

The Use of Sodium Enoxaparin in the Treatment of Tinnitus

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Abstract: Tinnitus is a pathological event caused by abnormal stimulation of any point along the acoustic pathway. Generally, it produces a sharp tone accompanied by hearing impairment. Currently, no widely used standard protocol for treatment of this condition exists, and vascular microthrombotic factors are considered as the main determinants. Prompted by such observations, we implemented a protocol using an anticoagulant, sodium enoxaparin. It is a kind of heparin with a low molecular weight and is endowed with antithrombotic activity. We studied 40 patients (ages 20–65 years) who had been experiencing tinnitus for at least 2 months. We divided patients into two groups: To the first group, enoxaparin was administered for 10 days; the patients in the second group were treated with traditional therapy (corticosteroids, vasoactive agents, multivitamins, and anticoagulants). At the beginning and at the end of the therapy period, the patients were evaluated by instrumental examinations. All patients treated with anticoagulant therapy have shown an evident abatement of their tinnitus symptom. No patient experienced side effects from this treatment. The results indicate that administration of sodium enoxaparin is an excellent mode of therapy for patients with tinnitus.

Key Words: microthrombotic factors; sodium enoxaparin; tinnitus

Tinnitus is a pathological event caused by abnormal stimulation of any point along the acoustic pathway, from the organ of Corti to cortical areas. It generally produces a sharp tone and often is accompanied by hearing impairment. Moreover, as the tinnitus symptoms are typified by complex noise, their exact height cannot be determined. As tinnitus is often the generic result of a dysfunction of complex systems and apparatuses, identifying the point at which the pathological mechanism operates is difficult [1].

No widely used standard protocol for the treatment of this condition currently exists. The most commonly used medications are corticosteroids, vasoactive agents, multivitamins (A, E, B-complex), and anticoagulants. The condition may be determined by many, often unidentifiable causes. Vascular microthrombotic factors (whether primary or secondary to phlogistic or autoimmune responses) currently are regarded as the main determinants [1–3].

Prompted by such observations, we implemented a protocol using an anticoagulant, sodium enoxaparin. Sodium enoxaparin is indicated in the treatment of unstable angina in non-Q-wave acute myocardial infarction; prophylaxis of deep venous thrombosis; neoplasia; previous thromboembolism; obesity; varicose veins; hormone therapy; chronic myocardial insufficiency; chronic respiratory insufficiency; acute pulmonary embolism; diabetic micro- and macroangiopathy; endobulbar bleeding, particularly to facilitate postsurgical reabsorption in ophthalmic surgery; and prophylaxis of coagulation during hemodialysis (100 IU/kg into the arterial line at the start of the session [1,4–6]. Contraindications for a given patient include a history of thrombocytopenia after heparin treatment; hemorrhagic manifestations or tendencies due to disorders of hemostasis that are not heparin-dependent or related to consumption coagulopathy; organic injuries at risk for bleeding; acute infectious endocarditis (excluding endocarditis due to a mechanical prosthesis); hemorrhagic cerebrovascular events; allergy to enoxaparin; concurrent use of ticlopidine, salicylate, or nonsteroidal antiinflammatory drugs with sodium enoxaparin; and

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association with a platelet anticoagulant (dipyridamole, sulfinpyrazone, etc.) [6–9].

Collateral effects are slight hemorrhaging, usually due to preexisting risk factors; thrombocytopenia; sometimes serious cutaneous necrosis near the injection site; cutaneous or systemic allergy; and increased transaminase levels [3]. The objective of our study was to determine the efficacy and feasibility of administering enoxaparin for tinnitus.

PATIENTS AND MATERIALS

Patients were selected on the basis of the following inclusion criteria: were between 20 and 65 years of age, had experienced tinnitus and hearing loss of 30 dB of audibility threshold involving the medium frequencies (2,000–4,000 Hz) for at least 2 months, and had provided informed consent. We analyzed 40 patients divided randomly into two groups of equal number (group A and group B). All patients were hospitalized for 10 days. To those in group A, enoxaparin was administered subcutaneously at a dose of 2,000 IU twice daily for 10 days. Group B (control) patients received traditional therapy (intravenously): corticosteroids, vasoactive agents, multivitamins (A, E, B-complex), and anticoagulants [10,11].

