Original article

Hyperbaric oxygen therapy for acute noise-induced hearing loss: evaluation of different treatment regimens

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Key words
Hearing, injury, hyperbaric oxygen therapy, outcome, research

Abstract


Introduction: Impulse noise from firearms is a common cause of acute acoustic trauma (AAT), which is characterized by high-frequency hearing loss and tinnitus. Various treatment modalities have been proposed, some combining medical treatment with hyperbaric oxygen (HBOT) in various ways. We have reviewed the therapeutic effect of primary protocols, with or without HBOT, used in our hospital.

Methods: Sixty-eight soldiers for all of whom pre-AAT audiometry tests were available, were treated with one of three different regimens. Group 1 received oral medication only. Group 2 received HBOT twice a day for 3 days then once a day (7 days), combined with intravenous medication (5 days) followed by oral treatment. Group 3 received HBOT once a day and oral medication for 10 days. Medical treatment consisted of methylprednisolone and piracetam in all groups. Control audiometry was performed after 10 days. Average Hearing Gain (AHG) and Average Residual Hearing Loss (ARHL) were calculated.

Results: The mean AHG in Group 1 was +5.58 ± 3.58 dB (mean ± SD); in Group 2 it was +20.62 ± 17.68 dB; and in Group 3 +17.0 ± 14.0 dB (P = 0.001, Kruskal-Wallis test). The mean ARHL without HBOT was -14.7 ± 8.27 dB (Group 1), and respectively -2.36 ± 10.69 dB (Group 2) and -5.0 ± 8.0 dB (Group 3) in the HBOT groups (P = 0.001, Kruskal-Wallis test).

Conclusion: These results indicate a significant benefit for the combination of HBOT and medical therapy over medical treatment alone. Which of the two HBOT regimens is the more effective, remains to be determined.
employed by the Belgian Armed Forces on active military
duty. Their average age was 20.9 ± 4.6 years, average height
176.2 ± 13.4 cm and average weight 75.2 ± 6.9 kg. Ethical
approval was obtained from the Military Hospital Bio-
Ethical Committee. Each patient was informed and gave
consent for use of their data in studies where only group data
are reported. Clinical information for each case was loaded
into a database that was stripped of individual identifiers.

All soldiers had suffered AAT during practice firing; all
firing was done with similar ammunition (NATO [North
Atlantic Treaty Organisation] 5.56 mm caliber) either with
an FNC assault rifle (FN, Herstal, Belgium) or a Minimi
light machine gun (FN, Herstal, Belgium). While appropriate
noise protection is provided during military shooting
exercises, this failed for a variety of reasons (improper
placement of ear plugs, non-adapted ear-plug size, accidental
removal or loss of ear plugs). The number of rounds shot
before suffering AAT could not be determined with accuracy
but, in most cases, AAT was provoked by one or two
impulse noises (125 dB at 10 cm).9 Once the soldiers were
symptomatic they were immediately removed from duty and
directed to sickbay where the first clinical evaluation took
place. When NIHL was suspected, they were immediately
transferred to the nearest hospital for audiometry and
treatment. All patients thus received treatment within 48
hours after AAT and were formally tested at least 24 hours
after the noise exposure. All patients were referred as soon
as possible to the Military Hospital in Brussels; depending
on logistic and practical considerations, some patients were
examined locally at the nearest other hospital. When NIHL
was suspected, medical treatment was started immediately in the patient’s military unit,
and consisted of a combination of oral corticosteroids
(methylprednisolone) in a decreasing daily dosage (64 mg
reducing to 8 mg over 10 days) and piracetam (2400 mg three
times a day) for 10 days. This specific treatment regimen
was found to be effective in reducing hearing loss in the Belgian Armed Forces since the 1970s; it
has been enforced by a military directive in 1994 and
has recently been endorsed by the Belgian Society of ENT Physicians after a consensus conference.10

Group 1, ‘No HBOT’. Seventeen patients did not receive
HBOT because emergency evacuation to the Military
Hospital was less than 36 hours (6 to 36 hours) and they were aggressively treated. They were given
HBOT twice daily (pressure 253 kPa, 70 minutes of oxygen
breathing) for three consecutive days, followed by once
daily sessions for seven days. All patients received daily IV
corticosteroids (methylprednisolone 125 mg decreasing to
40 mg) and IV piracetam (12 g over 15 minutes) for 5 days,
followed by oral treatment for 5 days (methylprednisolone
32 mg decreasing to 40 mg and piracetam 2400 mg three
times a day).

