

Hyperbaric Oxygen (HBO₂) in tinnitus: Influence of psychological factors on treatment results?

P. STIEGLER², V. MATZI¹, C. LIPP¹, A. KONTAXIS³, H. KLEMEN¹, C. WALCH³, F. SMOLLE-JÜTTNER¹

¹Department of Surgery, Division of Thoracic Surgery and Hyperbaric Medicine, Medical University Graz, Austria; ²Department of Surgery, Division of Transplantation Surgery, Medical University Graz, Austria; ³Department for E.N.T., Medical University Graz, Austria.

Submitted - 11/18/06 - Accepted - 4/2/06

Stiegler P, Matzi V, Lipp C, Kontaxis A, Klemen H, Walch C, Smolle-Juttner F. Hyperbaric Oxygen (HBO₂) in tinnitus: Influence of psychological factors on treatment results? *Undersea Hyperb Med* 2006; 33(6):429-437. HBO₂ for subjective tinnitus has never been objectified, yet it is still advocated by many institutions. We analyzed the therapeutic effect of HBO₂ treatment in the context of accompanying factors, especially focusing on the patients' attitude towards HBO₂ prior to therapy. Methods: 360 patients suffering from tinnitus were investigated in this study. They were randomized into 2 hyperbaric treatment protocols, one at 2.2, the other at 2.5 bar, 60 min bottom time each. All patients were asked to fill in a questionnaire (social and medical history, tinnitus characteristics, pre-HBO₂ duration of tinnitus, prior therapy, pre-treatment expectation, accompanying symptoms) immediately before and one month after HBO₂ treatment. The subjective impact of tinnitus on daily life was assessed using a score from 1 to 10 prior to HBO₂ and one month after the treatment. Results: 12 patients (3.3%) experienced complete remission of tinnitus, in 122 (33.9%) the intensity lessened, and 44 (12.2%) had a subjectively agreeable change of noise characteristics. 157 (43.6%) stated no change and 25 (6.9%) experienced deterioration. There was no statistically significant difference between the two hyperbaric protocols ($p > 0.05$). Out of 68 patients with positive expectation towards HBO₂ therapy 60.3% stated that the tinnitus had improved whereas out of the patients who underwent therapy with indifferent (N=271) or negative expectations (N=21) only 47.2% and 19%, respectively, reported an improvement. The influence of both positive and negative anticipation on the outcome was statistically significant ($p < 0.05$). Conclusion: The therapeutic effects of HBO₂ on subjective tinnitus might be greatly due to psychological mechanisms triggered by the attitude of the patient towards HBO₂ therapy prior to the treatment.

INTRODUCTION

Tinnitus is one of the common symptoms of the hearing system (2). These patients may suffer from severe distress such as sleeping problems, concentration difficulties, anxiety and depression influencing not only private but also professional life (3) leading to working inability (5) and even suicide (4).

Therapeutic strategies include intravenous hemorheologic medication (IHM), (8) tinnitus retraining therapy, (9) masking

devices (4) or low-power laser (10). In spite of well founded considerations the therapeutic effects are hardly better than those of treatments that lack pathophysiologic rationale like ginkgo biloba, acupuncture, biofeedback or even placebo treatment (11). Moreover, according to the literature, spontaneous remissions in 30 to 90 percent of patients, often seen within the first few months after onset, create a bias (8).

Since a lack of oxygen appears to be crucial in the pathogenesis of tinnitus, hyperbaric oxygenation (HBO₂) seems

promising to increase the partial pressure of oxygen (PO₂). Breathing 100% oxygen at elevated ambient pressure causes oxygen to dissolve in the plasma and thereby increases the PO₂ according to Henry's Law. The amount of any gas that will dissolve in a liquid at a given temperature is a function of the partial pressure of the gas in contact with the liquid and the solubility coefficient of the gas in the particular liquid (21).

Additionally, HBO₂ causes a reduction in haematocrit, a reduction of platelet aggregation and an increase of the flexibility of erythrocytes, thereby improving hemorheology (13). The cochlea is one of the organs with the highest oxygen requirement (12). Therefore, the elevation of PO₂ in the cochlea and especially in the perilymphatic and endolymphatic fluid should have a strong influence on the impaired metabolic conditions of the sensory cells of the inner ear (14). These cells lack any direct blood supply and oxygen supply is totally dependent on diffusion (8) which is increased in parallel with the PO₂ in the plasma.