At the beginning and at the end of the therapy, all patients underwent the following instrumental examinations: liminal tonal audiometry; tympanometry (by Metz test); otoacoustic emission with linear click emission; otoacoustic products of distortion with the Macro system; hematocrit and hemoglobin levels; blood tests; and subjective assessment of symptoms on a scale from 0 to 4 (with 0 indicating absence of tinnitus, 1 denoting low tinnitus, 2 meaning medium tinnitus, 3 indicating high tinnitus, and 4 denoting incapacitating tinnitus). Daily during the treatment, we performed three of the

Table 2. Hearing Test Results Before and After Therapy (Group A)

Frequency	Hearing Improvement (Mean)	± SEM
2,000 Hz	19.5	4.84
4,000 Hz	23.6	4.52

SEM = standard error of the mean.

aforementioned examinations: liminal tonal audiometry, otoacoustic emission with linear click emission, and otoacoustic products of distortion with the Macro system (Table 1).

RESULTS

On discharge, all patients treated with enoxaparin presented a subjective abatement of symptoms. The mean value of scores on the subjective symptom scale fell from 3.8 to 1.5. (In group B, the mean value fell from 3.7 to 3.1.) From an objective point of view, 16 patients in group A (80%) showed an improvement in auditory function; mean hearing improvement for these patients ranged from 19.5 to 23.6 dB across the 2,000- to 4,000-Hz range examined. The characteristics of the hearing test are summarized in Table 2 (respectively showing means plus or minus the standard error of the mean).

Comparison of groups was made by the unpaired *t*-test, and correlations were analyzed by regression analysis: probability values at less than .05 were regarded as significant. Comparisons of groups also were made for repeated measures by analysis of variance. In the same patients, the evoked otoacoustic emissions revealed an improvement from "fail" to "pass," and otoacoustic distortion products, which were previously absent, were evoked at frequencies of the tonal field normally examined. In group B, no patient showed an improvement in auditory function.

DISCUSSION

Sodium enoxaparin is a particular kind of heparin with a low molecular weight and is endowed with a high antithrombotic activity. Like all other types of heparin, it belongs to the class of anticoagulants but offers a number of clinical advantages over other agents in this class and has therapeutic effects. It is superior to the other types of unfractionated heparin, because this drug exerts its effects essentially on capillary blood viscosity, erythrocyte deformability, and thrombocyte aggregation.

Table 1. Results of Testing

	Mean	SEM
Patient characteristics		
Age (years)	42.3	4.20
Vertigo	0	
Smoking	7	
Other diseases	0	
Blood test (group A)		
Pretreatment prothrombin (%)	98.7	0.72
Posttreatment prothrombin (%)	98.6	0.64
Change in prothrombin (%)	0.1	0.9
Pretreatment fibrinogen (mg/dl)	310.5	12.23
Posttreatment fibrinogen (mg/dl)	312.6	12.13
Change in fibrinogen (mg/dl)	2.1	7.65

SEM = standard error of the mean.

In addition, it is reported to have an antiinflammatory action in subcutaneous and inhalational administration [12].

As the causes of tinnitus may include viral and bacterial infection, an increase in blood viscosity, or modifications in the microcirculation due to posttraumatic inflammation, we consider this type of treatment with sodium enoxaparin to be highly efficacious and innovative [9,11]. The literature does not report any therapeutic protocols for tinnitus treatment with enoxaparin or other kinds of unfractionated heparin. Our decision to use enoxaparin in tinnitus therapy was based both on the pathogenesis of this condition and on evaluation of the other classes of drugs currently used.

CONCLUSIONS

We have tested sodium enoxaparin in all our patients affected by tinnitus, and all have shown a marked improvement of their symptoms. Because of that outcome, we believe it has a very important role in the therapeutic management of tinnitus. Also, we find the use of these low-molecular-weight heparins to be very easy. Avoidance of the need for monitoring anticoagulation appears to be the major advantage of this agent over unfractionated heparins.

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