Group 2, ‘HBOT+IV’. For 32 patients, the delay in transfer
to the Military Hospital was less than 36 hours (6 to 36
hours) and they were aggressively treated. They were given
HBOT twice daily (pressure 253 kPa, 70 minutes of oxygen
breathing) for three consecutive days, followed by once
daily sessions for seven days. All patients received daily IV
corticosteroids (methylprednisolone 125 mg decreasing to
40 mg) and IV piracetam (12 g over 15 minutes) for 5 days,
followed by oral treatment for 5 days (methylprednisolone
32 mg decreasing to 40 mg and piracetam 2400 mg three
times a day).

Group 3, ‘HBOT+PO’. For 19 patients the delay of transfer
was 36 hours or more (36 to 43 hours). They were given daily
HBOT (pressure 253 kPa, 70 minutes of O2 breathing) for 10
days, combined with oral treatment as for Group 1.

Results were analysed with GraphPad Prism software
(version 5) on a PC, using the Kruskal-Wallis test (one-
way ANOVA) and Dunn’s multiple comparison tests (the
groups failed to pass the Kolmogorov-Smirnov normality test,
preventing assumption of a Gaussian distribution).

Figure 1
Comparison between the pure tone audiogram on
enlistment into the army (baseline) and after
acute acoustic trauma in the affected ear
(all patients; *** P < 0.0001)
Results

The three treatment groups were comparable as far as age, gender and weight were concerned.

Figure 1 shows the averaged pure tone audiograms of the injured ears compared to the induction PTA for the same ear. These confirm that the primary damage following acoustic trauma occurred at the high frequencies, from 2 kHz to 8 kHz (P < 0.0001, Wilcoxon test, two-tailed).

The initial hearing loss is illustrated in Figure 2. The mean (± SD) AHL in Group 1 (No HBOT) was -25.83 ± 11.70 dB; Group 2 (HBOT+IV), -31.35 ± 19.0 dB; and Group 3 (HBOT+PO), -29.68 ± 15.68 dB. There was no statistical difference between the three groups (Kruskal-Wallis test, P = 0.6603). The Dunn’s multiple comparison test likewise failed to demonstrate statistical significance.

The average hearing gain is shown in Figure 3. Group 1 (No HBOT) had an AHG of +5.58 ± 3.58 dB; Group 2 (HBOT+IV), +20.62 ± 17.68 dB; and Group 3 (HBOT+PO), +17.0 ± 14.0 dB. The difference between the three groups was statistically significant (Kruskal-Wallis test, P = 0.001). Dunn’s multiple comparison test failed to demonstrate statistical difference between the two HBOT groups but confirmed that both HBOT groups were statistically different from Group 1 (P < 0.05).

The average residual hearing loss is shown in Figure 4. For Group 1 (No HBOT), ARHL was -14.7 ± 8.27 dB; for Group 2 (HBOT+IV), -2.36 ± 10.69 dB; and for Group 3 (HBOT+PO), -5.0 ± 8.0 dB. ARHL was statistically significantly different for the three groups (Kruskal-Wallis test, P = 0.001). Again, the difference between both HBOT groups and the group without HBOT is significant (P < 0.05), but Dunn’s multiple comparison test failed to demonstrate a statistical difference between the two HBOT groups.

Discussion

The optimal treatment of NIHL has not been well defined. In analogy with sudden sensorineural hearing loss, various treatment regimens have been proposed. The most common approach to the treatment of SSHL is the use of systemic steroids, which have been deemed by some authors to be the ‘gold standard’ of treatment.11,12 However, a recent meta-analysis was unable to definitely support this statement.13 Some authors recommend pentoxifyllin, and others...
have reported that 12 g of piracetam administered as an intravenous infusion over 15 minutes significantly increased the chance of complete recovery for patients with SSHL. As it is a widely accepted and recommended treatment, the ‘standard’ approach for AAT in the Belgian Armed Forces is high-dose corticosteroids combined with piracetam, a strategy that has been endorsed recently by the Belgian ENT Society.

