Value of hyperbaric oxygen therapy in the management of malignant otitis externa patients
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Introduction
Malignant external otitis is an infection that affects the external auditory canal and temporal bone. The causative organism is usually Pseudomonas aeruginosa, and the disease commonly manifests in elderly patients (pt) with diabetes. The infection begins as an external otitis that progresses to an osteomyelitis of the temporal bone. Spread of the disease outside the external auditory canal occurs through the fissures of Santorini and the osseocartilaginous junction [1]. Malignant external otitis is a rapidly spreading bacterial infection that accounts for a relatively small proportion of infections, but arise aggressive in nature and may be fatal if left untreated [2].

Hyperbaric oxygen therapy (HBOT) is a medical treatment in which the entire body is placed in an airtight chamber at increased atmospheric pressure. In this chamber, the patient is surrounded by and breathes 100% pure oxygen. This treatment has been proven effective for a number of different medical conditions either as a primary or as an adjunctive treatment. The pressure can be increased to as much as three times the normal atmospheric pressure (although the usual treatment pressure is 1.5–2.0 atmospheric depending on the diagnosis). Pure, 100% oxygen is continuously maintained and circulated throughout the chamber during the treatment [3].

HBOT is an effective treatment for acute and chronic damaged tissue of all types — any cause, any duration, any location. The underlying causes can be trauma, infection, autoimmunity, ischemia, hypoxia, toxins, or something similar [4].

Background
Malignant external otitis is a rapidly spreading bacterial infection that is aggressive in nature and may be fatal if left untreated. Hyperbaric oxygen therapy (HBOT) is a medical treatment in which the entire body is placed in an airtight chamber at increased atmospheric pressure and has been proven to be effective for a number of different medical conditions.

Objective
The aim of this study was to assess the usefulness of HBOT as an adjunctive treatment in patients with malignant otitis externa.

Patients and methods
Forty-three diabetic patients, who had malignant otitis externa, underwent control of diabetes mellitus and were treated with ciprofloxacin. HBOT was administered to 15 patients as an adjunctive treatment. All the patients were evaluated clinically (in terms of ear discharge, granulations, and pain severity) and radiologically by a temporal bone computed tomography scan. The minimum follow-up duration in both groups was 2 months. HBOT was administered in one session every other day for 2 months, resulting in a total of 30 sessions. Patient factors analyzed included age, sex, ear discharge, and pain severity.

Results
A total of 43 patients (28 men, 15 women) were divided into two groups: group A (28 patients) only received the antibiotic ciprofloxacin and group B (15 patients) was treated with ciprofloxacin and hyperbaric oxygen. The severity of pain improved considerably and the pain score decreased markedly from score 3 (severe) to score 0 (no pain) after 1 month in 46.7 and 93.3% of the patients by the end of the second month in comparison with patients treated only with the antibiotic: 0% after 1 month and 28.5% after 2 months. On clinical and microscopic examination, both ear discharge and granulations in the external canal had improved considerably. There was no ear discharge in 80% of patients in group B after one month treatment, 93.3% after 2 months, in comparison with 0% after 1 month, 28.5% after 2 months treatment in group A, highly statistically significant (P<0.001).

Conclusion
The addition of HBOT to medical treatment is highly effective and has facilitated considerable improvement in patients.

Keywords:
hyperbaric oxygen therapy, malignant, otitis externa
These infections may be single aerobic or anaerobic, but are more often mixed infections. They are often observed in compromised hosts who have diabetes or a vasculopathy of another type. These infections are named on the basis of their clinical presentation and include malignant external otitis [5]. Irrespective of the depth of the tissue invasion, these infections have similar pathophysiology that includes local tissue hypoxia, which is exacerbated by a secondary occlusive endarteritis [5].

Multiple clinical studies suggest that HBOT is efficacious in the treatment of necrotizing soft tissue infections [6–15]. These include case series, retrospective and prospective studies, and nonrandomized clinical trials. They suggest significant reductions in mortality and morbidity.

It is also used to treat many other medical conditions that are still considered experimental by the mainstream medical establishment – despite decades of reported benefits.

The aim of this article is to assess the value of hyperbaric oxygen (HBO) as an adjunctive treatment of malignant external otitis along with antimicrobial agents.

