Multimodal Therapy for Chronic Tinnitus

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Abstract: From 2001 to 2006, we performed a retrospective study of patients suffering from chronic unilateral or bilateral tinnitus that was previously ineffectively treated by oral drugs [betahistine (Betaserc), extract of Ginkgo biloba (EGb 761), tanakan (Tebokan), and cinnarizine-dimenhydrinate (Arlevert), singly or in combination]. We divided 150 tinnitus patients (80 men, 70 women) into seven treatment groups. Treatments consisted of application of intravenous pentoxifylline, lidocaine, or vinpocetine (Cavinton) and combination of these agents with physiotherapy and soft laser. Mean duration (± standard deviation) of tinnitus in these patients was 7.4 ± 6.0 years; their mean age was 55.6 ± 12.5 years. The aim of our study was to compare treatment modalities and define their effectiveness for tinnitus relief. The most effective treatment was defined as a combination of Cavinton and physiotherapy. We evaluated pure lidocaine infusion therapy as ineffective. None of the treatment modalities had an objective correlate of improvement, though improvement was reported by a visual analog scale.

Key Words: chronic tinnitus; infusion therapy; physiotherapy; soft laser

Tinnitus is the phantom perception of sound in the absence of overt acoustic stimulation [1]. It is well known that chronic tinnitus is difficult to treat, though lots of modalities are used for treatment. Guidelines for inclusion of each patient into an appropriate treatment group are still missing. In our study, we evaluated some of the current treatment modalities to define the most effective for a certain group of patients.

Current possibilities for chronic tinnitus treatment vary from neuroprotective substances [2], calcium-channel blockers, corticosteroids, glutamate agonists, and thrombolytic drugs [3–5] to intravenous or intratympanic lidocaine application [6–10]; vinpocetine (Cavinton), pentoxifylline (Agapurin, Trental), or piracetam infusions [4]; low-level laser therapy (so-called soft laser) [11–13]; physiotherapy, acupuncture, tinnitus retraining therapy, or other approaches. Because the studies available on MEDLINE report different outcomes [8,10–12,14], we tried to evaluate the most widely used therapeutic approaches in our hospital: drop infusion of lidocaine, vinpocetine, or pentoxifylline and combination of these drugs with low-level laser therapy and physiotherapy.

SUBJECTS AND METHODS

Patient Population

We divided 150 chronic tinnitus patients (80 male, 70 female; mean age, 55.6 ± 12.5 years) into seven study groups (Table 1). The mean duration of treatment was 9.2 ± 3.2 days, and the mean duration of tinnitus was 7.4 ± 6.0 years. All patients had previously been treated ineffectively by various oral drugs [betahistine (Betaserc), extract of Ginkgo biloba (EGb-761), tanakan (Tebokan), cinnarizine-dimenhydrinate (Arlevert)], or their combination for at least 6 months. Patients with decompensated systemic or psychiatric disease were excluded from the study.

Study Design

Permanent tinnitus remaining for more than 6 months was considered to be chronic. Before and after treatment, each patient underwent basic ear, nose, and throat examination, including otomicroscopy, basic vestibular examination, pure-tone audiometry, and tinnitometry.
We randomly divided the patients into seven distinct treatment groups and administered treatment as specified.

- The pentoxifylline (PTX) group received daily for 10 days an intravenous infusion of 100 mg pentoxifylline and 250 ml physiological saline.
- Those in the Cavinton group received daily for 10 days an intravenous infusion of 20 mg Cavinton plus 250 ml physiological saline, and oral Cavinton 2/100 mg (0–2–2).
- To those in the lidocaine group, we gave a daily intravenous infusion of 40 mg lidocaine hydrochloride plus 250 ml physiological saline, and oral Cavinton 2 × 10 mg (0–2–2).
- Those in the lidocaine–RHB group were given a daily intravenous infusion of 40 mg lidocaine plus 250 ml physiological saline, combined with physiotherapy, for 10 days.
- To those in the lidocaine–RHB–soft laser group, a daily intravenous infusion of 5000 BTL; 400 mW/830 nm; pulse beam, 30 J/cm²) once daily for 10 minutes and physiotherapy, all for 10 days.
- Those in the lidocaine–RHB–soft laser group received a daily intravenous infusion of 20 mg Cavinton plus 250 ml physiological saline, and oral Cavinton 2/100 mg, combined with physiotherapy and soft laser (for soft-laser specifications, see earlier in this paragraph), were given for 10 days.

