Original article

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

Pierre Lafère, David Vanhoutte and Peter Germonpré

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

Abstract
(Lafère P, Vanhoutte D, Germonpré P. Hyperbaric oxygen therapy for acute noise-induced hearing loss: evaluation of different treatment regimens. *Diving and Hyperbaric Medicine*. 2010;40(2):63-7.)
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.

Introduction

Impulse noise from firearms is a common cause of acute acoustic trauma (AAT), which can cause rupture of cell membranes and decreased cochlear blood flow. This leads to decreased oxygen tension in the inner ear and reduction of oxygen-dependent cellular activities.[1] Symptoms are, typically, a high-frequency hearing loss ('noise-induced hearing loss', NIHL) and tinnitus. Different degrees of NIHL are described; in minor cases, the hearing loss is temporary (temporary threshold shift – TTS), recovering within 24 hours of the trauma.[2] In more severe cases, the hearing loss is permanent (permanent threshold shift – PTS).

The optimal treatment for NIHL has not been defined. In some animal models, it has been shown that hyperbaric oxygen treatment (HBOT), combined with corticosteroids, seems to improve the functional and morphological recovery.[3] Only the therapeutic regimens that include HBOT have shown a sustained therapeutic effect on noise-induced cochlear hypoxia.[4] Despite the first reports of HBOT as a treatment for NIHL being published 20 years ago, few human trials have been reported.[5,6]

It was proposed in 1995 that, in AAT, minimal therapy or waiting for spontaneous recovery is not the treatment of choice, because recovery is mostly incomplete, leaving a residual hearing loss and disabling tinnitus.[7] Analogy has been drawn with another acute hearing disorder, sudden idiopathic hearing loss. In human trials in those patients, 65% of poly-pragmatically treated patients demonstrated a hearing improvement independent of the drugs administered, whilst 61% of placebo-treated patients also demonstrated improvement.[8] Whereas the optimal medical therapy, if any, seemed unclear, a large review seemed to confirm that, in patients not responding to medical treatment, HBOT, even if given late, was still of benefit in about 45% of cases.[8]

There is a need to formally evaluate the therapeutic effect of HBOT in hearing loss, both idiopathic and noise-induced. Having at our disposal a unique cohort of patients for whom treatment is standardized and previous pure tone audiogram (PTA) is available, it was possible for us to analyse the results of the treatment protocols for AAT in a military hospital, including those using HBOT.

Subjects and methods

For this study, patient records from all cases with AAT treated between January 2006 and December 2008 at the Queen Astrid Military Hospital in Brussels, Belgium were retrieved. All 121 patients were professional soldiers

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 treated locally with a standard medication schedule including corticosteroids and piracetam (see below).

For this study, only patients with hearing loss of at least -25 dB in at least one frequency (as compared to their baseline PTA) were included. Those with less severe hearing loss, or (to exclude those with only TTS) with improvement in hearing of more than 20 dB in any frequency in the first 24h after AAT, were excluded. Furthermore, patients with a history of previous AAT, even if fully recovered, were also excluded. This left 68 patients with unilateral NIHL, who were available for assessment of the effect of therapy with or without HBOT. They were divided into three groups:

Group 1, 'No HBOT'. Seventeen patients did not receive HBOT because emergency evacuation to the Military Hospital was not possible or practical. 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 has been used 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 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 O_2 breathing) for 10 days, combined with oral treatment as for Group 1.

All patients were evaluated using PTA from 250 Hz to 8 kHz at the start of the treatment and after 10 days. These PTA curves were compared to the baseline PTA upon their enlistment into the Belgian Armed Forces. The average hearing loss (AHL) at frequencies of 2, 4 and 8 kHz (the only frequencies statistically different from the baseline PTA) was calculated with the enlistment PTA as a baseline. In order to compare the effect of the different treatment regimens, the average hearing gain (AHG) and the average residual hearing loss (ARHL) on these three frequencies were calculated in the same way as for the AHL. AHG was calculated with the initial loss as a basis, ARHL with the enlistment PTA as the baseline.