In spite of its clear-cut rationale, the effectiveness of HBO₂ has only been proven for acute hearing loss (18, 20), whereas it has never been objectified for subjective tinnitus. Nevertheless, HBO₂ for tinnitus is still advocated by many institutions. The treatment protocols applied in the literature are usually limited to 60 min HBO₂ at pressures between 2.0 and 2.5 bar. Most authors report amelioration in about 30 to 50% of patients, while the others remain unchanged or even deteriorate (18).

Furthermore, psychological factors play a major role in the treatment of tinnitus accounting for the high success rate of placebo treatment (19). Most patients readily adopt and favour any treatment, they consider promising, its rationale notwithstanding. Since the physician is dependent on the patients' assessment of success, an objective evaluation of treatment results is very difficult.

Based upon these considerations we analyzed the effectiveness of HBO₂ treatment on tinnitus in the context of pre-treatment expectations. Other subjective phenomena such as noise quality and type of onset were included. In order to assess possible differences between treatment protocols patients were randomized into two hyperbaric treatment groups (2.5 bar vs. 2.2 bar).

MATERIALS AND METHODS

Patients

360 (230 male, 130 female) patients suffering from tinnitus underwent HBO₂ treatment from 1998-2003 at the Division of Thoracic and Hyperbaric Surgery at the Department for Surgery, Medical University Graz, Austria.

Questionnaire

All 360 patients filled in a questionnaire before and one month after the HBO₂ treatment focusing on noise characteristics of tinnitus, interval between the onset of tinnitus and the beginning of hyperbaric therapy, subjective impairment by tinnitus, subjective expectation of the probability of success of HBO₂ prior to treatment and patients' characteristics such as professional or private stress and accompanying symptoms.

For evaluation of the subjective impact of tinnitus on daily life, patients documented the degree of their impairment using a score from 1 to 10 before and after HBO₂ therapy.

HBO₂ treatment

Hyperbaric facility

HBO₂ was administered in a multiplace facility accommodating a group of 10 patients and one attendant. Tinnitus patients were allowed to listen to music through ear phones and to drink, and they were provided with

reading material throughout the treatment sessions. Face-masks were used for oxygen administration.

Hyperbaric protocols

After obtaining informed consent the patients were randomized into one of two treatment protocols, diving protocol A (DPA) at 2.2 bar for 60 min bottom time and diving protocol B (DPB) at 2.5 bar for 60 min bottom time. HBO₂ was administered regularly on 15 consecutive working days.

Follow-up

One month after the end of the HBO₂ treatment the therapeutic effect was evaluated according to the patients' subjective assessment of tinnitus documented by a second questionnaire.

Statistics

The data were stored on a spreadsheet and evaluated using the SPSS statistical program package 12.0 (SPSS Inc., Sunnyvale, USA). Basic statistics including mean, standard deviation and range, student's t-test and chi²-test were used where necessary. A p value of less than 0.05 was considered statistically significant.

RESULTS

Pre-treatment characteristics

Patients' characteristics

The median age at the time of HBO₂ treatment was 49.2 (+/- 14.5) years. 156 patients underwent DPA (2.2 bar for 60 min bottom time), 156 were assigned DPB (2.5 bar for 60 min bottom time). These 312 patients underwent 15 treatments on 15 consecutive working days. 48 patients were treated inconsistently according to DPA or DPB, respectively leaving out single days of treatment, but no patient had less than 12 treatment sessions. Table 1 (see page 5)

shows detailed patients' characteristics.

Type of onset of tinnitus

230 patients reported a sudden onset of their sound perception, whereas 130 remembered an initial on-and-off situation with symptom-free intervals until tinnitus definitively established itself.

Subjective tinnitus characteristics

The quality of the subjectively experienced noise was described by 311 patients. 157 patients heard a murmuring, 38 a ringing, 86 chirping and 27 patients suffered from trilling. 3 patients reported to hear a noise similar to a hammer.

179 patients experienced a high pitched tone, 62 a medium pitched tone and 14 a noise of low pitch tone quality. 53 patients suffered from a noise changing in pitch. 52 patients did not answer the question related to the pitch.

