Treatment of SSNHL in the COVID-19 pandemic—time for changes

Leczenie SSNHL w dobie pandemii COVID-19—czas na zmiany

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ABSTRACT:

Our work aimed to review the literature about sudden sensorineural hearing loss (SSNHL) treatment and the approach to this problem during the COVID-19 pandemic. Current knowledge on SSNHL was sought and presented based on literature published in English-language journals from the Master Journal List. We searched for articles in the MEDLINE, PubMed, and Scopus databases. Sudden sensorineural hearing loss (SSNHL) is a relatively common pathology in otolaryngology. The American Academy of Otolaryngology-Head and Neck Surgery published guidelines for managing SSNHL, specifying systemic and intratympanic (IT) steroid therapy and hyperbaric oxygen therapy (HBOT) as the optional adjunctive treatment. However, due to the COVID-19 pandemic, the standard treatment of SSNHL needed to be verified to identify possible interference of virus infection with pharmacological and hyperbaric therapy. The general use of standard treatment of SSNHL with steroids and HBO according to internationally approved guidelines should ensure safe medical procedures due to epidemiological restrictions. Potential relations between COVID-19 and SSNHL, as well as concomitant use of anticoagulants, should be investigated.

KEYWORDS:

hyperbaric oxygen therapy, SARS-CoV-2, steroid therapy, sudden hearing loss

STRESZCZENIE:


SŁOWA KLUCZOWE:

nagła utrata słuchu, SARS-CoV-2, sterydoterapia, tlenoterapia hiperbaryczna

ABBREVIATIONS

ACE2 – angiotensin-converting enzyme 2
ARDS – acute respiratory distress syndrome
ATA – atmosphere absolute
COVID-19 – coronavirus disease-19
DNA – deoxyribonucleic acid
HBO – hyperbaric oxygen
HBOT – hyperbaric oxygen therapy
IT – intratympanic
RNA – ribonucleic acid

SARS-CoV-2 – severe acute respiratory syndrome coronavirus 2
SSNHL – sudden sensorineural hearing loss
WHO – World Health Organization

INTRODUCTION

SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) is a virus that causes severe acute respiratory syndrome — a disease entity called COVID-19 (coronavirus disease-19). The first cases of COVID-19 were reported in December 2019 in China. In January
2020, the disease spread rapidly throughout mainland China, with the Wuhan epicenter [1]. The SARS-CoV-2 virus has proven to be highly infectious, and it is transmitted from person to person by airborne droplets. Just two months after the outbreak in Wuhan, COVID-19 has reached pandemic proportions, announced on March 11, 2020, by the World Health Organization (WHO) [2].

Symptoms reported by people infected with SARS-CoV-2 (over 200 registered) are very diverse: from no symptoms to fever, dry cough, fatigue, muscle pain, breathing problems, loss of smell, and taste. However, in some patients, the central and peripheral nervous system’s symptoms dominate, including cerebrovascular disease, impaired consciousness, and visual disturbances [3]. In addition, there are reports about the possible high value of other symptoms (including hearing and balance) as signaling SARS-CoV-2 virus infection [4].

Sudden sensorineural hearing loss (SSNHL) is a hearing loss of at least 30 dB in at least three consecutive frequencies that develop within up to 3 days. It is a relatively common pathology in otolaryngology, with a worldwide incidence of 5–20 cases per 100,000 people per year. Until the first decade of the 21st century, the disease was treated in various ways, and pharmacotherapy often took the form of polypharmacy to therapeutic nihilism. In 2012, a team of experts from the American Academy of Otolaryngology-Head and Neck Surgery developed guidelines for managing SSNHL, specifying systemic and intratympanic (IT) steroid first-line therapy. Clinicians should not routinely prescribe antivirals, thrombolytics, vasodilators, vasoactive substances, or antioxidants to patients with SSNHL. If there is a possibility of application – steroid therapy can be supplemented with hyperbaric oxygen treatment. Clinicians may offer hyperbaric oxygen therapy within three months of diagnosis of SSNHL [5].

In 2019, a team of experts from the American Academy of Otolaryngology-Head and Neck Surgery in a similar composition made changes to these recommendations, including leaving hyperbaric oxygen therapy as an option but only when combined with steroid therapy for either initial treatment or “salvage therapy”. The timing of initial therapy is within two weeks of onset, and that of “salvage therapy” is within one month of sudden sensorineural hearing loss [6]. These recommendations have been widely accepted and introduced into clinical practice. Since 1997 at the Department of Otolaryngology Medical University of Gdańsk, patients with SSNHL have been treated with high doses of steroids and, at the same time, with hyperbaric oxygen [7–9].

