of amikacin (AK), an exclusive cochleo-toxic aminoglycosidic antibiotic (AA), and of gentamicin (GM), which is both cochleo- and vestibulo-toxic, has been studied in cochlear and vestibular hair cells. Guinea pigs were treated during six days with one daily injection of AK (450 mg/kg/day) or GM (60 mg/kg/day). AAs were detected, using immunocytochemical technique with scanning laser confocal microscopy, in isolated cells from guinea pigs sacrificed from 2 to 30 days after the end of the treatments. Results demonstrate a rapid uptake (as soon as after 2-day treatment) of both AAs by cochlear and vestibular hair cells and a very slow clearance. Particularly GM and AK are detected in type I and type II hair cells of the utricles and cristae ampullaris. The presence of these two molecules with different toxic potentialities towards cochlear and vestibular hair cells indicates that the selective ototoxicity of aminoglycosides cannot be explained simply on the basis of particular uptake and accumulation in the different sensory hair cells.

Aminoglycoside ototoxicity and the medial efferent system: II. Comparison of acute effects of different antibiotics.

Lima da Costa D, Erre JP, Pehourq F, Aran JM Laboratoire d'Audiologie Experimentale et Clinique, Universite de Bordeaux II, Hopital Pellegrin, France.

Gentamicin (GM) has been shown to reversibly reduce the ability of contralateral noise to suppress ipsilateral cochlear activity, in a dose-dependent manner. However, during chronic administration of lower doses (60 mg/kg) the involvement of medial efferents could not be demonstrated. The purposes of the present study were to determine whether other aminoglycosides would display the same acute effects as GM and whether there was any correlation between their specificity and degree of cochlear and vestibular toxicity and their potency of blockade of the medial efferent system. Thus, we observed changes in ipsilateral ensemble background activity (EBA) of the VIIIth nerve without and with contralateral low level (55 dB SPL) broadband noise stimulation, in awake guinea pigs (GPs), before and after one single high-dose intramuscular injection of different aminoglycoside antibiotics (AAs) (gentamicin, amikacin, neomycin, netilmicin, streptomycin, tobramycin). For comparison, the effects of strychnine, a known antagonist of the efferent transmission and of cisplatin, an antineoplastic agent with cochleotoxic properties were also studied. Netilmicin displayed blocking properties similar to GM, although less pronounced, while amikacin and neomycin had no effect on medial efferent function. With tobramycin and streptomycin a decrease in suppression was usually associated with a reduction of the EBA measured without acoustic stimulation. However, with cisplatin, suppression was still effective when EBA was severely decreased. We could not observe specific effects of strychnine on medial efferent function. In conclusion, no correlation was found between specificity and degree of AA ototoxicity and their action on the medial efferent system.

[Ginkgo extract EGb 761 (tenobin)/HAES versus naftidrofuryl A randomized study of therapy of sudden deafness]

Hoffmann F; Beck C; Schutz A; Offermann P Universitäts-HNO-Klinik Freiburg im Breisgau.

Laryngorhinootologie (Germany) Mar 1994, 73 (3) p149-52

80 patients with idiopathic sudden hearing loss existing no longer than 10 days were included in a randomised reference-controlled study. The therapeutic value of Ginkgo EGb 761 (Tebonin) + HAES was compared to that of Naftidrofuryl (Dusodril)+HAES. The main mechanisms of action of EGb 761 are a vasoregulating activity (increased blood flow), the platelet activating factor antagonism and a prevention of membrane damage caused by free radicals. Naftidrofuryl has antiserotonergic and therefore vasodilatory properties. The statistical analysis of the audiometric data was performed in measuring the relative hearing gain as described by Eibach 1979. After one week of observation, 40% of the patients in each group showed a complete remission of hearing loss. This was also observed by other authors who had compared other drugs. Therefore, in these cases, it is most likely that spontaneous recovery is the most important factor. After two and three weeks of observation, measuring the relative hearing gain, there was a significant borderline benefit of EGb 761 ($p = 0.06$) without any side effects. Some patients of the reference group developed side effects such as orthostatic dysregulation or headache or sleep disturbances. Minimising side effects should be one of the most important goals in therapy of sudden hearing loss until the efficiency of infusion therapy is proved.

[Therapeutic trial in acute cochlear deafness. A comparative study of Ginkgo biloba extract and nicergoline]

Dubreuil C

Presse Med (France) Sep 25 1986, 15 (31) p1559-61

Ischemia and the metabolic disorder it entails would seem to be the pathogenic mechanism behind acute cochlear deafness, irrespective of the triggering process. The prognosis is entirely dependent on the rapid initiation of an effective treatment. At the end of a double-blind therapeutic trial comparing Ginkgo biloba extract and a standard alpha blocker (nicergoline), a significant recovery was observed in both therapeutic groups, but improvement was distinctly better in the Ginkgo biloba group.

All Contents Copyright © 1995-2009 Life Extension Foundation All rights reserved.

LifeExtension®

These statements have not been evaluated by the FDA. These products are not intended to diagnose, treat, cure or prevent any disease. The information provided on this site is for informational purposes only and is not intended as a substitute for advice from your physician or other health care professional or any information contained on or in any product label or packaging. You should not use the information on this site for diagnosis or treatment of any health problem or for prescription of any medication or other treatment. You should consult with a healthcare professional before starting any diet, exercise or supplementation program, before taking any medication, or if you have or suspect you might have a health problem. You should not stop taking any medication without first consulting your physician.