Impact of tinnitus on daily life

331 patients completed the question concerning their subjective assessment of the impact of tinnitus on everyday life prior to HBO₂. 23 (6.9%) felt not disturbed at all, 51 (15.4%) felt occasional trouble but without significant impact on daily life, 71 (21.4%) experienced a medium, 95 (28.7%) a high grade, and 91 (27.5%) patients experienced a very severe impact on their daily life (see figure 1, triangles, black line).

Pre-treatment interval

In 92 patients HBO₂ therapy was begun within the first 14 days after the onset of the disease, in 93 there was an interval of up to 6 months, in 41 between 6 and 12 months and in 126 patients HBO₂ was not done but after more than one year after onset of tinnitus. 8 patients could not remember the time when their tinnitus occurred for the first time.

Patients' pre-HBO₂-treatment expectation

All 360 patients completed the question focusing on their expectations towards HBO₂ therapy success prior to the first HBO₂ treatment. 21 patients had negative expectations regarding HBO₂ therapy success, 271 were indifferent towards HBO₂ treatment and 68 patients underwent HBO₂ therapy with positive expectations.

TREATMENT RESULTS

Overall effect of HBO₂ on tinnitus

12 patients (3.3%) experienced complete remission of tinnitus, 122 (33.9%) felt a decrease of tinnitus intensity and 44 (12.2%) patients experienced a change of the quality of noise, which they subjectively interpreted as amelioration. 157 (56.3%) patients did not notice any change in the disease whereas 25 (6.9%) patients complained that their tinnitus had increased in intensity following HBO₂ (see table 2).

Influence of different HBO₂ treatment protocols

The post therapeutic changes of tinnitus observed by the patients were evenly distributed between the two treatment groups DPA (2.2 bar; valuable: N=156) and DPB (2.5 bar; valuable: N=156) ($p > 0.05$) (see table 1).

Influence of sex

110 out of 230 male patients (47.8%) and 61 out of 130 females (46.9%) experienced an overall amelioration of tinnitus after HBO₂ ($p > 0.05$) (see table 1).

Influence of age

Patients aged younger than 60 (N=234) experienced amelioration of tinnitus in 36.3%, whereas those aged over 60 (N=126) felt an

improvement in only 19.0% ($p < 0.001$) (see table 1).

Subjective tinnitus characteristics and HBO₂ effect

No significant correlation between the different noise characteristics experienced and positive therapy outcome was found.

Patients who experienced tinnitus at a low pitch were more likely to feel an amelioration after HBO₂ ($p = 0.01$) than those with a high pitched noise (see table 1).

Influence of time interval until the first HBO₂ therapy

Out of 12 patients who had a complete remission of tinnitus after HBO₂, 10 (83.3%) underwent HBO₂ within the first two weeks after the onset of tinnitus and 2 (16.6%) within the first 6 months.

27 (22.13%) of the 122 patients who felt that their tinnitus had muted after treatment underwent HBO₂ therapy within the first 14 days after the onset of tinnitus and 2 (16.6%) within the first 6 months ($p < 0.001$). The overall rate of improvement (complete remission and subjective amelioration) was 64.1% for patients treated within the first 14 days and 57% for those undergoing HBO₂ between 14 days and 6 months after onset of tinnitus.

In contrast, only 31.7% of patients treated between 6 and 12 months after the onset of symptoms and 38.8% of those in whom HBO₂ was initiated after more than one year felt amelioration (see table 1).

Out of the 25 patients who indicated deterioration after HBO₂, 2 (8%) were treated within the first 14 days, 4 (16%) within the first 6 months, 5 (20%) within 1 year and 14 (56%) underwent HBO₂ treatment more than 12 months after the onset of their disease. No statistical significance was found between the time interval until start of the HBO₂ therapy and the overall success rate (see table 1).

Table 1. Treatment, patient and tinnitus characteristics. Percentages of amelioration and complete remission.