The COVID-19 pandemic has changed our everyday lives and forces us to change our perspective, e.g., ways of treating many diseases. As the pathophysiology of SARS-CoV-2 infections becomes known, measures are being implemented to limit their negative effects. As a result, we learn more and more about this infection. As shown by the latest histological studies of Bussani et al., SARS-CoV-2 infection mainly affects the lungs, with little involvement of other organs (heart, brain, kidney, and liver). On the other hand, COVID-19 is a unique disease characterized by extensive lung thrombosis, long-term persistence of viral RNA in pneumocytes and endothelial cells, along with the presence of infected cell syncytia [10].

We know that SARS-CoV-2 penetrates the cell through the ACE2 receptor, and its damaging effect is based on supporting vascular endothelial inflammation leading to systemic coagulation disorders [11]. As a result, platelet function disorders, fibrin formation, and sepsis occur, followed by local hypoxemia and activation of cytokines [12]. These changes can also develop in various parts of the hearing organ (cochlea, cochlear nerve, central hearing center), eventually leading to hearing loss.

Data such as the proven influence of other viral infections (cytomegalovirus, rubella, measles) on hearing loss [13], finding DNA fragments of the herpes simplex virus in the vestibular nerve fibers of patients with vertigo [14], finding cells in the brain that can express the ACE2 receptor [15], showing an increase in ACE2 receptor expression in the epithelium of the middle ear, vascular stria tum and spiral ganglion of mice infected with SARS-CoV-2 [16], demonstrating the association of SARS-CoV-2 infection with loss of smell [17–19] and inflammation of the optic nerve [20] indicating the possibility of exerting a similarly damaging effect on other cranial nerves, including the VIII nerve, suggest a possible relationship between SSNHL and SARS-CoV-2 infection.

AIM

Our comments focus on two issues related to the management of SSNHL in the COVID-19 pandemic: the quality of pharmacotherapy and the method of conducting hyperbaric oxygen (HBO) therapy.

MATERIALS AND METHODS

We sought literature on SSNHL published in journals from the Master Journal List in English. In addition, we searched for articles in the MEDLINE, PubMed, and Scopus databases using the following keywords: “sudden hearing loss”, “sensorineural hearing loss”, “steroid therapy”, “hyperbaric oxygen therapy”, “COVID-19” and “SARS-CoV-2”. Inclusion criteria were: articles in English, meta-analysis, and literature review; individual case reports were valuable for us. Exclusion criteria were: articles in languages other than English; case reports, apart from those that seemed very interesting and valuable for us.

RESULTS

Steroids therapy

Systemic and intratympanic (IT) steroid therapy is SSNHL’s first-line therapy. The use of steroids in treating patients infected with SARS-CoV-2 has not always been widely accepted. The Lancet journals published in February and March 2020 claimed that corticosteroids should not be used to treat Covid-19 because they have no benefit in terms of mortality or viral RNA clearance delay, and cause serious side effects. The authors of these reports based their opinions on previous studies’ results indicating that steroids increase mortality among patients with influenza and other viruses [21, 22]. Later studies conducted among over 11,000 patients with COVID-19 showed that dexamethasone reduced deaths by a third in ventilated patients and a fifth in patients receiving oxygen alone.
Steroids did not affect patients with mild COVID-19 who were not treated with oxygen [23].

The distrust towards the effectiveness of steroids used in COVID-19 was dispelled by WHO experts’ recommendations published in September 2020. Corticosteroids were recognized by the WHO as potentially useful in treating COVID-19 and readily available, with low production costs. WHO experts formulated two recommendations to dispel any doubts, especially regarding the side effects related to high doses of these drugs. There are strong recommendations for systemic (intravenous or oral) corticosteroid treatment (e.g., 6 mg of dexamethasone orally or intravenously daily or 50 mg of hydrocortisone intravenously every 8 hours) for 7 to 10 days in patients with severe and critical COVID-19 and a conditional recommendation not to use corticosteroids in patients with less severe COVID-19 [24].

