

Is effective the hyperbaric oxygen therapy for the treatment of ischemic lower extremity ulcers?—new insights from a multicenter study

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Provenance: This is a Guest Editorial commissioned by Section Editor Qi-Nan Wu, MD, PhD (Endocrine Department, the First Affiliated Hospital of the Third Military Medical University, Chongqing, China).

Comment on: Iribarne A, Schmoker JD, Malenka DJ, *et al.* Does Use of Bilateral Internal Mammary Artery Grafting Reduce Long-Term Risk of Repeat Coronary Revascularization? A Multicenter Analysis. *Circulation* 2017;136:1676-85.

Submitted Mar 21, 2018. Accepted for publication Apr 16, 2018.

doi: 10.21037/atm.2018.04.37

View this article at: <http://dx.doi.org/10.21037/atm.2018.04.37>

Diabetes is a non-stop growing epidemic, that instead of getting better is getting worse, prevalence of diabetes has increased in the developed and developing countries during the last four decades. According to International Diabetes Federation, nowadays, 425 million people worldwide, or 8.8% of adults 20–79 years, are estimated to have diabetes.

The number of people with diabetes increases to 451 million if the age is expanded to 18–99 years. If these trends continue, by 2045, 693 million people, will have Diabetes. It has been estimated that globally 212.4 million people are unaware of their disease. This grim scenario has led 4.0 million deaths from diabetes in 2017, all of them aged between 20 and 79 years (1).

Although diabetes by itself is a huge health problem, this metabolic disease does not come alone, when glycemic levels are not well managed, all types of diabetes can lead to complications, resulting in frequent hospitalizations and early death. People with diabetes have an increased risk of developing a number of serious life-threatening health problems increasing medical care costs such as vascular damage and peripheral neuropathy. Peripheral neuropathy is the most common form of diabetic neuropathy which affects the distal nerves of the limbs, particularly those of the feet (1,2), nevertheless, peripheral arterial disease, often caused by accelerated atherosclerosis, is present in up to 50% of patients with diabetic foot ulcers (DFU). This arterial disease is an important risk factor for impaired wound healing and lower extremity amputation,

however, most of the DFUs have both aggravating factors: neuropathy and ischemia.

There is a whole guidance for the treatment of DFU (2), which includes relief of pressure, metabolic control, treatment of infection, local wound care, patient's education and restoration of skin perfusion to promote oxygenation. Within this last point is included revascularization and hyperbaric oxygen therapy (HBOT), which is a way of systemic supplemental oxygen administration in which patients breathe 100% oxygen at a pressure greater than one atmosphere.

The effects and exact mechanisms of the HBOT are still unclear, several experimental and clinical studies have investigated the effects of these therapies on wound healing, nonetheless, the results are ambiguous. Some of these studies reported positive results, whereas others reported none, or negative results (3,4).

The HBOT is widely used worldwide since several decades ago, thus it was important to provide clinical evidence to assess its clinical usefulness. In the study presented by Santema *et al.*, they sought to determine whether additional HBOT would benefit patients with diabetes and ischemic leg ulcers (5). Previous studies have shown a promissory use of HBOT, nonetheless, the conclusion of these trials is of limited value in making clinical recommendations because of short-follow periods, methodological weakness or small number of individuals involved in the study (6-8). The present trial was a well-conducted and robust multi-centric study (25

hospitals), all patients data were well collected and analyzed for a period of 12 months. Patients (120 individuals) with an ischemic wound were randomized divided into two groups: all of them with standard care and with or without HBOT. For those whom were included into de HBOT group, therapy was scheduled for 5 days per week until a maximum 40 sessions or until complete wound healing was achieved. Afterwards, a very comprehensive analysis was carried out to compare several critical points among groups such as complete wound healing at the end of follow up, median time to complete wound healing, amputation index, additional revascularization, limb salvage index, amputation-free survival etcetera. Their results indicate that among individuals with diabetes with ischemic DFU, HBOT do not confer statistically benefits in terms of limb salvage or wound healing. They also observed that most patients may not be able to undergo a complete HBOT regimen due to their unfavorable overall medical condition. This important point must be taken into account in clinics, since most of the patients have more than a decade of diabetes progression which is an important factor to impair health, certainly, it has been widely documented that HBOT has several side effects such as pulmonary edema, blood pressure effects, retrorenal fibroplasia, pulmonary oxygen toxicity, pulmonary barotrauma, central nervous system oxygen toxicity and even dental barotrauma (9), all of them, instead of being a benefit for patients could impair their health. Indeed, in the present study even though patients were deeply evaluated by specialized physician previous to HBOT treatment, there were adverse events, this highlights the imperious need for a deeply evaluation of patients prior, during and after HBOT, which not always is performed properly in the hospitals worldwide.

Although in Netherlands the HBOT is variable used and used as an alternative to therapy, in several countries HBOT is taken as an important option for the treatment of DFUs, the present study shows that HBOT does not improve clinical outcomes of DFU, this is an important knowledge to evaluate its use, since besides its side effects increases the cost of treatment substantially. In high income countries, the annual ulceration among people with diabetes is about 2% whereas in low and middle-income countries DFUs reach up to 30% in diabetic patients, therefore, similar multi-centric studies must be performed in such countries to evaluate cost-benefit, however is likely that result are going to be similar.

In conclusion, new evidences are showing that HBOT do not improves the therapy in DFUs, instead, new efforts must be directed towards new research to find effective therapies for diabetic wound healing.

Acknowledgements

None.

Footnote

Conflicts of Interest: The author has no conflicts of interest to declare

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Cite this article as: Rivas-Santiago B. Is effective the hyperbaric oxygen therapy for the treatment of ischemic lower extremity ulcers?—new insights from a multicenter study. *Ann Transl Med* 2018;6(11):226. doi: 10.21037/atm.2018.04.37