

## Case Series

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# The effect of hyperbaric oxygen therapy on post stroke aphasia

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### Abstract

**Background:** Ischemic stroke is the third cause of mortality in the world even though it decreased over the last decade, it remains a major etiology of a lifelong handicap. In fact, approximately one third of the patients will experience aphasia, a devastating impairment for the patient and his family. The language rehabilitation enable variant degrees of recovery and mild improvement occurs within the first six months but results still less efficient than desired.

**Objective:** The aim of the study is to assess the effects of hyperbaric oxygenotherapy in post stroke aphasia during the chronic phase.

**Methods:** We report a case series of 3 patients suffering from post-ischemic stroke Broca's aphasia, all hospitalized and taken in charge in the neurology department of the military hospital of Tunis, between 2018 and 2020. Each patient had around 30 to 40 sessions of Hyperbaric Oxygenotherapy (HBO). The evaluation of the language was performed with the Montreal Toulouse MT 86 using the Arabic version before and after HBO.

**Results and discussion:** Recovery after HBO was recorded in the three patients with the improvement of variant dimension of the language: Output of spontaneous speech besides oral and written expression. HBO through hyperoxia, induces several effects permitting the restoration of cerebral cell metabolism and blood brain barrier structure.

**Conclusion:** The presented results suggest that HBO could be an efficient and reliable therapy that helps recover from post stroke aphasia sequelae. Even though its mechanisms aren't well elucidated, further studies are needed to confirm its benefits.

**Keywords:** Stroke; Aphasia; Sequelae; Hyperbaric oxygenotherapy.

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### Introduction

Ischemic stroke continues to be an important public health issue. Even though the decreasing lethality over the last decade, it remains a devastating disease through its handicap affecting motricity and language.

It has been stated that, "one never recovers from aphasia; one recovers with aphasia [1]", emphasizing the long term poor prognosis of recovering from post stroke language disorders.

The neurologists are striving to validate pharmacological and non pharmacological therapies that would improve the outcome of these patients and minimize sequelae.

Since ischemic stroke physiopathology is characterized by abrupt blood vessel occlusion [2], the available therapies focus on restoring the brain blood flow. Hyperbaric Oxygenotherapy (HBOT) has emerged more than a decade ago [3], as a non-invasive therapy to improve brain tissue oxygenation and thus

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reduce the consequences of hypoxemia and facilitate recovery.

To date, only the European consensus conference on hyperbaric medicine Recommend its use in chronic phase stroke but with weak evidence of beneficial actions. The U.S Food and Drug Administration (FDA) only approved this therapy in 13 disorders that do not include stroke sequelae [4,5].

However, according to different clinical trials on stroke, HBOT results are promising.

### Methods

We report a case series of 3 patients suffering from post-ischemic stroke Broca's aphasia, all hospitalized and taken in charge in the neurology department of the military hospital of Tunis, between 2018 and 2020. Each patient had around 30 to 40 sessions of hyperbaric oxygenotherapy. The evaluation of the language was performed with the Montreal Toulouse MT 86 using the Arabic version before and after HBOT.

The Montreal Toulouse MT 86, is a tool that allows language evaluation by the detection of linguistic impairments in it's different dimension.

Patients were informed of the study procedure and its potential outcomes before giving their consent.

The follow-up was made regularly to detect any clinical modifications or possible adverse events.

### Results

**Case 1:** A forty -year-old right handed woman was brought to our department of neurology, in November 2019, because of acute onset of slurred speech and right side heaviness. She had a personal history of thyroid nodule, hypertension since August 2019, without significant family history.

The clinical examination revealed Broca's aphasia and right hemiparesis. After performing a cranial Computed Tomography (CT) scan, the diagnosis of ischemic stroke in the territory of the left superficial middle cerebral artery was established. The investigations concluded to double heterozygous mutation of factor II and Methylene Tetrahydrofolate Reductase (MTHFR). The OHB was initiated sixteen months after the onset of stroke with secondary improvement.

**Case 2:** A forty three-year-old right handed woman with no significant family nor personal history, abruptly developed in 2019, heaviness of right side of the body and difficulty in speaking. The diagnosis of ischemic stroke in the territory of the left superficial middle cerebral artery was made based on the clinical findings and CT scan of the brain. The stroke was secondary to celiac disease associated with antiphospholipid syndrome and vitamin B12 deficiency. The OHB was initiated fifteen months after the onset of stroke with secondary improvement.