The intratympanic steroid administration is a valuable supplement to steroid therapy methods in SSNHL in patients infected with SARS-CoV-2. This steroid administration route’s advantages are minimal systemic absorption, reduced risk of systemic side effects, and higher concentrations of steroids in the cochlear lymph. In addition, intratympanic steroid administration can be performed as monotherapy in the first line or in conjunction with the administration of oral steroids or as “salvage therapy” if initial treatment has failed [25].

Hyperbaric oxygen therapy

Hyperbaric oxygen therapy (HBO) has been commonly used for many different clinical indications for a long time. In the treatment of SSNHL, it was first used in the late 1970s by Goto et al. [26] and Vincey [27]. The primary rationale was to increase perilymph oxygenation. Similar results were reported by Lamm et al., who showed that HBO therapy would increase the perilymph oxygen tension and improve microcirculation of the inner ear [28]. Regardless of the increase in the partial pressure of oxygen (pO2) in the inner ear, HBO improves hemorheology and contributes to improved microcirculation, lowers the hematocrit, and entire blood viscosity improves erythrocyte elasticity [29, 30]. It also induces cell metabolism in the inner ear, even if the blood supply is insufficient [28, 31, 32]. HBO may also influence the disease by exerting anti-inflammatory, immunomodulating, and lipid peroxidation-reducing effects [33, 34].

Clinical evidence for HBO in SSNHL is so strong that several international organizations have already recommended HBO for SSNHL, including the American Academy of Otolaryngology-Head and Neck Surgery [5, 6], the European Committee for Hyperbaric Medicine [35], as well as Undersea and Hyperbaric Medical Society [36].

For all clinical indications, including SSNHL, HBO is conducted in the hyperbaric chamber. The ambient pressure is increased up to 2.0–2.5 ATA. The patient breathes for 60 to 120 minutes 100% oxygen through fit masks or oxygen hoods to deliver high partial pressure to tissues via capillaries. In Europe and Australia, most treatments were conducted in the large walk-in multiple chambers under medical attendants’ direct supervision. In contrast, in the USA, most sessions are conducted in small monoplane chambers where patients are left alone inside [30, 35].

As compared to 2019, since the COVID-19 pandemic in March 2020, HBOT sessions have been modified to meet the epidemiological requirements for infection identification (temperature scanning, surveys), distancing (patients are seated in a chamber every second seat), and isolation (patients breathe with oxygen masks from the beginning of session without any air breaks) to avoid breathing using internal chamber atmosphere [9].

A look to the future

Fighting the COVID-19 pandemic comes with many challenges. Lung lesions caused by SARS-CoV-2 are a problem for doctors involved in HBO. The diffuse alveolar damage is a classic histopathological pattern related to ARDS, divided into two phases [37]. The exudative phase is mainly characterized by hyaline membrane formation from fibrin polymerization in the plasma liquid that leaked into the interstitial/alveolar space and alveolar-capillary barrier injury with red blood cell extravasation, and intense inflammatory cells infiltration into the intra-alveolar area corresponding to the first ten days of viral infection.

On the other hand, the second or proliferative phase is distinguished by an exacerbated fibroblast and myofibroblast proliferation. It can form acute fibrous organizing pneumonia or organizing pneumonia with subsequent extracellular matrix deposition, resulting in parenchymal remodeling and pulmonary fibrosis as well as pneumocytes squamous metaplasia and proliferation of multinucleated giant cells. Interestingly, the sequence of those pathophysiological changes is very similar, if not identical, to the one described in pulmonary oxygen toxicity [38]. Therefore, some concerns have been raised for the safety of HBO sessions in patients with severe pulmonary tissue involvement in COVID-19 [39].

Interestingly, HBO has already been suggested to treat SARS-CoV-2 infections, and some clinical studies have already been commenced [40]. However, precautions must be taken before starting HBO until the results come.

The second, unresolved problem, significant for doctors treating SSNHL in the pandemic era, is to supplement the currently used therapy with anticoagulants. This therapy method for patients infected with SARS-CoV-2 was recommended, among others, by the International Society on Thrombosis and Haemostasis and the American College of Chest Physicians [41, 42]. Essential elements of these considerations are the knowledge of the pathophysiology of SARS-CoV-2 and the existing experimental and clinical observations indicating the possibility of a relationship between SSNHL and SARS-CoV-2 infection.

CONCLUSIONS

According to internationally approved guidelines, the standard treatment of SSNHL with steroids and HBO should be maintained with ensuring safe medical procedures due to epidemiological restrictions. Potential relations between COVID-19 and SSNHL, as well as concomitant use of anticoagulants, should be investigated.