In addition, there were groups treated by pentoxifylline plus physiotherapy (PTX–RHB) and pentoxifylline plus physiotherapy and soft laser (PTX–RHB–soft laser), which consisted of a total of 9 persons. As the outcomes were considered to be statistically insignificant, the findings from these groups are not evaluated further.

The visual analog scale from 0 (no tinnitus) to 10 (unbearable tinnitus) was used for daily evaluation. Patients’ symptoms were evaluated as improved if their tinnitus was perceived to be better by two or more points on this scale.

### STATISTICAL EVALUATION

We used an enhanced method for construction of a binary classification tree—a regression method computed by condition of maximized homogeneity of treatment methods used [by Agapurin (Trental), Cavinton, lidocaine] in terminal leaves. We had four metrics—age, duration of tinnitus, gender, and audiometry—each of which could be used to divide cases into branches. According to audiometry, we had three subgroups: bilateral normal hearing, unilateral normal hearing, and bilateral hearing loss. We crossed all boundaries that are created as a midpoint between all recorded numerical data on all metrics.

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**Table 1. Demographic and Anamnestic Data of the Patient Population**

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Male/ Female</th>
<th>Age ± SD (yr)</th>
<th>Duration of Tinnitus ± SD (yr)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTX</td>
<td>22/8/14</td>
<td>55.6 ± 11.1</td>
<td>9 ± 6.5</td>
</tr>
<tr>
<td>Lidocaine</td>
<td>17/9/8</td>
<td>54.7 ± 12.6</td>
<td>4.0 ± 2.8</td>
</tr>
<tr>
<td>Lidocaine–RHB</td>
<td>28/17/11</td>
<td>54.4 ± 9.5</td>
<td>5.3 ± 5.2</td>
</tr>
<tr>
<td>Lidocaine–RHB–soft laser</td>
<td>29/13/6</td>
<td>51.8 ± 16.4</td>
<td>6.8 ± 6.6</td>
</tr>
<tr>
<td>Vinpocetine</td>
<td>17/9/8</td>
<td>58.7 ± 14.2</td>
<td>9.2 ± 7.5</td>
</tr>
<tr>
<td>Vinpocetine–RHB</td>
<td>20/14/6</td>
<td>59.1 ± 12.0</td>
<td>8.8 ± 7.1</td>
</tr>
<tr>
<td>Total</td>
<td>150/80/70</td>
<td>55.6 ± 12.5</td>
<td>7.4 ± 6.0</td>
</tr>
</tbody>
</table>

PTX = pentoxifylline; RHB = physiotherapy; SD = standard deviation.
and sought maximized homogeneity. When we finished dividing by all metrics (or when it was superfluous to continue with such division), we decided on classification of terminal leaf by the bayesian method.

In computing progress, we found that treatment PTX and age metric were ambiguous and so we dropped them, with no effect on our results. The boundary in the age metric was found at 62 years; in tinnitus duration, the value was 15 months. The output classification tree divided the patients into groups according to the metrics (Fig. 1) treated by lidocaine (contains lidocaine infusion, lidocaine–RHB, and lidocaine–RHB–soft laser groups) or by Cavinton (contains Cavinton, Cavinton–RHB, and Cavinton–RHB–soft laser groups).

RESULTS AND DISCUSSION

Combination of Cavinton and physiotherapy was the most effective treatment seen in all the groups (see Fig. 1). As we compared the groups of either Cavinton or lidocaine infusion alone with groups who received one of these agents combined with physiotherapy with or without soft laser, the effectiveness of combination therapy was assessed as being better. The multimodal approach of tinnitus treatment is widely accepted. We did not find any additional effect of soft laser, but we expect that the effect of soft laser on biostimulation cannot be observed during 10 days of therapy.

The groups treated by pentoxifylline plus physiotherapy (PTX–RHB) and pentoxifylline plus physiotherapy and soft laser (PTX–RHB–soft laser) consisted of a total of 9 persons, and the outcomes were considered to be statistically insignificant. Only 1 patient of those 9 experienced a decrease in tinnitus intensity; the rest saw no change.

We found no effect of plain lidocaine infusion (see Fig. 1). The combinations of lidocaine with RHB and with RHB plus soft laser were assessed by the classification tree as being effective for patients younger than 62 years who had tinnitus lasting for more than 15 months (Fig. 2).

Because tinnitus is a subjective symptom, we used the subjective scale—the visual analog scale—as the only parameter. Many patients with positive tinnitus changes (according to the visual analog scale) experienced changes in quality of life, so the quality-of-life questionnaire should be used in further studies. We hope that our outcomes will be helpful for patients suffering from chronic tinnitus, and we encourage our colleagues to undertake further research.

REFERENCES