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 Kolmgorov-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)**

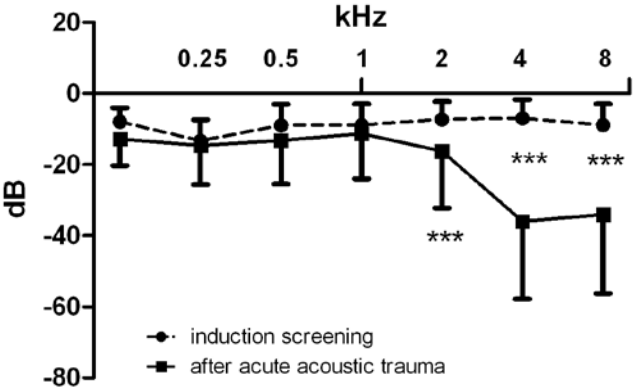


Figure 2
Average hearing loss at presentation for the three treatment groups (see text; $P = 0.66$)

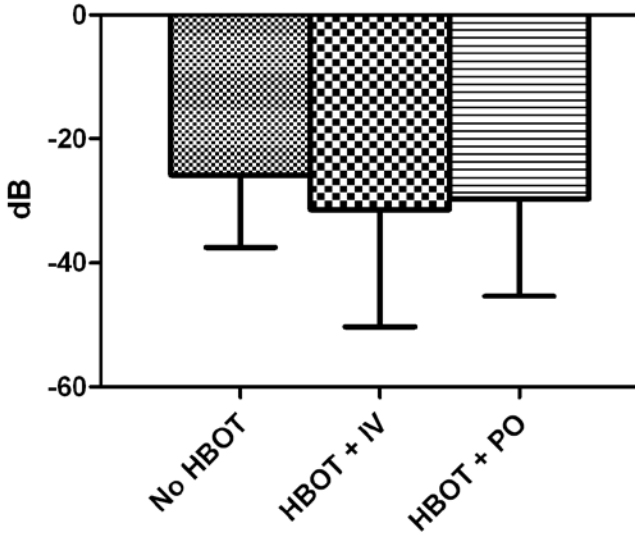
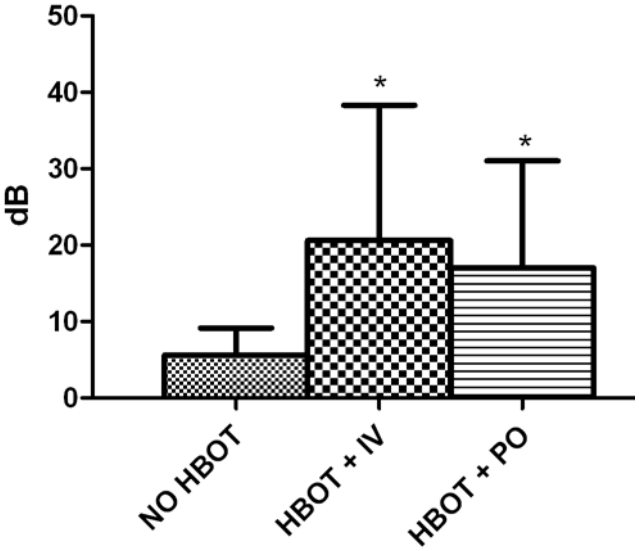


Figure 3
Average hearing gain in the three treatment groups (* $P < 0.05$)



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.