**Case 3:** A thirty eight -year-old right handed man, without any significant history was admitted to our neurological department for an ischemic stroke in the territory of the left middle and anterior cerebral arteries. The stroke was due to a post traumatic dissection of the left internal carotid artery. The OHB was initiated twenty six months after the onset of stroke with secondary improvement.

### Discussion

Hyperbaric oxygenotherapy was initiated in the post-stroke late chronic stages. All the subjects received around 30 to 40 sessions and had regular evaluation of the language using the objective test, MT 86. The added value of these findings is related to the recorded benefit during chronic stage indeed confirmed in variant studies [6,7].

It was believed, years ago, the earlier the treatment was set, the better the outcome will be. But, there is no definitive proof for the efficacy of HBO treatment in acute ischemic stroke and instead its early use is correlated to a higher risk of side effects [5].

Even though our patients were treated after a median of 19 months, improvement of language disorder was the rule regardless of variation of its efficacy among them (Table 1).

The lack of significant differences regarding HBO favorable effects to stroke's etiology could be explained by the final common pathophysiological path of injury which an ischemic lesion.

Only few clinical trials tested HBOT, as an adjuvant treatment, in chronic stroke sequelae.

In fact, in vascular dementia, the addition of HBOT to conventional therapy was associated with a better income objectified through the following screening tools "Mini Mental State examination" (MMSE) and Activities of Daily Life (ADL) [8].

For aphasia, patients were treated after 2 to 9 years after brain ischemic injury with an average of 20 to 30 sessions [9,10] and relative improvement was the major constatation.

Until the present day, there is no specific time window for HBOT. A better understanding of its mechanisms will allow the identification of the adequate delay for therapy onset.

Effects of HBO on the brain after ischemic lesions vary from neuroprotection effects to neuroregeneration empowerment. Several specific effects of hyperoxia are described. The primordial mechanism is to improve the oxygen delivery in the injured area followed by the major responses that would target neurons and oligodendrocytes.

Neuroprotection is likely mediated by anti-oxidative and anti-inflammatory impact, both promoting neurobehavioral functional recovery. This action is made through decreased lipid peroxidation, inhibition of leukocyte activation and regulation of cell function and metabolites. Mitigating the inflammatory response reduces apoptosis and enable to preserve more brain tissue [11,12].

Once all these factors combined, they allow the restoration of the functional blood-brain barrier [13] and thus enhance neuronal viability.

Along with the structural changes demonstrated with brain microstructure imaging [14], HBO can induce neuroregeneration. In fact, microangiogenesis and hyperoxia serve as an infrastructure for the neuroplasticity process. On the cellular scale, the key stakeholders are mitochondria and growth factors [15]. Mitochondria transfer from astrocytes to neurons when being exposed to hypoxic condition or to an inflammatory insult both

found after stroke [16]. This redistribution allows neurons to be better equipped to regulate their metabolism and delay apoptosis. This transfer was more robustly recognized when treated with HBO. In vitro, growth factors levels were boosted while injured cells exposed to HBO [17].

Such cell-to-cell exchange ability for the benefit of neurons support the theory of neuroregeneration.

While high oxygen levels are maintained, a paradoxical event of oxidative stress may occur and worsen the clinical evolution. It is thought to be secondary to an overproduction of oxygen radicals and inefficiency of its detoxification system [16].

Antioxidants products could replenish in the brain tissue and harm its function.

Back to our cases, aphasia known as one the most long lasting post stroke handicap was sensible to HBO. The initial size of the brain lesions did not interfere with the language prognosis. It's disputable whether the observed amelioration resulted from the natural course of the disease or accelerated by HBO. Considering the discussed mechanisms above, the improvement is believed to be due to neuroprotection and neuroregeneration mechanisms that made its efficacy notable even in the chronic stage of a brain lesions.

### Conclusion

The application of HBO to promote post stroke language recovery is still controversial and its supposable mechanisms are not fully understood. Nonetheless, neuroprotection remain as an elusive concept and more studies are needed for better explanation and though a better care.

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