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Original Article

Effects of Oxygen Therapies in Experimental Acute Acoustic Trauma

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BACKGROUND: Acute acoustic trauma is defined as a sudden sensorineural hearing loss that occurs after an exposure to acoustic overstimulation. Increasing the oxygen in perilymph can be a treatment modality. Our study aims to investigate the influence of normobaric oxygen therapy on the recovery of acute acoustic trauma and to compare it with the hyperbaric oxygen therapy.

METHODS: Three groups of rats (5 rats each) were exposed to white noise for 1 hour. Sensorineural hearing loss was identified using distortion product otoacoustic emission. Subsequently, the first group was treated with hyperbaric oxygen therapy, the second group was treated with normobaric oxygen therapy, and the third group did not receive any treatment and was used as a control group.

RESULTS: There was a statistically significant difference within time for frequencies of 1, 1.5, and 2 kHz, but there was no statistically significant difference between groups. For frequencies of 3, 4, 5, and 6 kHz, there was a statistically significant difference within time and between groups. Between groups, recovery of distortion product otoacoustic emission values in all frequencies was better in the control group by the third, fifth, and seventh days. Comparing the values of hyperbaric oxygen therapy and normobaric oxygen therapy groups, it was observed that by the third day, the hyperbaric oxygen therapy values were better than those of the normobaric oxygen therapy values. However, by the fifth and seventh days, the normobaric oxygen therapy values were better (except at a frequency of 1 kHz).

CONCLUSION: Because there is a high rate of spontaneous recovery, physicians should be more selective to treat patients with oxygen therapies.

KEYWORDS: Acute acoustic trauma, hearing loss, hyperbaric oxygen therapy, normobaric oxygen therapy

INTRODUCTION

Acute acoustic trauma (AAT) is defined as a sudden sensorineural hearing loss that occurs after an exposure to acoustic overstimulation.[1,2] In industrialized societies, exposure to intense noise is one of the major causes of hearing loss in adults. Acute acoustic trauma may occur in occupational (military, construction, etc.) or recreational (concerts, etc.) activities.[1,3,4] The reported prognosis for AAT ranges from total recovery to no improvement.[1,2,5,6]

Cell death after AAT is related to hypoxia and the formation of free radicals.[7] Following an oxygen deficiency, in addition to a decrease in perilymph PaO_2, there is also a swelling of nuclei of sensory cells of the inner ear.[3,8-14] Therefore, increasing the oxygen in perilymph becomes a treatment modality. The most commonly used medical treatment of AAT is corticoids, alone or in conjunction with hyperbaric oxygen therapy (HBOT). Clinicians usually offer corticoids as initial therapy for patients with sudden sensorineural hearing loss.[15,16] Also, clinicians may offer HBOT combined with steroid therapy as an initial or salvage therapy.[16] Steroids appear to be the mainstay of pharmacological therapy. However, some physicians have taken a conservative approach to using steroids in some cases.[17,18]

Hyperbaric oxygen therapy is a treatment in which a patient breathes 100% oxygen intermittently while he or she is inside a sealed chamber at a pressure higher than the sea level. Exposure to acoustic trauma induces cochlear hypoxia, and the increase

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in perilymphatic oxygenation by HBOT is the most efficient treatment for preventing the loss of the outer hair cells due to hypoxia.[8,19] Hyperbaric oxygen therapy is aimed to increase perilymphatic oxygen pressure and prevents the oxidative stress secondary to cochlear hypoxia.[2,5,8,20] Although normobaric oxygen therapy (NBOT) is not as effective as HBOT, it has also shown to be effective in treatment.[1] However, it is not a common therapeutic approach in today's daily practice for the treatment of AAT.

Many patients with AAT are not referred to an HBOT center or are sent after considerable delay. The cost and limited availability of HBOT facilities as well as the lack of adequate evidence make HBOT impractical for some patients.[21]

There are very few studies comparing the effectiveness of HBOT and NBOT in AAT. The majority of these studies are retrospective in nature.[1] In our study, we decided to treat similar hearing loss in a homogenous group exposed to the same noise with HBOT and NBOT. Today, many AAT patients are treated with HBOT and steroids. There is conflicting scientific evidence regarding the effectiveness of HBOT in the management of AAT.[5,22] In some publications, it is stated that the negative effect of HBOT is prevented with steroids.[23] Due to this confusing effect of the steroid, we found it appropriate to apply HBOT and NBOT alone and make a more accurate comparison. This study aimed to investigate the influence of NBOT on the recovery of AAT and to compare it with the effect of HBOT.