**Patients and methods**

**Patients’ selection criteria**

This is a retrospective study. It was carried out at the Otorhinolaryngology Department, Ain Shams University Hospitals in the period between January 2011 and December 2014 with Institutional Review Board approval. An informed written consent was obtained from all participants. Forty-three patients (pt) were examined and treated for malignant otitis externa; they all had diabetes mellitus, and were undergoing treatment for control of diabetes mellitus. They were divided into two groups: group A (28 pt) only received the antibiotic ciprofloxacin and group B (15 pt) was treated with ciprofloxacin and HBO as an adjunctive treatment. The minimum follow-up duration in both groups was 2 months. Their ages ranged from 56 to 72 years. Both groups were similar in age, ear discharge bacteriology, and antimicrobial therapy.

The Student 𝑡-test was used for statistical analysis. Skewed numerical data are presented as median and interquartile range. Qualitative data are presented as number and percentage. A 𝑃 value less than 0.05 was considered statistically significant.

**Treatment strategy**

*Control of diabetes:* All patients were treated with insulin injections and diabetes mellitus was strictly controlled.

Ear discharge culture and sensitivity were assessed for all patients, which indicated growth of pseudomonas.

Computed tomography (CT) scan temporal bone was performed before (Fig. 1a and b) and 2 months after treatment (Fig. 2a and b). All patients were administered an antibiotic (ciprofloxacin). HBOT was administered at 2.0–2.5 ATA for 90 min per session. HBOT was administered for one session every other day for 2 months. HBOT was administered in the Naser National Institute in Sechrist hyperbaric oxygen chamber (Sechrist Monoplace Hyperbaric Chambers H-Series) (Fig. 3).

**Comparison criteria**

*Clinical microscopic examination* (ear discharge, external canal edema, and granulations). Figure 4 showed granulations filling the external ear canal and purulent discharge (Table 1).

*Pain severity* (pain was scored for assessment of severity of pain and degree of improvement and cure).

A pain score of 3 indicated severe pain (preventing patients from sleep and normal activities), a pain score of 2 indicated moderate pain (controlled sometimes...
Tables 1

| Table 1 Comparison criteria | Group A | Group B |
|----------------------------|---------|---------|
| Treatment                  | Antibiotic only (n = 28) | Antibiotic + HBOT (n = 15) |
| Clinical examination [n (%)]|         |         |
| Ear discharge and granulations | 21 (75) (profuse) | 7 (25) (moderate) |
| Pain severity [n (%)]      | 20 (71.4) | 8 (28.6) |
| Score before treatment     | 3        | 2       |
| CT temporal bone scan      | Before and after 2 months of treatment |         |

CT, computed tomography; HBOT, hyperbaric oxygen therapy.

Results

A total of 43 patients had malignant external otitis; these patients were divided into two groups: group A (n = 28) received antibiotics only (18 men, 10 women; median age 64 years, interquartile range 58–70) and group B (n = 15) received HBO (90 min at 2.5 ATA) in addition to antibiotics (10 men, five women; median age 62 years, interquartile range 56–72) (Table 2).

A total of 43 patients were identified, including 15 patients who underwent HBOT with antibiotics. The degree of improvement of patients after treatment with adjunct HBO with antibiotic was high both symptomatically and clinically, and for CT scan of temporal bone (Tables 3–6). Pain severity improved markedly and the pain score decreased considerably from 3 (severe) to 0 (no pain) after 1 month in 46.7 and 93.3% of the patients by the end of the second month in comparison with patients treated only with an antibiotic: 0% after 1 month and 28.5% after 2 months. Pain score in group B patients was greatly shifted toward score 0 (no pain) more than three to five folds by the end of treatment; 93.3% were pain free in group B compared with 28.5% in group A, and this was highly statistically significant (Figs. 5 and 6). On clinical and microscopic examination, both ear discharge and granulations in the external canal were markedly improved. In group B, 80% of patients had no discharge after 1 month and 93.3% after 2 months, in comparison with 0% after 1 month and 28.5% after 2 months treatment in group A; this was highly statistically significant (P < 0.001) (Figs. 7 and 8). Also, there was radiological improvement in mastoid opacity and fluid and granulations in the mastoid and the middle ear.

