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TINNITUS: THE PHANTOM SOUND (PART III)

PHARMACOLOGICAL TREATMENT OF TINNITUS

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Tinnitus: The phantom sound (part III). Pharmacological treatment of tinnitus

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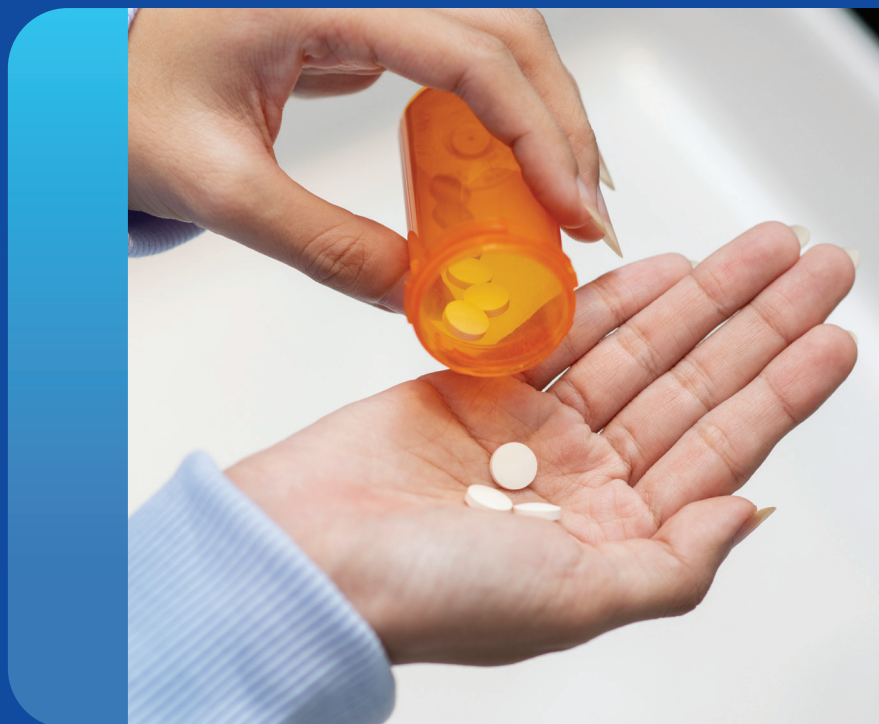
The topic of tinnitus has already been discussed in two of our previous newsletters. We therefore recommend you read the previous editions if you would like to go deeper into the subject; it will also make the current newsletter more understandable.

TINNITUS IS A VERY INTRIGUING AND CHALLENGING PATHOLOGY, BUT HAVE YOU EVER WONDERED WHAT TYPES OF MEDICATIONS ARE MOST EFFECTIVE?

Here we will present the options for the pharmacological treatment of tinnitus. Because the causes of tinnitus are complex, none of the drugs listed have been approved for treatment of this disease by the Food and Drug Administration (FDA) or the European Medical Agency (EMA).



ONE REASON IS THAT THE CHARACTERISTICS AND SYMPTOMS OF TINNITUS VARY SO WIDELY FROM PATIENT TO PATIENT, SO TREATMENT IS VERY CHALLENGING.



The groups of medical substances that may be beneficial in treating tinnitus are:

- anticonvulsants,
- vasodilators,
- tranquilizers,
- antihistamines,
- antiarrhythmic agents,
- antianxiety medicines,
- antidepressants,
- local anesthetics,
- vitamin pills,
- ginkgo biloba extracts,
- anesthetics,
- antipsychotics,
- calcium channel blockers,
- cholinergic antagonists,
- NMDA antagonists (N-methyl-D-aspartate receptor antagonists)
- muscle relaxants.

Double-blinded clinical trials are needed to determine safety and efficacy. The literature appears to indicate that, based on clinical experience, a combination of drugs may be more beneficial than only one. Pharmaceutical factors that should be taken into consideration are:

- (1) dose (the most effective and safe),**
- (2) duration of treatment,**
- (3) potential side-effects (permanent or temporary),**
- (4) the risk of drug addiction or dependence,**
- (5) possible interactions between drugs,**
- (6) possible withdrawal symptoms or tolerance.**

Importantly, tinnitus may lead to comorbidities such as depression, insomnia, or anxiety.

One should also keep in mind that drugs used to treat other diseases may themselves cause unwanted tinnitus. These include alcohol, antineoplastic

chemotherapeutic agents, heavy metals, antimetabolites, antitumor agents, antibiotics, caffeine, cocaine, marijuana, nonnarcotic analgesics and antipyretics, ototoxic antibiotics and diuretics, oral contraceptives, quinine and chloroquine, and salicylates.