METHODS

Animals

We used 21 rats in our study. All rats were male and weighing approximately 300-350 g. They were housed in a controlled room. The research was approved by the Animal Experiments Local Ethics Committee. The rats' ears were examined with otoscopes before and after administering treatments.

Distortion Product Otoacoustic Emission

We preferred distortion product otoacoustic emission (DPOAE) to evaluate the function of hair cells. Rats with any ear pathology as well as those in which DPOAE measurements could not be obtained before noise exposure were excluded. We recorded DPOAEs with the Otodynamics ILO v6 system (Otodynamics Ltd., Hatfield, Herts, UK) by using a newborn probe. DPOAEs were measured before and after noise exposures and on days 3, 5, and 7. The analysis of the DPOAE results is based on the signal-to-noise ratio values that indicate the difference between the otoacoustic emission (OAE) response and the noise level at a particular frequency.

Acoustic Trauma

The frequency range of white noise to simulate acoustic trauma was between 1 and 12 kHz bands. The rats were subjected to a 110 dB sound pressure level. It was measured by a sound level meter for an hour by use of a loudspeaker placed at a distance of 2 cm. The laboratory's background noise was kept below 35 dB.

Groups

Two rats with ear pathology and 4 rats in which DPOAE measurements could not be obtained were excluded. The 15 rats were distributed into 3 groups. The first group (5 rats, 10 ears) was treated with HBOT, the second group (5 rats, 10 ears) was treated with NBOT, and the third group (5 rats, 10 ears) was used as a control group and did not receive any treatment.

Hyperbaric Oxygen Treatment

We used an experimental hyperbaric chamber for HBOT. The chamber was pressurized to 2.4 ATA in 5 minutes and ventilated during the treatment. After 60 minutes at 2.4 ATA, the chamber was decompressed to the normal atmospheric pressure over a period of 5 minutes. The first HBOT was administered sixth hour after noise exposure. HBOT continued once a day for seven days.

Normobaric Oxygen Therapy

We used an experimental chamber for NBOT. At ambient pressure, 100% oxygen was given for 60 minutes into the chamber. The chamber was ventilated during NBOT. The first NBOT was administered sixth hour after noise exposure. NBOT continued once a day for seven days.

Statistical Analysis

For the analysis of the data, differences between the 3 groups were tested using analysis of variance (ANOVA) followed by the post hoc Tukey's test. Pre- and post-exposure differences between groups were assessed using paired *t* test. Repeated-measure ANOVA was used to compare measurements made pre-exposure, post-exposure, and on days 3, 5, and 7 between the groups. Shapiro–Wilk's test was performed to evaluate the normality of data distribution, and it was seen that data were normally distributed. Data were expressed as mean ± standard deviation. The *P* values less than .05 were accepted as statistically significant. IBM SPSS 19.0 for Windows (IBM SPSS Corp.; Armonk, NY, USA) was used for statistical analysis.

RESULTS

Frequencies

Pre-exposure and Post-exposure Differences

Analysis of pre-exposure DPOAE measurements indicated that the pre-exposure recordings were normal for each rat, and pre-exposure recordings between HBOT, NBOT, and control groups were not significantly different ($P > .05$). Analysis of the post-exposure data set indicated that all rats had AAT due to noise exposure with statistically significant differences between pre- and post-exposure measurements ($P < .05$). Post-exposure measurements between the groups were not significantly different ($P > .05$) (Figure 1).

Low Frequencies Comparison (1,1.5, and 2 kHz)

There was a statistically significant difference within time ($P < .05$), but there was no statistically significant difference between groups ($P > .05$) (Figures 2-4).

High Frequencies Comparison (3, 4, 5, and 6 kHz)

There was a statistically significant difference within time and between groups ($P < .05$) (Figures 5-8).