Discussion

Necrotizing invasive pseudomonal infection of the external auditory canal (malignant external otitis) is an uncommon, but major disorder in the elderly. The high morbidity, and even mortality, of this disorder has been reduced by the early and intensive use of combination antipseudomonal antibiotics. However, in severely immunocompromised patients or in infections involving the base of the skull, multiple...
cranial nerves, or the meninges, conventional therapy is prolonged, intensive, and relatively ineffective [6]. Prompt identification, antibiotic therapy, control of medical condition, and HBOT have reduced the mortality resulting from this infection. Oxygen, at increased pressures, augments tissue oxygen partial pressure, allowing increased bacterial killing by providing a substrate for the formation of oxygen free radicals and augmenting respiratory burst [16]. During the healing process, hyperoxia causes increased formation of capillaries for oxygen, nutrient, and antibiotic delivery, leading to increased efficacy of some antibiotics in the high-oxygen environment, and possibly more rapid overall wound healing [17,18]. HBOT can enhance host immune systems [19]. There is limited evidence showing that HBOT may facilitate antibiotic penetration or action in several classes of antibiotics, including aminoglycosides [20], cephalosporins, sulfonamides, and amphotericin [19].

### Table 2 Demographic data of the study groups

| Patient data | Group A | Group B |
|--------------|---------|---------|
| Number of patients | 28 | 15 |
| Sex | 18 M, 10 F | 10 M, 5 F |
| Age | 58–70 (64) | 56–72 (62) |
| DM | ++++ | ++++ |
| Treatment | Antimicrobial therapy | Antimicrobial therapy+HBOT |
| Ear discharge bacteriology | ++ Pseudomonas | ++ Pseudomonas |
| Pain | Main C/O | Main C/O |

DM, diabetes mellitus; HBOT, hyperbaric oxygen therapy.

### Table 3 Results after 1 month of treatment

| Results after 1 month of treatment | Group A | Group B |
|-----------------------------------|---------|---------|
| Number of patients | 28 | 15 |
| Clinical examination [n (%)] | | |
| Ear discharge | | |
| No | 12 (80) | 7 (46.7) |
| Mild | 8 (28.6) | 2 (13.3) |
| Moderate | 14 (50) | 1 (6.7) |
| Profuse | 6 (21.4) | 0 (0) |
| Pain severity score [n (%)] | | |
| 0 (no pain) | 0 (0) | 7 (46.7) |
| 1 (mild pain) | 9 (32.1) | 6 (40) |
| 2 (moderate pain) | 17 (60.7) | 2 (13.3) |
| 3 (severe pain) | 2 (7.2) | 0 (0) |

### Table 4 Pain severity score after 1 and 2 months of treatment

| Group | Group A (28 patients) | Group B (15 patients) |
|-------|------------------------|-----------------------|
|       | No | Mild | Moderate | Severe | No | Mild | Moderate | Severe | P |
| After 1 month | 0 | 9 | 17 | 2 | 7 | 6 | 2 | 0 | <0.001 |
| After 2 months | 0% | 32.1% | 60.7% | 7.2% | 46.7% | 40% | 13.3% | 0% | <0.001 |

Pain Score: N0 = 0,Mild = 1,Moderet = 2,Sever = 3.
Value of HBOT in otitis externa patients

Infections for which HBOT has been studied and is recommended by the Undersea and Hyperbaric Medicine Society include necrotizing fasciitis, gas gangrene, chronic refractory osteomyelitis (including malignant otitis externa), mucormycosis, intracranial abscesses, and diabetic foot ulcers that have concomitant infections [7]. In all of these processes, HBOT is used adjunctively along with antimicrobial agents and aggressive surgical debridement [7].

This study evaluates how the addition of HBOT to antibiotic treatment has affected improvement, cure, and infection control in these patients.