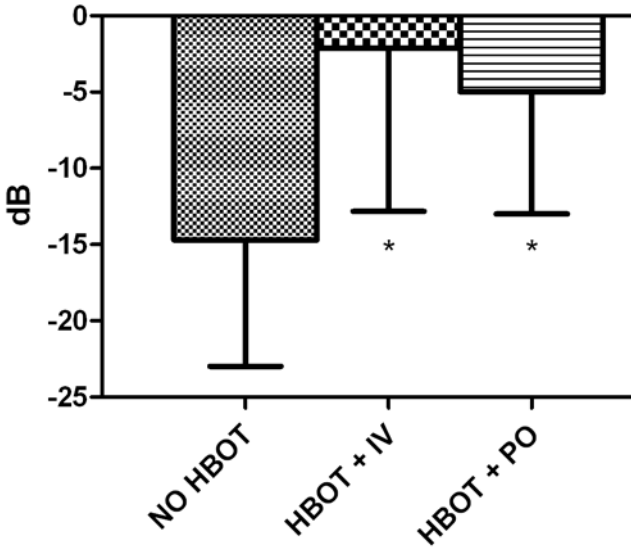
The average hearing gain is shown in Figure 3. Group 1 (No HBOT) had an AHG of +5.58 ± 3.58 dB; Group 2 (HBOT+IV), +20.62 ± 17.68 dB; and Group 3 (HBOT+PO), +17.0 ± 14.0 dB. The difference between the three groups was statistically significant (Kruskal-Wallis test, $P = 0.001$). Dunn's multiple comparison 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

Figure 4
The average residual hearing loss in the three treatment groups (see text; * $P < 0.05$)



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.[14,15] 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.[10,16]

Whereas for SSHL, scientific understanding of its cause or a rational approach to its treatment is lacking,[13] 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.[16,17] It has also been shown that noise can induce hypoxia in the auditory cortex, the hippocampus and the inferior colliculus.[18] 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.[19] 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.[20,21]

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.[22] 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.[22] 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.[23] 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.[22]

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.[24] 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.[25] 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

1 Kuokkanen J, Aarnisalo AA, Yiloski J. Efficiency of hyperbaric oxygen therapy in experimental acute acoustic trauma from firearms. *Acta Otorlayngol Suppl*. 2000;543:132-4.

2 Dancer A, Grateau P, Cabanis A, Vaillant T, Lafont D. Delayed temporary threshold shift induced by impulse noises (weapon noise) in men. *Audiology*. 1991;30(6):345-56.

3 D'Aldin C, Cherny L, Devriere F, Dancer A. Treatment of acoustic trauma. *Ann N Y Acad Sci*. 1999;884:328-44.

4 Lamm K, Arnold W. Successful treatment of noise-induced cochlear ischemia, hypoxia and hearing loss. *Ann N Y Acad Sci*. 1999;884:233-48.

5 Demaertelaere L, Van Opstal M. Behandeling van acoustische trauma's met hyperbare zuurstof (HBO). *Acta Otorhinolaryngol Belg*. 1981;35(3-4):303-14.

6 Pilgramm M, Schumann K. Hyperbaric oxygen therapy for acute acoustic trauma. *Arch Otorhinolaryngol*. 1985;241(3):247-57.

7 Vavrina J, Muller W. Therapeutic effect of hyperbaric oxygenation in acute acoustic trauma. *Rev Laryngol Otol Rhinol (bord)*. 1995;116(5):377-80.

8 Lamm K, Lamm H, Arnold W. Effect of hyperbaric oxygen therapy in comparison to conventional or placebo therapy or no treatment in idiopathic hearing loss, acoustic trauma, noise-induced hearing loss and tinnitus. A literature survey. *Adv Otorhinolaryngol*. 1998;54:86-99.

9 De Heyn G, Van Opstal M. [Comparative study of acoustic trauma caused by blasts, treated by vasodilators or by a combination of vasodilators and hyperbaric oxygenation]. *Acta Otorhinolaryngol Belg*. 1976;30(3):251-9. French

10 Levie P, Desgain O, de Burbure C, Germonpré P, Monnoye JP, Thill MP, et al. Sudden hearing loss. *B-ENT*. 2007;3(suppl 6):33-43.

11 Conlin A, Parnes L. Treatment of sudden sensorineural hearing loss I. A systematic review. *Arch Otolaryngol Head Neck Surg*. 2007;133:573-81.