Time

Between groups, recovery of DPOAE values in all frequencies except 1 kHz was better in the control group during the third, fifth, and seventh days. When the values of HBOT and NBOT groups were compared, we found that on the third day, HBOT values were better than

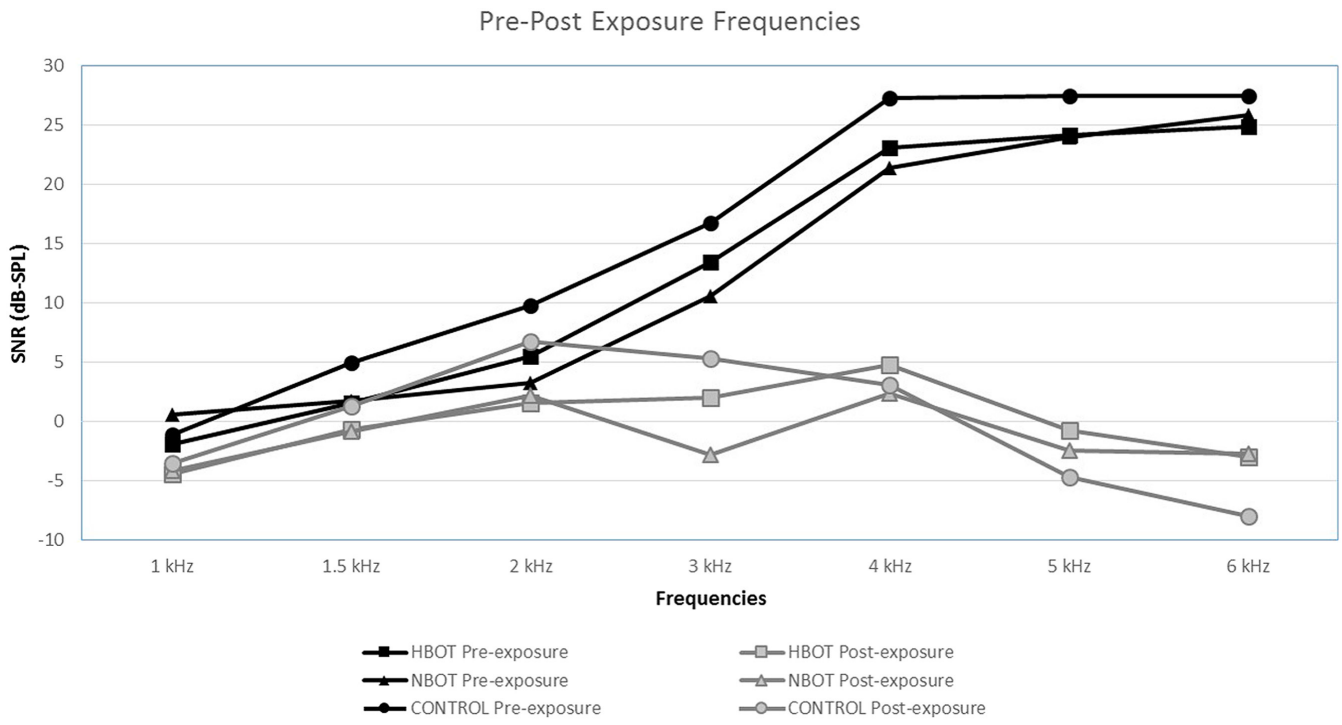

Figure 1. Line graphic of pre- and post-exposure measurements.

NBOT values, but on the fifth and seventh days, NBOT values were better than HBOT values (except frequency of 1 kHz) (Figures 2-8).

Groups

Hyperbaric Oxygen Therapy

On day 3, a significant recovery in DPOAE was seen at 5 and 6 kHz (Figures 7 and 8).

Normobaric Oxygen Therapy

On day 5, a significant recovery in DPOAE was seen at 3, 4, 5, and 6 kHz (Figures 5-8).

Control

On day 3, a significant recovery in DPOAE was seen at 3, 4, 5, and 6 kHz (Figures 5-8).