BETAHISTINE FOR TINNITUS (BASED ON COCHRANE ANALYSIS)

In a Cochrane analysis, inclusion criteria to randomised controlled trials (RCTs) were acute or chronic subjective idiopathic tinnitus in patients of any age.

All studies comparing interventions with betahistine or placebo were included (that is, all courses of betahistine, regardless of dose regimen or formulation and for any duration of treatment).

In summary, 5 clinical studies were included (making a total of over 300 participants), in

which 4 were parallel-group randomised clinical trials and 1 was a cross-over design. The risk of bias was unclear in all of them.

The results were that, compared to placebo, there was no evidence of betahistine being effective in treating subjective idiopathic tinnitus.

Nevertheless, betahistine is well-tolerated in patients and the risk of side effects is similar to placebo.

At the same time, on the GRADE scale, the quality of the evidence of the reported outcomes ranged from moderate to very low. Moreover, betahistine may benefit patients who suffer from tinnitus as a result of Ménière's disease.

GINGKO BILOBA FOR TINNITUS (BASED ON COCHRANE ANALYSIS)

According to the Cochrane database, 12 studies (with a total of 1915 participants) were involved in this analysis: 11 compared the effects of Ginkgo biloba with placebo, and 1 study compared the effects of Ginkgo biloba combined with hearing aids to hearing aids alone.

The result was that the benefits or harms of Ginkgo biloba

for treating tinnitus when compared to placebo were uncertain.

Similarly, conclusions were difficult to draw regarding the benefits and harms of Ginkgo biloba when used concurrently with hearing aids.

On the GRADE scale, the quality of evidence of the reported outcomes ranged from moderate to very low, due to the methodology (in future studies the research methodology needs to be more rigorous).

ANTICONSULSANTS FOR TINNITUS (BASED ON COCHRANE ANALYSIS)

In this review 7 trials (453 patients) were included, and 4 different anticonvulsants were investigated: gabapentin, carbamazepine, lamotrigine, and flunarizine. The risk of bias

in most studies was 'high' or 'unclear'. Three studies included a validated questionnaire (primary outcome).

None of them showed a

significant positive effect of anticonvulsants.

A meta-analysis of “near or total eradication of tinnitus annoyance” showed no effect of anticonvulsants (risk difference

(RD) 4%, 95% CI -2% to 11%).

Side-effects of anticonvulsants were experienced by 18% of patients.

EFFECTIVENESS OF THE PHARMACOLOGICAL TREATMENT OF TINNITUS

Here, 36 RCTs were included with 2,761 participants. The main result revealed that interventions with certain brain-acting pharmaceuticals were associated with less tinnitus severity and better response rate compared to placebo/control.

The pharmaceuticals were amitriptyline (a tricyclic antidepressant), acamprosate (a GABA analog), gabapentin (another GABA analog), and drugs with anti-inflammatory or anti-oxidant effects (e.g. intra-tympanic dexamethasone

injection plus orally administered melatonin).

Orally administered amitriptyline was associated with the biggest reduction in tinnitus severity and the fourth highest response rate. None of the interventions were associated with changes in quality of life compared to placebo/control.

All the investigated treatments were associated with similar drop-out rates to placebo/control.

The current network meta-analysis suggests that there is a potential role for brain-acting drugs (especially amitriptyline, acamprosate, and gabapentin) or those with anti-inflammatory or anti-oxidant effects (for example, intra-tympanic dexamethasone injection plus oral melatonin) as the preferred treatment for tinnitus of nonspecific origin.