Whereas for SSHL, scientific understanding of its cause or a rational approach to its treatment is lacking, in NIHL, it has been shown that one of the first effects of AAT is a decrease in the oxygen supply to the organ of Corti. It has also been shown that noise can induce hypoxia in the auditory cortex, the hippocampus and the inferior colliculus. The rationale for using HBOT is based on the fact that inhalation of pure oxygen under pressure causes an increase in the arterial partial pressure of oxygen and an increase in the oxygen diffusion distance in tissues. These principles, enhancing tissue oxygenation, are complemented by blood-flow redistribution to hypoxic areas. As a consequence, and in contrast to vasodilatation treatment, HBOT treatment increases oxygen tension in the endo- and perilymph and might in this way help hypoxic cells to survive.

An animal study of HBOT for NIHL suggested that HBOT immediately after AAT (one and two hours post exposure) may have an adverse effect, probably by an increase of oxygen free radical production. When HBOT was started later (at 6, 24 or 48 hours post-exposure) this adverse effect seems to be absent, and in these groups hearing was back to the pre-exposure level, as demonstrated by levels of signal-to-noise ratio, within 10 days post exposure. This positive effect has also been suggested in another recent animal study in which only a regimen of combined HBOT and corticosteroids provided significant protection from NIHL, especially when started one day post exposure. Hearing recovery induced by this treatment regimen was about 10–15 dB. These two animal studies support our strategy to use HBOT as a primary tool in association with corticosteroids in the treatment of AAT. Our current treatment protocols adhere to a therapeutic window from 6 to 48 hours, as suggested by Cakir et al.

In this study a significant therapeutic effect on noise-induced hearing loss was only achieved in the HBOT groups. This supports the idea that HBOT therapy is an important therapeutic tool and that medical therapy alone, like minimal therapy or no therapy (waiting for spontaneous recovery), is not the treatment of choice. HBOT was associated with significant improvement in PTA thresholds, although full recovery had not occurred by 10 days post injury. Compared to the baseline PTA at enlistment, even the HBOT groups were left with a residual loss. However, both HBOT groups have gained statistically significant better hearing recovery than the group not receiving HBOT.

When comparing both HBOT groups, a combination of aggressive HBOT and initial treatment with intravenous corticosteroids seems to be the best option. This could be interpreted as a confirmation that HBOT started as early as possible, but not in the first 6 hours post injury to avoid any possible adverse effect of HBOT, produces better results, while therapy started later (after sensory cell death) produces poorer results. The relatively small numbers of patients in the HBOT groups may have been insufficient to demonstrate a significant difference. Alternatively, it is possible that there is indeed no difference between the two HBOT regimens; this would mean that the ‘HBOT+IV’ group was treated unnecessarily aggressively. From this study, it is not possible to obtain a clear-cut recommendation as to the best HBOT regimen.

This retrospective study on the treatment of AAT has limitations. Despite the fact that clear guidelines for the approach to AAT are available in the Belgian Armed Forces, and that all patients received a standardised emergency treatment, the study was neither prospective nor randomised. Therefore, it is possible that some referral bias played a role in the decision to refer patients acutely for HBOT. Although the differences in AHL in the three groups were statistically not significant, Group 1 had slightly less hearing damage than the other groups. It is possible, although improbable, that the presence or severity of other symptoms (such as tinnitus) may have played a role in the decision to refer patients over an often considerable distance. We tried to minimise the influence of these confounding factors by selecting only those patients who had a severe decrease in their hearing and who failed to improve within the first 24 hours (to exclude patients with TTS only). This, however, reduced the number of patients available for analysis, decreasing the power of the study.

Performing a randomised controlled trial with a placebo group in this disease would probably be inappropriate because several treatments have been shown to have some degree of efficacy. Furthermore, the practical implementation of sham hyperbaric treatment is difficult, and its validity has been questioned. Therefore, in order to obtain evidence regarding the efficacy of a new treatment, it is acceptable that it is tested against the best available treatment. A randomised, prospective study is being conducted in our hyperbaric unit. We hope to open this to multicentre collaboration among military centres in NATO countries and beyond. This study will compare different combinations of HBOT and intravenous or oral corticosteroids, in a similar group of well-defined ‘ears’ and AAT.

**Conclusions**

This study demonstrates a clear benefit from the combination of HBOT and medical therapy over medical treatment alone. It suggests that the more aggressive the combined treatment is at an early stage, the better the results. However, at this stage, strong evidence to demonstrate the superiority of one HBOT protocol over another is lacking.
References


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