with a TSH value greater than 2.0 mIU/liter and/or a high titer of thyroid antibodies [2]. In view of the negative maternal and fetal outcomes of hypothyroidism, carefully monitored thyroid hormone treatment of TPO antibody positive pregnant patients might be a prudent measure.

Subclinical hypothyroidism is defined as increased TSH with normal concentrations of FT4. Women with subclinical hypothyroidism are more likely than euthyroid women to have TPO antibody positivity. Etiology is similar to overt hypothyroidism. Since multiple studies have shown that subclinical hypothyroidism is associated with an adverse outcome for the mother and offspring, most guidelines recommend thyroxine replacement in women with subclinical hypothyroidism. However, while thyroxine treatment has been shown to improve obstetrical outcome, it has not been proven to modify long-term neurological development in the offspring [3].

Isolated maternal hypothyroxinemia is defined as a low FT4 and normal TSH, which can be found in approximately 1 to 2 % of pregnancies. In the Faster study, among the women with hypothyroxinemia and normal TSH, there was an increased odds ratio for preterm labor (1.62, 95 % CI 1.00–2.62), macrosomia (1.97, 95 % CI 1.37–2.83), and gestational diabetes (1.70, 95 % CI 1.02–2.84), but these results were not consistent. A study by Casey et al. concluded that isolated maternal hypothyroxinemia in the first half of pregnancy has no adverse effects on pregnancy outcome [4].

In some study infants and toddlers whose mothers had reduced serum free T4 concentrations (with normal TSH) during gestation (12 to 20 weeks) had lower mean intelligence, psychomotor, or behavioral scores compared with children born to women with normal thyroid function during gestation. However, till date, no study has shown benefit from levothyroxine treatment of isolated hypothyroxinemia during pregnancy, on pregnancy outcome or subsequent infant development.

Conclusion

The impact of maternal hypothyroidism on the fetus depends on the severity of the condition. A. Uncontrolled hypothyroidism: miscarriage, anaemia, intrauterine fetal demise and stillbirth preterm delivery, low birth weight, preeclampsia, developmental anomalies including reduced IQ. Maternal and congenital hypothyroidism resulting from severe iodine deficiency: profound neurologic impairment & mental retardation. If the condition is left untreated. Congenital cretinism: growth failure, mental retardation, and other neuropsychologic deficits including deaf-mutism. If cretinism is identified & treated in the first 3 months of life: near-normal growth and intelligence can be expected. For this reason, newborn screening for congenital hypothyroidism. B. Asymptomatic overt hypothyroidism. Women who had previously been diagnosed with hypothyroidism, (abnormal TSH and FT4 levels), but who do not have symptoms. Impaired psychomotor development at 10 months in infants born to mothers who had low T4 during the first 12 weeks of gestation. Low IQ scores in the offspring at 7 to 9 years of age was correlated with elevated maternal TSH levels at less than 17 weeks’ gestation. An inverse correlation between a woman’s TSH level during pregnancy and the IQ of her offspring confirmed that maternal hypothyroxinemia is a risk for neurodevelopmental abnormalities that can be identified as early as 3 weeks of age.

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HYPERBARIC OXYGEN THERAPY IN ISCHEMIC STROKE

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Introduction

Stroke is one of the leading causes of death in the world and the 5th cause of death in the United States. According to the American Stroke Association, 87 % of stroke cases are ischemic
stroke. When ischemic stroke occurs, there are blockage of blood supply and stoppage or reduction of oxygen delivery to the particular area of the brain and subsequent cell death. Hyperbaric oxygen therapy has been frequently applied and investigated in stroke since 1960s. It was suggested that hyperbaric oxygen therapy (HBOT) may reduce the volume of brain that will die by increasing available oxygen, and it may further improve outcomes by reducing brain swelling. In August 2013, the US Food and Drug Administration declared artery occlusion as one of the 13 specific indications for HBOT. This provides opportunities for the further development of hyperbaric medicine.

**Aim**
To review clinical trials and researches done with hyperbaric oxygen therapy, and determine its therapeutic effects in stroke.