DISCUSSION

A literature review was carried out to determine the noise for producing AAT. Colombari et al[2] used 4 kHz octave band noise with a 110 dB intensity for 72 hours, Cakir et al[5] used 1-12 kHz white noise with a 110 dB intensity for 25 minutes, and Fakhry et al[24] used 8 kHz one-third octave band noise with a 115 dB intensity for 3 hours.[2,5,24] We decided to use 1-12 kHz white noise with a 110 dB intensity for 60 minutes. The post-exposure DPOAE data set indicated that all rats had AAT due to noise exposure. The best recovery was observed in the control group. It is possible that noise exposure might have induced a temporary threshold shift (TTS) in the rats' hearing. Although a gap of 48 hours is essential to differentiate between TTS and permanent threshold shifts (PTS), this delay is generally not possible in actual clinical practice. Hence, in order to replicate actual clinical practice conditions, HBOT and NBOT were started at 6 hours.

Cochlear damage due to intense noise can cause the loss of the outer hair cells of the organ of Corti, and DPOAEs seem to be the most suitable test to use to provide further information about the function of outer hair cells in cases of AAT.[25-27] Because of that, the effect of the acoustic trauma on the hearing was monitored with measurements of DPOAEs which is an accurate, objective, fast, and noninvasive

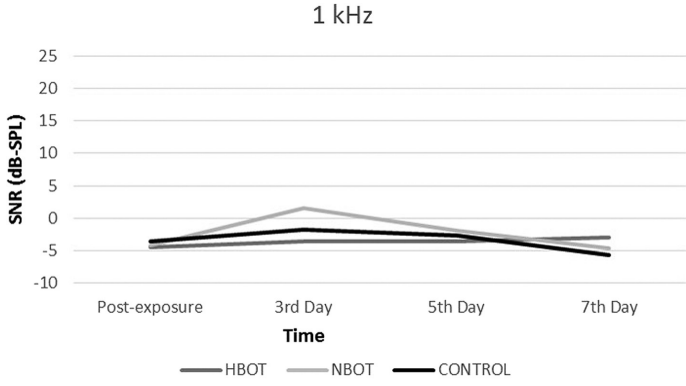

Figure 2. Line graphic of 1 kHz on the first, third, fifth, and seventh days.

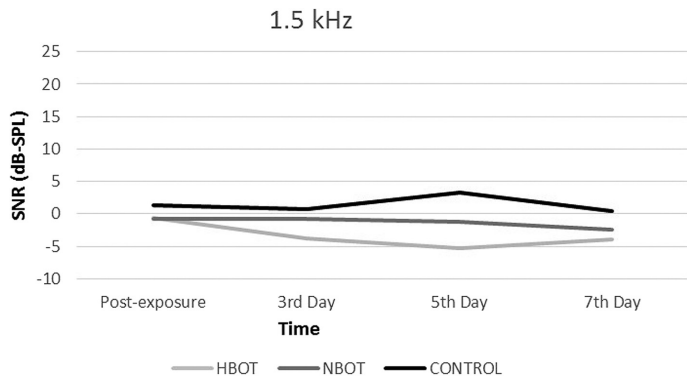

Figure 3. Line graphic of 1.5 kHz on the first, third, fifth, and seventh days.

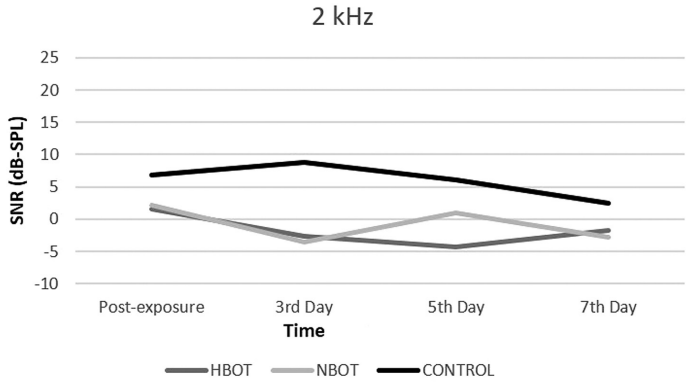

Figure 4. Line graphic of 2 kHz on the first, third, fifth, and seventh days.