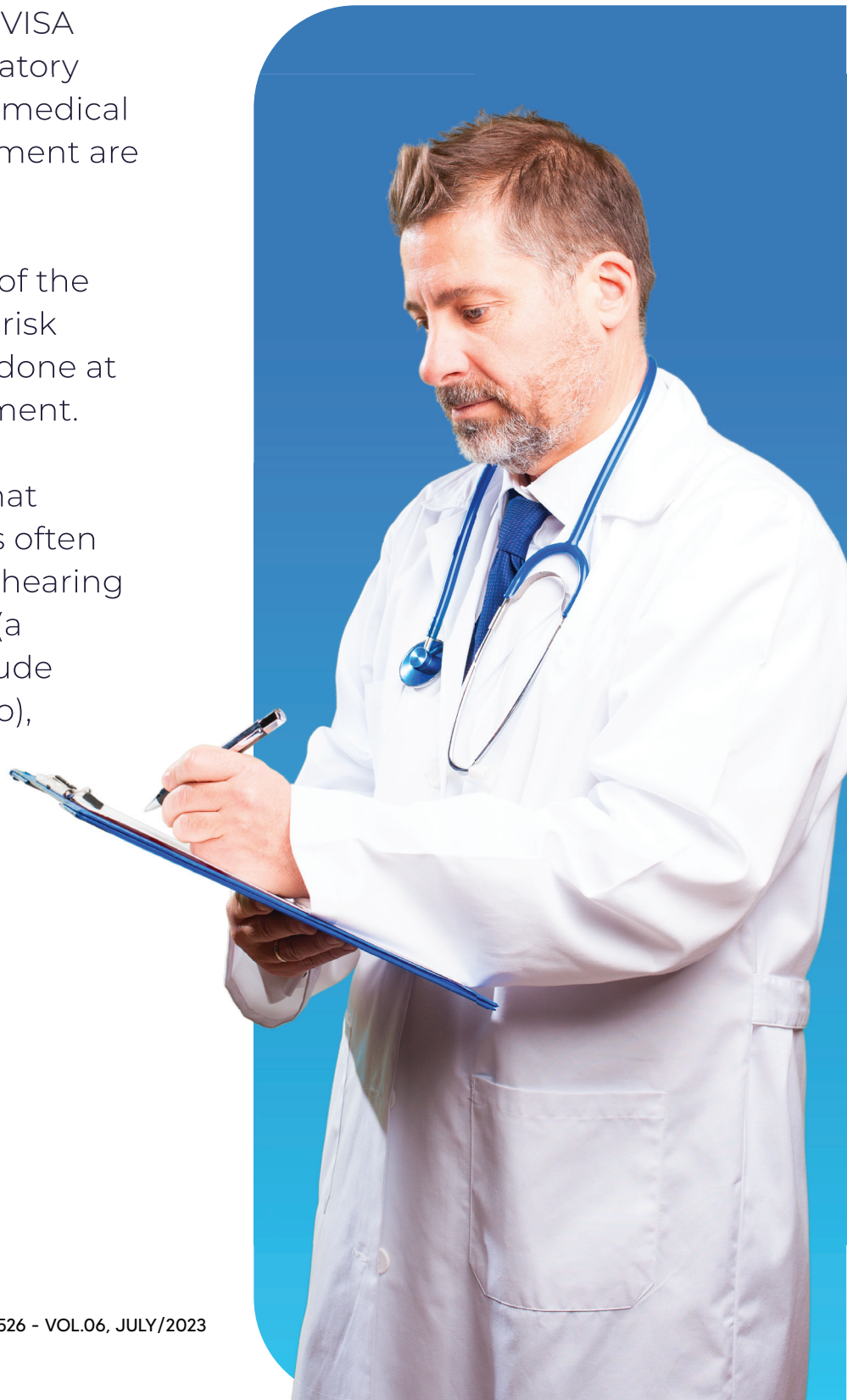
TIPS FOR PHARMACOLOGICAL TREATMENT OF TINNITUS

1. No drugs have been approved by the FDA (Food and Drug Administration), EMA (European Medical Agency), or ANVISA (Brazilian Health Regulatory Agency). As a result, all medical drugs for tinnitus treatment are administered off-label.

2. Individual diagnosis of the cause of tinnitus and a risk assessment should be done at the beginning of treatment.

It is not always clear what causes tinnitus, but it is often linked to some form of hearing loss, Ménière's disease (a condition that can include hearing loss and vertigo), comorbidities such as diabetes, thyroid disorders, multiple sclerosis, anxiety, insomnia, or depression.

Tinnitus is often associated with age-related hearing loss, inner ear damage caused by repeated exposure to loud noises, build-up of earwax, middle ear infection, or otosclerosis.



3. Tinnitus can be a side-effect of some chemotherapy medicines, antibiotics, non-steroidal anti-inflammatory drugs (NSAIDs), and aspirin.

4. When starting tinnitus treatment, take into consideration:

- a) dose (the most effective and safe),
- b) the duration of the treatment,
- c) side-effects (permanent or temporary),
- d) the risk of drug addiction or dependence,
- e) potential interactions between drugs,
- f) possible withdrawal symptoms or tolerance of the drug.

5. If tinnitus is caused by Ménière's disease, both pharmacological and surgical treatments may be appropriate.

Pharmacotherapy in the treatment of Ménière's disease includes drugs against vertigo (thiethylperazine, promethazine), diuretics (acetazolamide, hydrochlorothiazide, furosemide), and drugs that improve blood circulation in the inner ear (betahistine). Diuretics relieve dizziness in about 60% of patients.

We invite you to follow our new monthly newsletters! If you have any suggestions for topics you would like to see discussed, please send an e-mail to misanfins@gmail.com

See you in our next newsletter!

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