**Materials and methods**
Reviews, analysis and data processing of scientific literature on HBOT in stroke.

**Results**
Most innovative researches started with experimental studies. In an experimental study by Li Sun et. al., mice were subjected to filament-induced middle cerebral artery occlusion for 2 hours. Twenty-five minutes after the induction, they breathed 100 % oxygen at 3 absolute atmospheres (ATA) for 95 minutes. Hypoxic regions were mapped on tissue sections after preischemic infusion of the in vivo hypoxia marker. Hypoxia-inducible factor-1 protein was measured after 2-hour of middle cerebral artery occlusion, using immunofluorescence and immunoblotting. The results showed that HBOT significantly reduced the area of hypoxia in focal cerebral ischemia.

A pilot study with 46 participants was also done in Taiwan between February 2007 and April 2010 by Cheng-Hsin Chenet al. Out of the 46, 16 underwent hyperbaric oxygen therapy, while 30 belonged to the control group. All the participants were 48 hours post ischemic stroke and had ‘mild’ stroke according to the National Institute of Health Stroke Scale (NIHSS). The HBOT group was given HBOT with 2 ATA. Treatments lasted 60 minutes for 10 sessions, once a day, for two weeks. The results of the treatment were based on NIHSS score which was evaluated at Day — 10 of the HBOT and one month after the therapy. The results in the control group showed the average NIHSS score after 10 days decreased, but there was no significant decrease in the score after one month. Whereas, in the HBOT group, NIHSS score decrease after one month was more significant than the control group. This lead to the thought of late efficiency of HBOT and some of the supposed reasons were that low pressure of HBOT was used (2.0 ATA) to avoid possible oxidative stress. Generally, NIHSS score improved more in the HBOT group than in the control group.

A review by Bennett et al., which was first published in 2005, updated in 2014 and later in 2015, reported about an extensive research carried out of 11 randomized clinical trials having 705 participants. The review included all randomized controlled trials that compared the effect of adjunctive HBOT with either no treatment or sham and in which death or functional scales were assessed as outcomes. Significant differences weren’t revealed in the case fatality rate at six months in those receiving HBOT compared with the control, but 4 out of 19 scale measures of disability and functional performance indicated improvement following HBOT. These improvements were not evident in earlier assessments in the relevant trials. Possibility of co-administration of HBOT and Tissue Plasminogen Activator (TPA) was also considered. A review about it was done in Chongqing Medical University, Chongqing, China. HBOT and TPA were used for myocardial infarction, so it was also thought to use it for stroke. In 1999, a research team initiated r-TPA and HBOT simultaneously 2 hours after ischemia onset in rat models. The combination greatly improved the neurological deficits within 24 hours. It was suggested that HBOT has maximum efficacy when given within the first 3 hours post stroke. It was suggested that HBOT might extend time window and increase the efficacy of TPA thrombolysis after acute ischemic stroke.

Another review by Zheng Ding et al. in 2014 revealed some possible effects of HBOT. One of its effects considered was on oxidative stress. In animal models, HBOT at 2.5 ATA, one hour each day for 2 days reduced the ischemia-reperfusion injury of the middle cerebral artery occlusion (MCAO) via increasing the expression of antioxidant enzymes. However, longer duration of HBOT may upregulate the expression of oxidase in permanent ischemic stroke models. Inhibition of Apoptosis and HBOT’s neuroprotective effect was also suggested. This was said because Li et
al. showed that HBOT preconditioning can reduce cytochrome C in the hippocampus and ischemic penumbra analyzed by Western blot in an MCAO model.

Simultaneously, several studies have shown that HBO therapy inhibits the expression of caspase-3 in the cortex and hippocampus of an ischemic model. Several other researchers suggest that HBO significantly reduces the expression of hypoxia-inducible factor 1-alpha (A transcription factor which promotes the neovascularization by stimulating the expression of vascular endothelial growth factor) and its downstream effector proteins and suppresses apoptosis. Other effects include alleviation of inflammation, improvement of brain metabolism and blood flow.

**Conclusion**

According to the researches reviewed, hyperbaric oxygen therapy continues to show its therapeutic effect in acute ischemic stroke and therefore, it can be recommended for use in stroke patients alongside other stroke therapy.

**LITERATURE**