Feature		Number of patients	Percentage of amelioration or complete remission	Significance
HBO₂ protocol	2.2 bar	156	49.3%	
	2.5 bar	156	48.1%	n.s.
Sex	Female	130	46.9 %	
	Male	230	47,8 %	n.s.
Age	< 60	234	36.3 %	
	> 60	126	19.0 %	P < 0.001
Noise characteristics	Murmuring	157	49.0 %	
	Ringing	38	52.6 %	
	Chirping	86	39.5 %	
	Trilling	27	59.3 %	
	Hammering	3	66.7 %	n.s.
	High pitched tone	179	45.3 %	
	Medium pitched tone	62	38.7 %	
	Low pitched tone	14	85.7 %	P < 0.01
	Changing noise	53	58.5 %	
Type of onset	Sudden onset	230	53.9 %	
	Non-sudden onset	130	36.2 %	P < 0.001
Time until HBO₂ therapy	Less than 2 weeks	92	64.1%	
	2 weeks to 6 months	93	57%	
	6 to 12 months	41	31.7%	
	More than 12 months	126	38.8%	
Anticipation	Negative	21	19.0 %	P < 0.01
	Indifferent	271	47.2 %	
	Positive	68	60.3 %	P < 0.05

Table 2. Overall effect of HBO₂ on tinnitus. Patients were asked to indicate the subjective change of tinnitus after HBO₂ therapy.

Effect of HBO ₂ on patients	Number of patients	Percentage
Complete remission	N = 12	3,30 %
Decrease in tinnitus intensity	N = 122	33,90 %
Positive change of noise	N = 44	12,20 %
No impact of HBO ₂ on tinnitus	N = 157	56,30 %
Increase of tinnitus intensity	N = 25	6,90 %

Subjective impact of tinnitus on daily life after HBO₂

339 patients completed the question focusing on the subjective impact of tinnitus on daily life after HBO₂ therapy. 25 (7.37%) patients felt undisturbed, 121 (35.6%) reported no significant impairment, 96 (28.3%) felt a medium, 69 (20.3%) a high grade burden, and 28 (8.25%) experienced a severe impact on daily life after HBO₂ treatment (see figure 1, squares, spotted line).

Influence of the patients' expectation on HBO₂ therapy success

Out of 21 patients with negative expectations towards therapy success, 4 (19 %) experienced an amelioration of tinnitus ($p < 0.01$). 133 patients (49.1 %) reported an improvement of symptoms despite of indifferent attitude towards HBO₂ (N=271). Statistical analysis showed no significance in this group. 41 (60.3 %) patients out of 68 who indicated a positive expectation concerning therapy success prior to therapy had an improvement of the disease after HBO₂ indicating a significant correlation between psychological factors and the patient's expectation prior to therapy on the therapeutic effect ($p < 0.05$) (see table 1, figure 2).

DISCUSSION

Tinnitus is defined as a phantom perception of sound in the absence of overt acoustic stimulation (1-4). It can be caused by different diseases originating along the auditory path, including cochlear lesions, disease of the auditory nerve, central auditory damage or psychological and neurovegetative factors (7). Studies have shown that common pharmacological therapy did not achieve effects beyond placebo therapy (6, 11, 15, 19).

Despite intensive research, the exact

pathophysiology of subjectively disturbing tinnitus is still unknown. However, a decrease in PO₂ is the most accepted pathophysiological thesis (8). Under therapeutic HBO₂ conditions with oxygen physically dissolving in the plasma, PO₂ is increased to values by far exceeding the physiological conditions (13). This leads to an increased PO₂ in the cochlea (14). In contrast, IHM and other non-HBO₂ treatment regimens depend on erythrocytes as transport vehicles, what is the reason why the PO₂ attainable by these models is limited at a maximum PO₂ of 1.0 bar (15). However, an improvement in cochlear function has never been observed below the limit of 2.2 bar PO₂ in the perilymph (8) which can only be achieved using HBO₂.

To the disappointment of investigators, HBO₂ in patients with tinnitus has not fulfilled the high expectations deriving from its theoretic rationale. There are a number of studies on HBO₂ for tinnitus therapy performed at pressures between 2.0 and 2.5 bar (8). Though the authors report various degrees of improvement in up to 50% of patients (8), actual cure of tinnitus is rare under HBO₂: Complete remission does not exceed 3%, which is similar to other treatment options or placebo (6, 11, 15, 19, 22). Moreover, even the rate of partial remission may be biased by the high rate of spontaneous improvement observed in the course of tinnitus (8, 23).