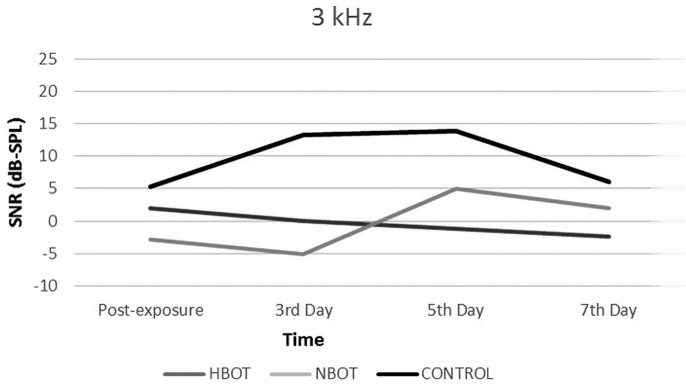

Figure 5. Line graphic of 3 kHz on the first, third, fifth, and seventh days.

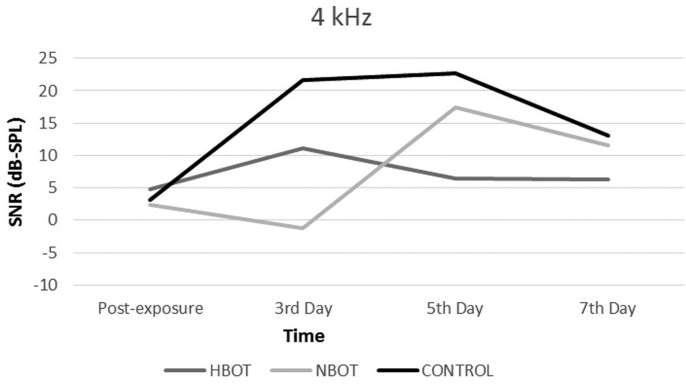

Figure 6. Line graphic of 4 kHz on the first, third, fifth, and seventh days.

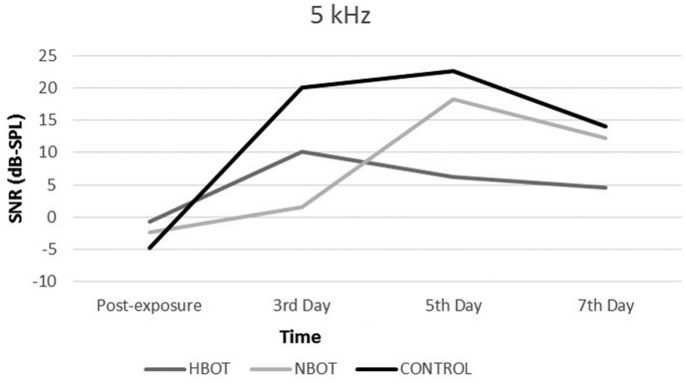

Figure 7. Line graphic of 5 kHz on the first, third, fifth, and seventh days.

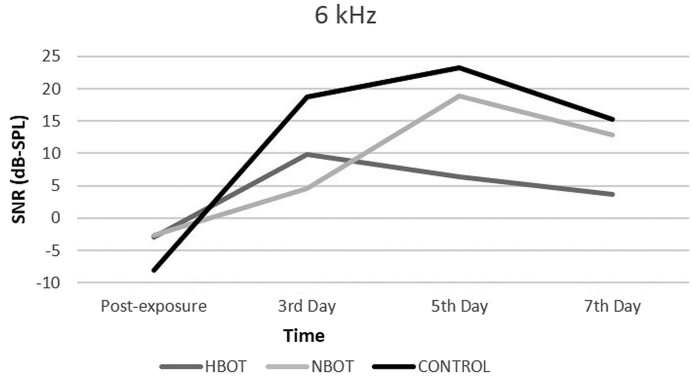

Figure 8. Line graphic of 6 kHz on the first, third, fifth, and seventh days.

measurement method. A problem encountered in the DPOAE measurements in a rat is the difficulty of placing the probe in the rat's narrow external auditory canal. To overcome this problem, a neonatal probe was used in this study.

