Hyaluronic acid in skin aging

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SKIN AGING

Understanding the aging process is crucial to attaining optimal results with facial rejuvenation procedures. A variety of theories has been proposed to explain aging phenomena in general, and some of them may be applicable to innate cutaneous aging as well (1) .According to one of the most popular aging theory, free radicals (FR) are the cause of aging.There are two sources of FR, endogenous and exogenous. Endogenously, the two main sources of FR are mitochondria and detoxification reactions mediated by cytochrome p450. Other sources of FR are immune reactions and alcohol metabolism. In order to minimize the FR deleterious effect, we have to avoid the exogenous sources of FR, but also we have to control the endogenous sources (Figure 1)

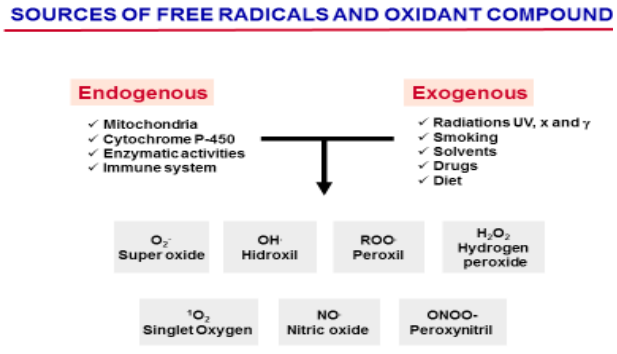

Figure 1. Main sources of Free Radicals.

Most changes in aging skin result from a combination of endogenous (e.g., gene mutations, cellular metabolism, hormone changes, etc) and exogenous (e.g., chemicals, toxins, pollutants, UV, ionizing radiation, smoking, excessive alcohol consumption, poor nutrition, etc) factors. Among the external factors, sun exposure is considered to be the most significantly deleterious to the skin. Indeed, 80% of facial ageing is believed to be due to chronic sun exposure (2).

Exposed areas of the skin, typically the face, chest and extensor surfaces of the arms, display the majority of extrinsically aged skin, which results from the cumulative effects of life-long ultraviolet radiation exposure. Rhytides, pigmented lesions and depigmented lesions comprise the clinical presentation of photo-aged skin. Losses in tone and elasticity are also observed in photo-aged skin, along with increased skin fragility, areas of purpura due to blood vessel weakness, and benign lesions (egacrochordons, keratoses, and telangiectases)

Skin that ages intrinsically is smooth with some exaggerated expression lines. Histologically, such skin manifests epidermal and dermal atrophy, flattening of the epidermal rete ridges, as well as reduced numbers of fibroblasts and mast cells. In addition, increases are seen in the number of collagen fibrils as well as the ratio of collagen III to collagen I.

The changes undergone by skin as it ages occur throughout the epidermis, dermis and subcutaneous tissue and can manifest in discrete and broad alterations in skin.

GLYCOSAMINOGLYCANS

Glycosaminoglycans (GAGs), along with collagen and elastin, are the primary constituents of dermal skin and are responsible for conferring the outward appearance of the skin (3). Changes in these three primary structural components of the dermis have been the subjects of the majority of anti-ageing research pertaining to the skin.

There are numerous members in the GAG family, including hyaluronic acid (HA), dermatan sulphate (both of which are two of the most prevalent GAGs) and chondroitin sulphate. These compounds render normal skin plump, soft and hydrated, and are believed to assist in maintaining proper salt and water balance. HA provides structure and holds moisture within the dermis (4). It not only improves wrinkles but also restores volume. In addition, HA interacts with proteins and functions in growth, development, inflammation, immune responses and regeneration of damaged tissues (5). HA exhibits no species and no tissue specificity. HA is an essential component of the extracellular matrix of all animal tissues and is an abundant component of this matrix. The average human body contains 15 g of HA, 50% of which is located in the skin (primarily dermal) (6, 7). In its natural form HA is highly soluble, not immunogenic and has a rapid turnover through enzymatic and free radical degradation with a half-life of 24 h in vivo. HA is synthesized by membrane-bound synthases (HASs) at the inner surface of the plasma membrane of fibroblasts and the chains are extruded through pore-like structures into the extracellular space by In vivo, HA can be rather rapidly degraded and is ultimately metabolized in the liver .

Several studies suggest that GAGs, particularly HA, have been found to be reduced in amount in photoaged skin. This is the rational for using HA as a temporary dermal filling agent in soft tissue augmentation procedures (8, 9).

HA DERMAL FILLERS

Ideally, an injectable implant should be easy to inject, produce reproducible results, and produce an acceptably long period of volume retention (10). Also, the filler would be painless on injection and nonallergenic, noncarcinogenic, nonteratogenic, and not to migrate once injected, nor produce local adverse events.

Although the HA fillers appear to be similar, their physical characteristics and methods of manufacture are not the same (8, 11). The main differentiators for HA fillers are: source of HA; concentration of HA in each syringe being utilized; the particulate size of the HA; whether the HA is cross-linked; the type of cross-linking agent used in the HA; and whether there is an anesthetic in the HA syringe. These differences affect injection technique, usage, and the quality of the outcome. Each current approved filler exhibit differences in these basic characteristics. All physicians must understand the physical and biological properties of the intended filler before its clinical use. Of the available products, nonanimal stabilized hyaluronic acid (NASHA), derived from bacterial fermentation in cultures of a Streptococcus species, is one of the products least likely to produce allergic reactions (12).

The concentration of HA fillers is also important. Those HA fillers with higher HA concentrations displace more tissue and are felt to equate to longer duration of effect. Particle size is important: Larger gel particles are more difficult to push through a small-bore needle. A filler with a high average particle size will be more difficult to extrude. Larger particles can last longer. Larger particles can create a firmer result

so are usually reserved for deeper dermal use. Smaller particles are reserved for more superficial indications, and may dissipate earlier.

Another important feature of HA fillers is their elastic modulus, expressed as G'. This is essentially a measure of the gel's ability to withstand changes from external mechanical forces. Coupled with the measure of cohesivity, which reflects resistance to mechanical breakdown, G' can be an indicator of a gel's lifting effect. Lift capability increases as G' and cohesivity increase.

As can be seen, there are very good aesthetic treatments available for aged skin based on fillers. However, prevention strategies are also needed to avoid both a premature aging and potentiate these aesthetic interventions based on fillers. In order to promote the integral health of the skin this entails avoiding exposure to the sun, using sunscreen when sun avoidance is impossible, avoiding cigarette smoke and pollution, eating a diet high in fruits and vegetables, and taking oral anti-oxidant supplements or topical anti-oxidant formulations. All these intervention strategies are basic in anti-aging skin care.

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