In the present study complete remission which amounted to 3.3% was found almost uniquely in those who started treatment within 14 days after the onset of the disease. Though the association of complete remission with this factor was statistically significant, it highlights the possibility that these were spontaneous remissions. At pre-treatment intervals longer than 14 days, complete response was found in only 2 patients, whereas 46.1% of the others had some "amelioration" for which no significant impact of the length of time elapsed before HBO₂ on the results could be documented.

Analyzing the impact of tinnitus on

Fig. 1. Impact of tinnitus on the patients' daily life presented in a polynomic regression curve. Patients were asked to give scores from 1 (no impact on daily life) to 10 (severe impact on daily life) prior and one month after HBO₂ therapy. There is a trend towards amelioration after HBO₂ treatment. Triangles: Mean values prior to HBO₂; Black line: polynomic regression curve prior to HBO₂; Squares: Mean values after HBO₂; Spotted line: polynomic regression curve after HBO₂.

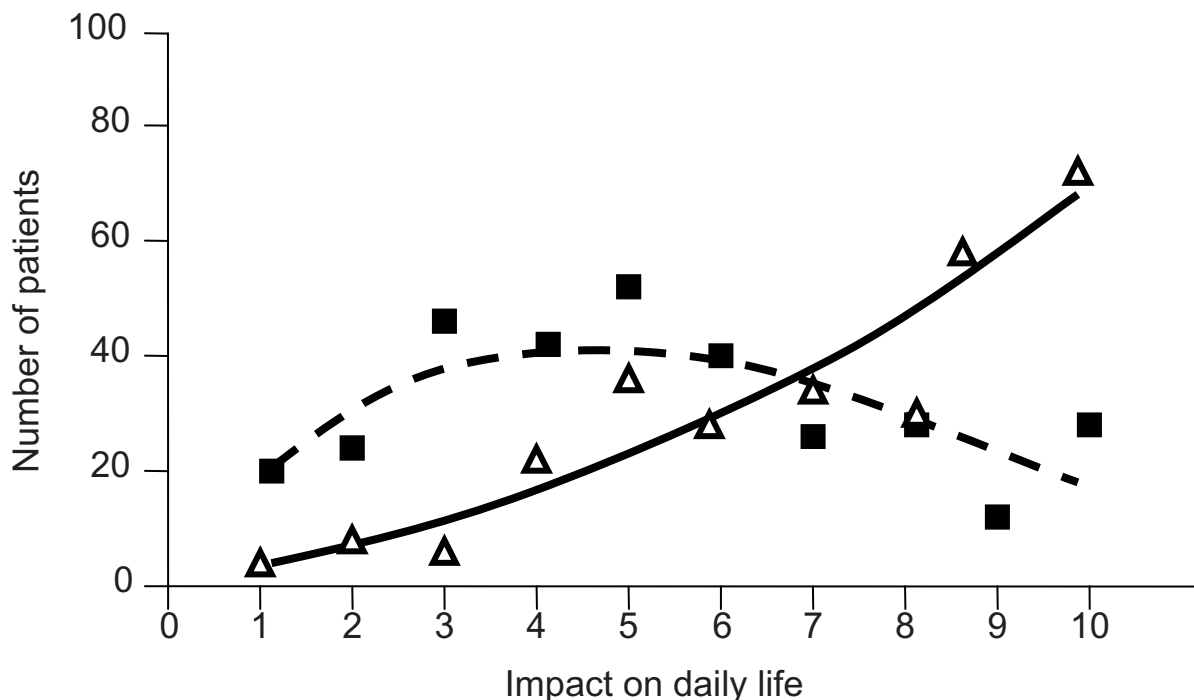
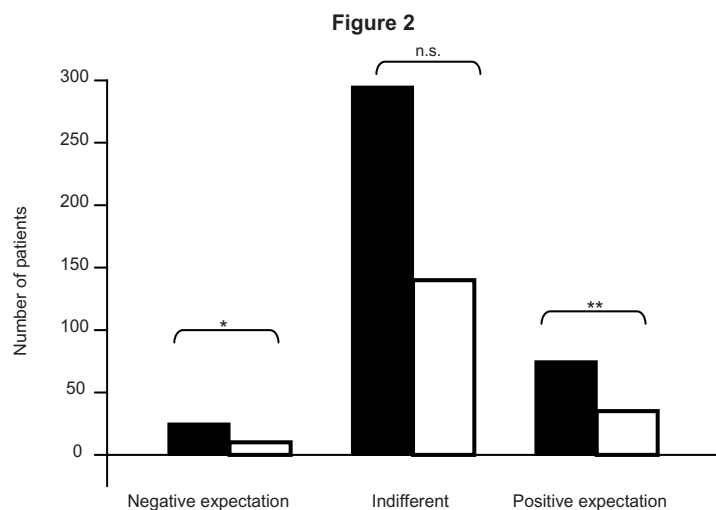


