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A BRIEF REPORT ON

THE IMPACT OF HYPERBARIC OXYGEN THERAPY

on Skin Aging Pathophysiology

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BACKGROUND

Intrinsic and extrinsic aging are two different types of skin aging. Extrinsic aging, also known as photoaging, is specific to the skin and is linked to the effects of ultraviolet (UV) radiation (primarily from the sun) and other environmental agents that the skin is exposed to. Intrinsic aging, also known as chronological aging, includes the pathophysiological processes common across most organs with us humans.

Intrinsic aging is related to well-known cellular and genetic aging hallmarks, including cell senescence, telomere shortening, genomic instability, inflammation, and mitochondrial dysfunction. Another important factor is changes in extracellular matrix molecules such as collagen, providing strength for elastin and ensuring proper skin elasticity. The most remarkable historical feature occurs within the basal layer where there's a rampant proliferation of keratinocytes, fibroblasts, and melanin pigment-producing cells, reducing the epidermis' thickness and resulting in decreased contact surface area between the dermal and epidermis layers.

The width of the papillary dermis increases as you have fewer collagen fibers, elastic fibers, mast cells, and fibroblasts. There is also a significant decrease in skin blood supply of the reduced number of dermal blood vessels. This happens because the endothelial cells don't work well, resulting in a reduced ability to form new blood vessels, abnormal expression of molecules that hold things together, and problems with getting the blood vessels to relax. This leads to clinical signs like dermal atrophy and loss of elasticity.

Extrinsic aging is related to the long-term effects of exposure to ultraviolent radiation and other environmental agents. Due to failed corneocyte desmosome degradation and an impaired epiderma keratinocyte differentiation process, the UV-radiated epidermis thickens compared to the thinner epidermis in intrinsically aged skin. Photoaged skin showed decreased expression of type VII collagen in keratinocytes as well as an aggregation of unusual elastic tissue deep in the dermis, a pathologic phenotype named solar elastosis.

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INTRODUCTION

Hyperbaric oxygen therapy (HBOT) uses 100% oxygen in a pressure chamber with more than one absolute atmosphere. This boosts the amount of oxygen that is dissolved in the body's tissues. When people do this therapy often, it has been shown to cause effects called "hyperoxic-hypoxic paradox," which is the induction of physiological effects that normally occur during hypoxia in a hyperoxic environment by the relative hypoxia exposure that normally happens when there is not enough oxygen. These include restoring mitochondrial function and increasing biogenesis, simulating stem cell proliferation, migration, differentiation, and angiogenesis. Recently, clinical trials have also shown that HBOT can target aging hallmarks at the cellular level, including telomere shortening and senescent cell clearance.

Subjects:

As per the paper published on NCBI.

The study was conducted over 3-4 years, i.e., between 2016-2020, in the Shamir (Assaf-Harofeh) Medical Center, Israel. The study included patients who were adults, living independently, in good functional and cognitive status without pathological cognitive decline, aged 64 and older. The following were the exclusion criteria: if there was any previous treatment with HBOT for any reason during the last three months, any malignancy history in the previous year, any decline in pathological cognitive aspects, severe chronic renal failure (GFR <30), uncontrolled diabetes mellitus (HbA1C>8, fasting glucose>200), taking immunosuppressants, MRI contraindications (including BMI>35), active smoking, or pulmonary diseases.

Study Design:

The study was approved by the Institutional Review Board at the Shamir Medical Center in Israel. The subjects signed a pre-informed consent before undergoing a baseline evaluation. The subjects were then assigned to a three-month control period that was followed by three months of Hyperbaric oxygen therapy sessions. Measurement points were evaluated at baseline, after three

months of no intervention (control), and 1-2 weeks following the last HBOT session.

This study cohort, which is part of a larger cohort of the average aging population studied at the Shamir Medical Center, Israel (NCT02790541), includes only patients who agreed to have skin biopsies. The original design and sample size were meant to evaluate the primary endpoint related to cognitive function. Skin biopsies were a secondary endpoint and optional due to their invasiveness.

Method:

The study was performed as a clinical trial. After signing informed consent and undergoing baseline evaluations, the subjects were assigned to three months without any intervention. They then had three months of daily HBOT sessions. Skin biopsies were taken at baseline, after three months of no intervention (control), and 1-2 weeks following the last HBOT session. Trichrome, Orecin, lipofuscin, and CD31 staining were used to evaluate

- Collagen fibers staining
- Epidermis layer thickness
- Papillary layer thickness
- Papillary layer collagen fibers thickness
- Reticular layer collagen fibers thickness
- Elastic fibers staining
- Reticular layer elastic fibers thickness and length
- The area occupied by elastin in the reticular dermis
- Tissue senescent cells count
- Tissue blood vessels count

Result:

From the cohort of 70 participants in the usual aging population study, thirteen male patients (age 68.07±2.5y) consented to repeat skin biopsies.

Following HBOT, there was a drastic boost in:

- collagen density (p<0.001, effect size(es)=1.10)
- elastic fiber length (p<0.0001, es=2.71)

And:

- number of blood vessels (p=0.02, es=1.00)

There was a considerable decrease in fiber fragmentation (p=0.012) and in tissue senescent cells (p=0.03, es=0.84) post-HBOT. There weren't any notable changes in elastic fiber density or thickness.

To study the results in detail, you can visit the link: NCBI.

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CONCLUSION

Skin aging is a natural process that starts at birth and can be accelerated by intrinsic and extrinsic factors. We focused on the former type, which includes increased levels of senescent cells (fibroblasts) as well as epidermal thinning; dermal tissue loss with increases in papillary layer thickness, among other things—all happening at your skin's surface level! This accessible method allowed us to better understand how HBOT affects these tissues, specifically deep within our bodies, where it'll affect you long after treatment ends. Angiogenesis and the elimination of senescent cells are two methods that have been established, and their combined effects could improve the quality of recovery from wrinkles and other age-related changes.

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