In our study, we found that the addition of HBOT to the antibiotic therapy was very beneficial to the patients with malignant otitis externa in the control of infection, improvement of symptoms and signs, and cure of the condition. Clinically, in group B, 86.7% of the patients reported considerable improvement in pain after the first month of treatment (15 sessions), with 93.3% being pain free after the second month (30 sessions). On the other hand group A showed only 32.1% improved of pain after 1 month and 28.5% free of pain after 2 months those patients treated with antibiotic only ($P < 0.001$). On examination, purulent ear discharge was markedly reduced with HBOT therapy, there was no ear discharge in 80% of patients after the first month and in 93.3% of patients after the second month; without HBOT therapy, only 28.5% of patients were free of discharge after 2 months ($P < 0.001$). Radiologically, CT scan temporal bone indicated considerable improvement with HBOT treatment, with less infection, opacity, fluid in mastoid, and osteomyelitic changes. Generally, all cases treated with antibiotic and HBOT showed considerable improvement subjectively and objectively by examination and radiology, with more than 93% of cases cured and discharged early from the hospital. In contrast, those treated only with antibiotic showed slow improvement, low percent of complete cure (less than 30%), with persistent discharge and some degree of pain, and longer duration of hospitalization. No complications were reported with this treatment.

Davis et al. [6] reported that all 16 of their patients responded promptly when a 30-day course of HBO was added to the antibiotic regimen, and all patients remained free from infection during 1 to 4 years of follow-up. No complications were noted. Pilgramm et al. [8] also showed that hyperbaric oxygenation had a positive influence on the reduction of $P$. aeruginosa in the external auditory canal and on the symptoms of pain.

Mader and Love [9] reported control of $P$. aeruginosa infection in their patient when adjunctive HBOT was added to the treatment regimen. Also, Gilain et al. [10] found that the addition of HBO as a complementary treatment led to the regression of clinical signs and resolution of infection.

Tisch et al. [11] found, over a period of more than 5 years, that 16 of 22 patients treated on the basis of a multimodal

Table 5 Results after 2 months of treatment

| Results after 2 months of treatment | Group A | Group B |
|------------------------------------|---------|---------|
| Number of patients                 | 28      | 15      |
| Clinical examination [n (%)]       |         |         |
| Ear discharge                      |         |         |
| No                                 | 8 (28.5)| 14 (93.3)|
| Mild                               | 12 (42.9)| 1 (6.7) |
| Moderate                           | 6 (21.4)| 0 (0)   |
| Profuse                            | 2 (7.2) |         |
| Pain severity (score) [n (%)]      |         |         |
| 0 (no pain)                        | 8 (28.5)| 14 (93.3)|
| 1 (mild pain)                      | 15 (53.6)| 1 (6.7) |
| 2 (moderate pain)                  | 5 (17.9)| 0 (0)   |
| 3 (severe pain)                    | 0 (0)   | 0 (0)   |

Table 6 Ear discharge after 1 and 2 months of treatment

| Group   | Group A (28 patients) | Group B (15 patients) | $P$  |
|---------|-----------------------|-----------------------|------|
|         | No       | Mild     | Moderate | Profuse | No       | Mild     | Moderate | Profuse |      |
| After 1 month | 0 | 8 | 14 | 6 | 12 | 2 | 1 | 0 | <0.001 |
|          | 0%       | 28.6%    | 50%      | 21.4%   | 80%     | 13.3%    | 6.7%     | 0%      |      |
| After 2 month | 8 | 12 | 6 | 2 | 14 | 1 | 0 | 0 | <0.001 |
|          | 28.6%    | 42.9%    | 21.4%    | 7.2%    | 93.3%   | 6.7%     | 0%       | 0%      |      |
concept remained free from recurrences. Narozny et al. [12] have confirmed the role of HBO as a valuable, beneficial, and supporting classical treatment method in the treatment of bacterial-caused malignant otitis externa. Shupak et al. [13] treated two patients with extensive necrotizing otitis externa by hyperbaric oxygenation, followed by complete resolution, with no recurrence.

Heiden [14] confirmed in his study that multimodal therapy, with the inclusion of HBOT, enabled a reduction in mortality compared with earlier case reports without HBOT.

In the study of Saxby et al. [15], 70% of patients were considered cured of their disease, being disease free at follow-up. HBOT confers minimal morbidity, but its role in malignant external otitis (MOE) remains uncertain. The high mortality of MOE despite a maximal therapeutic intervention highlights the need for more effective treatment protocols.

**Conclusion**

The addition of HBOT to medical treatment is highly effective and has led to marked improvements in patients and the time required to achieve control of infection in these patients.

**Acknowledgements**

**Conflicts of interest**

None declared.

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