Fig. 2. Influence of the patients' expectations prior to HBO₂ treatment on the therapy success. Statistical analysis showed a significant impact of positive (** p < 0.05) and negative expectations (* p < 0.01) on the therapy outcome, whereas no statistical significance on the therapy success could be found in patients who were indifferent towards HBO₂. Black bars: Total number of patients with negative, indifferent and positive expectations. White bars: Number of patients who experienced complete remission or amelioration after HBO₂ therapy.



daily life experienced by the patients, a trend towards a lesser impairment of activities was found after HBO₂ treatment compared to pre-treatment evaluation. We could not confirm the presumption that according to Henry's Law patients might benefit more from the higher PO₂ achieved by treatment at 2.5 bar than at 2.2 bar. The results did not differ between the two treatment protocols.

Interestingly, patients experiencing a low pitched noise had a greater benefit from HBO₂ therapy than those who suffered from a high pitched one. The difference reached the level of significance. Equally significant was the overall rate of amelioration in patients who had experienced a sudden onset of tinnitus compared to those with gradual onset. It may be speculated, that in case of sudden onset there might be indeed a higher proportion of patients with a clear-cut pathology related to hypoxia in the inner ear (12, 14), which can be treated with HBO₂. Moreover, patients suffering from a sudden onset of the disease are more likely to consult a physician immediately shortening the time-interval between onset of the disease and HBO₂ treatment, compared to patients suffering from a gradual onset of tinnitus.

Apart from the few patients who experienced relief, others stated a positive effect of therapy if their tinnitus muted a little, and even reported therapeutic success if the noise characteristics of tinnitus changed. These subjective notions are likely to be influenced by psychological co-factors.

The high impact of placebo treatment in tinnitus might be due to the fact that tinnitus patients often have neuropsychiatric disturbances such as anxiety, depression, insomnia and stress. The sensation of tinnitus is modified by these factors (3, 5). Since patients with chronic tinnitus often consider the acoustic sensation as the main source of their distress, the psychological component is also influenced in a positive way once the tinnitus is "taken

care of". Most of our patients entered the HBO₂ treatment with an indifferent attitude towards its possible benefits, and only half of them experienced subjective benefit. Out of the 21 patients who had negative expectations towards HBO₂ only 4 felt amelioration, whereas 60% of those who initially believed in the effectiveness of treatment actually felt a positive effect.

These findings suggest a major influence of psychological factors and the anticipation towards the therapy success in the patients' subjective assessment of HBO₂ effects on tinnitus. The very situation that the patients entered treatment in groups, the caretaking by the attendant and the impressive surroundings of a hyperbaric chamber in combination with the fact that the treatment itself was agreeable and involved reading while listening to low music provided a setting that was likely to bring about placebo effects.

CONCLUSION

The success rate of HBO₂ for tinnitus seems to be highly influenced by psychological factors and by the expectations of the patient prior to HBO₂. Moreover, patients suffering from tinnitus are likely to be susceptible to the impressive surroundings of the hyperbaric chamber, the caretaking and the fact to be in a group of patients experiencing the same disease, enabling the patients to share the problems causing the disease or dealing with problems caused by the disease. The findings of this study and the high spontaneous remission rate of tinnitus (8) suggests the conclusion that HBO₂ therapy in patients suffering from tinnitus does not go beyond placebo effects.

REFERENCES

1. Jastreboff PJ. Phantom auditory perception (Tinnitus): mechanisms of generation and perception. *Neurosci Res* 1990; 8:221-254.