The treatments and measurements were limited to 7 days after noise exposure in this study. Certain studies have recorded measurements up to the 10th and 16th day after noise exposure or after the start of treatment.[6,24] However, there is no consensus among researchers regarding the duration of treatment after noise exposure. In this study, TTS had already come up on the fifth day. Measurements were recorded up to the seventh day only, to obviate the risk of the rats' death due to repeated interventions. The possibility of further recovery or threshold shifts after 7 days cannot be ruled out.

Although the spontaneous recovery rate is very high, there are various treatment modalities for AAT.[1,2,5,28-30] The most common approach to the treatment of AAT is the use of steroids. Some studies show that steroids combined with HBOT are useful in AAT.[1,2,19,24,25,28] By providing adequate oxygen supply, HBOT prevents oxidative stress secondary to cochlear hypoxia.[1,2,5,25] It shortens the duration of healing and reduces the relapse in AAT.[28] Despite all this evidence data, no significant difference was observed between the control and the animals treated with HBOT alone in Fakhry et al's research.[24] However, the results of this study were different from those of previous studies. The best recovery is observed in the control group. Maybe the reason for this difference is the time of commencement of the treatment. If HBOT is used alone immediately after AAT, it can cause a possible additional injury to cochlear hair cells and has a negative effect.[5,22] This is the reason why a delay of 6 hours was ensured before instituting treatment. Nevertheless, hyperbaric and normobaric oxygen therapy still had a deleterious effect. In our study, HBOT had a significant recovery effect on high frequencies by the third day. However, deterioration started to appear subsequently. Two previous studies may be a guide for the earlier recovery to deteriorate over time. In these studies which used patients' data, some individuals may have atrophy of stria vascularis. This atrophy leads to extensive damage.[13,31] It is difficult to conclude with this contradictory data. However, it is clear that HBOT and NBOT have a detrimental effect on recovery from AAT in some cases.

The negative effect of HBOT observed in our study was also observed in previous studies. In these studies, administration time of HBOT was

found to be a critical factor. Hyperbaric oxygen therapy was found deleterious when administered early.[5,22] Contrary to the assertions in previous studies that HBOT at 6 hours would not have any detrimental effects, our observations revealed that this is not the case. Hence, it is probably advisable to wait longer before starting HBOT.

In one study, researchers compared the effect of HBOT under different pressures.[32] They found that at low frequencies, high-pressure oxygen therapy and at higher frequencies, low-pressure oxygen therapy produced better results. In our study, we observed that the healing effect of NBOT at high frequencies is better than HBOT especially on the fifth and seventh days. At low frequencies (1 and 2 kHz), the healing effect of HBOT was better than NBOT on the seventh day. The results of this study and those of some earlier ones point to the fact that HBOT is more effective in AAT where low frequencies are affected. However, there is a need for more randomized controlled trials for this inference. On the other hand, if we had evaluated frequencies higher than 6 kHz (16-32 kHz) in our research, we could compare the effect of HBOT and NBOT at high frequencies more clearly. Since we planned to evaluate frequencies up to 6 kHz in our study, not evaluating high frequencies can be considered as a limitation of this study.

CONCLUSION

The best results were found in the control group. However, it does not mean that AAT patients should not be given any treatment. On the other hand, the first rule of medicine "do not harm" should not be forgotten, and physicians should be more selective to treat AAT patients with HBOT and NBOT. We did not use steroids in our study, as adding steroids to the treatment may affect the results. In a future study, adding steroids in addition to the treatments used here may result in better outcomes in the HBOT and NBOT groups than in the control group.

Ethics Committee Approval: All applicable international, national, and/or institutional guidelines for the care and use of animals were followed. This study protocol was approved by Institutional Local Animal Care and Use Committee of Eskisehir Osmangazi University (No: 224).

Informed Consent: N/A.

Peer Review: Externally peer-reviewed.

Author Contributions: Concept; Design; Supervision; Funding; Materials - N.A., E.K., A.I., E.Y.; Data Collection and/or Processing; Analysis and/or Interpretation; Literature Review; Writing - N.A., E.K., A.I.; Critical Review - N.A., E.K., A.I., E.Y.

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