12 Chandrasekhar SS. Updates on methods to treat sudden hearing loss. *Oper Tech Otolaryngol Head Neck Surg*. 2003;14:288-92.

13 Conlin A, Parnes L. Treatment of sudden sensorineural hearing loss II. A meta-analysis. *Arch Otolaryngol Head Neck Surg*. 2007;133:582-6.

14 Michel O, Jahns T, Joost-Enneking M, Neugebauer P, Streppel M, Stennert E. [The Stennert antiphlogistic-rheologic infusion schema in treatment of cochleovestibular disorders]. HNO. 2000;48(3):165-7. German

15 Gersdorff M, Franceschi D. Value of piracetam in the treatment of sudden idiopathic deafness. Preliminary report [in French]. *Ann Otolaryngol Chir Cervicofac*. 1986;103:283-5.

16 Axelsson A, Dengerink H. The effect of noise on histological measures of cochlear vasculature and red blood cell: a review. *Hear Res*. 1987;31:183-92.

17 Yamane H, Nakai Y, Konishi K, Sakamoto H, Matsuda Y, Iguchi H. Strial circulation impairment due to acoustic trauma. *Acta Otolaryngol (Stockh)*. 1991;111:85-93.

18 Kim YJ, Kang HH, Ahn JH, Chung JW. Hypoxic change in the central nervous system of noise-exposed mice. *Acta Otolaryngol Suppl*. 2007;(558):73-7.

19 Ratznhofer-Komeda B, Favory R, Weslau W, Smolle-Jüttner FM, Mathieu D. Physiologic effects of hyperbaric oxygen on oxygen transport and tissue oxygen pressure. In: Mathieu D, editor. Handbook on hyperbaric medicine. Doordrecht: Springer; 2006. p. 49-74.

20 Lehnardt E, Hesch RD. [Causes of inner ear deafness; a critique of therapy]. *HNO*. 1980;28(3):73-9. German

21 Pilgramm M. Clinical and animal experiment studies to optimize the therapy for acute acoustic trauma. *Scand Audiol*. 1991;Suppl 34:103-22.

22 Cakir BO, Ercan I, Civelek S, Körpinar S, Toklu AS, Gedik O, et al. Negative effect of immediate hyperbaric oxygen therapy in acute acoustic trauma. *Otol Neurotol*. 2006;7(4):478-83.

23 Fakhry N, Rostain JC, Cazals Y. Hyperbaric oxygenation with corticoid in experimental acoustic trauma. *Hear Res*. 2007;230(1-2):88-92.

24 Jansen T, Mortensen CR, Tvede MF. It is possible to perform a double-blind hyperbaric session: a double-blinded randomized trial performed on healthy volunteers. *Undersea Hyperb Med*. 2009;36(5):347-51.

25 Jaillon P. [Controlled randomized clinical trials]. *Bull Acad Natl Med*. 2007;191(4-5):739-56; discussion 756-8. French

Submitted: 15 June 2009
Accepted: 10 May 2010

Pierre Lafère, MD, is an anesthesiologist and a physician in diving and hyperbaric medicine at the Centre for Hyperbaric Oxygen Therapy of the Military Hospital in Brussels and an associate researcher at the Environmental & Occupational Physiology Laboratory of the Free University of Brussels.
David Vanhoutte, MD, is a physician in diving and hyperbaric medicine at the Centre for Hyperbaric Oxygen Therapy of the Military Hospital in Brussels.
Peter Germonpré, MD, is the Medical Director of the Centre for Hyperbaric Oxygen Therapy of the Military Hospital in Brussels and an associate researcher at the Environmental & Occupational Physiology Laboratory, Free University of Brussels.

Address for correspondence:
Lafère P, MD
Centre for Hyperbaric Oxygen Therapy
Military Hospital "Queen Astrid"
Rue Bruyn 1
1120 Brussels, Belgium
***Phone**: +32-2-264 48 68*
***Fax** +32-2-264 48 61*
***E-mail:** <doc.lafere@skynet.be>*