2. Jastreboff PJ, Gray WC, Mattox DE. Tinnitus and hyperacusis. *Otolaryngology head and neck surgery* 1998; 3rd ed. Mosby-Year Book 198-222.
3. Kröner-Herwig B, Frenzel A, Fritsche G. et al. The management of chronic tinnitus. Comparison of an outpatient cognitive-behavioral group training to minimal-contact interventions. *Journal of Psychosomatic Research* 2003; 54:381-389.
4. Lewis JE. Tinnitus and suicide. *J Am Acad Audiol* 2002; 13:339.
5. Poshnoi L, Carel R. Noise-induced hearing loss - factors affecting worker's decision to submit a disability claim. *Harefuah* 2004; 143(2):106-109.
6. Hesse G, Rienhoff NK, Nelting M, Brehmer D. Medikamentenkosten bei Patienten mit chronisch komplexem Tinnitus. *HNO* 1999; 47:658-660.
7. Bernhardt O, Gesch D, Schwahn C, et al. Signs of temporomandibular disorders in tinnitus patients and in a population based group of volunteers: results of the Study of Health in Pommerania. *Journal of Oral Rehabilitation* 2004; 31:311-319.
8. Biesinger E, Heiden C, Greimel V, Lendle T, Hönig R, Albegger K. Strategien in der ambulanten Behandlung des Tinnitus. *HNO* 1998; 46:157-169.
9. Jastreboff PJ, Jastreboff MM. Tinnitus retraining therapy (TRT) as a method for treatment for tinnitus and hyperacusis patients. *J Am Acad Audiol* 2000; 11:162-177.
10. Mirz F, Zachariae R, Andersen SE, et al. The low power laser in the treatment of tinnitus. *Clin Otolaryngol* 1999; 24:346-354.
11. Fish et al. Measurement of oxygen tension in human perilymph. *Acta Otolaryngol* 1976; 81:278-282.
12. Lamm K, Arnold W. Successful treatment of noise-induced cochlear ischemia, hypoxia, and hearing loss. *Ann N Y Acad Sci* 1999; 884:233-48.
13. Sahley TL, Nodar RH. Tinnitus models. *Hearing Research* 2001; 152:43-54.
14. Lamm H. Die Wirkung des hyperbaren Sauerstoff auf das normale Innenohr des Meerschweinchens (CM+AP). *Arch Otolaryngol* 1979; 222:145-151.
15. Lamm K. Rationale Grundlagen einer Innenohrtherapie. *tolaryngol Nova* 1995; 5:153-160.
16. Bock KH, Frey G, Lamp L. Hyperbare Oxygenation, Pathophysiologie und Nebenwirkungen. In: Lawin P, ed.: *Praxis der Intensivbehandlung*; 6. Auflage 415-437 ISBN 3-13-441806-1.
17. Feldmeier J, Carl U, Hartmann K, Sminia P. Hyperbaric oxygen: does it promote growth or recurrence of malignancy? *Undersea Hyperb Med* 2003; 30(1):1-18.
18. Lamm H. Der Einfluß der hyperbaren Sauerstofftherapie auf den Tinnitus und den Hörverlust bei akuten und chronischen Innenohrschäden. *Otolaryngol Nova* 1995; 5:161-169.
19. Lockwood AH, Salvi RJ, Burkhard RF. Tinnitus. *The New England Journal of Medicine* 2002; 347:904-910.
20. Kuokkanen J, Aarnisalo AA, Ylikoski J. Efficiency of hyperbaric oxygen therapy in experimental acute acoustic trauma from firearms. *Acta Otolaryngol Suppl* 2000; 543:132-134.
21. Van Poucke S, Hans G, Hens P. The release of dissolved gases from solution during decompression after hyperbaric treatment: effervescent tables and Henry's law. *Anesthesiology*. 2001; 95(3):816.
22. Park J, White AR, Ernst E. Efficacy of acupuncture as a treatment for tinnitus: A systematic review. *Arch otolaryngol* 2000; 126(4):489-492.
23. Anderson G, Vretblad P, Larsen H, Lyttkens L. Longitudinal follow-up of tinnitus complaints. *Arch otolaryngol* 2001; 127(2):175-179.