BRIEF COMMUNICATION

Hyaluronic Acid as a Treatment Option for Pressure Ulcers

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Abstract: Introduction. Health care professionals are constantly seeking novel approaches to treat pressure ulcers because of the impact they have on patient quality of life and health, as well as the costs associated with treating them. Methods. A review of the literature from 2002-2012 was conducted on the clinical usefulness of hyaluronic acid in tissue regeneration. Reports suggest that the therapeutic use of hyaluronic acid favors tissue regeneration by modulating the hydration and osmotic balance. Results. Different studies show that hyaluronan and derived-hyaluronic acid products are safe and free of adverse effects. Furthermore, a few studies examine the hyaluronic acids repercussions in pressure ulcer treatment. Conclusion. Reports suggest that this molecule could be successfully used to treat pressure ulcers in association with conventional measures.

Key words: pressure ulcers, hyaluronic acid, wound healing

Pressure ulcers (PUs) are skin lesions that may involve the epidermis and deeper layers of the skin, sometimes even causing damage to muscle or bone. Triggering factors include an increase in capillary pressure at skin level as a consequence of the action of 2 opposing forces, as in the case of pressure on a bone protuberance. Pressure ulcers compromise the health and quality of life of patients and entail high economic costs. Patients with a single PU are 3.5 to 5 times more likely to stay in the hospital than patients without an ulcer, and the development of novel approaches is of great interest to health care professionals, especially the nurses, who often treat them.

Pressure ulcers are currently treated with a moist environment, which high-level evidence has proved effective in reducing healing time. Hyaluronic acid is one of a group of molecules proposed to participate in the pathophysiological mechanisms underlying wound healing. More recent studies have shown that treatment with hyaluronic acids and their derivatives have an important role in the regeneration of various tissues, such as periodontal, bone, adipose, or cartilage regeneration.

The objective of this study was to review published reports on the clinical usefulness of hyaluronic acid in tissue regeneration and PU healing.
Material and Methods

Literature searches were carried out using the dialog interface in the following databases: PubMed and CINAHIL. Databases were searched from 2002 through 2012 for human studies. The following key words were covered in the search strategy: “hyaluronic acid,” “pressure ulcers,” “pressure sores,” “hyaluronic acid and pressure ulcers,” and “hyaluronic acid and pressure sores.” Titles and abstracts identified by the literature searches were read and reviewed. Those not appearing to meet key words were excluded and the others were reviewed in full.

Results

Hyaluronic acid is a natural biopolymer with a highly preserved molecular structure among mammal species. It was first reported in 1934 and was subsequently synthesized in the laboratory.8 It is a natural polymer of disaccharides, which are composed of alternating D-glucuronic acid and D-N-acetylglucosamine, linked together via alternating β-1,4 and β-1,3 glycosidic bonds. One of the components of the extracellular matrix, hyaluronic acid is present in skin, cartilage, bone, and brain, among other tissues. It has proved valuable in neurosurgery and dermatology because hyaluronic acid and degradation products can modulate wound healing.8 Numerous studies have demonstrated the usefulness of hyaluronic acid in skin lesions and cartilage defects, in glial cell culture, and in the regeneration/increase of sperm motility.9 Over the past few years, there has been a considerable increase in the use of hyaluronic acid in aesthetic plastic surgery.9 Physiologically, the key characteristic of this molecule is its high hydroscopicity, which serves to regulate tissue hydration and osmotic balance. It is also water soluble, enabling the formation of an easily handled and applied gel.10 In recent years, hyaluronic acid and its sodium salt have been applied for multiple clinical purposes.11,12

Discussion

Usefulness of hyaluronic acid and its sodium salt in tissue regeneration. The usefulness of hyaluronic acid and its derivatives in tissue regeneration, tissue engineering, epidermal diseases, ophthalmic surgery, and plastic surgery is well documented.9,11-14 Although the action mechanism of this molecule in tissue regeneration has not been fully elucidated, effects have generally been attributed to its lubricating, hydroscopic, and homeostatic properties.15 It can also interact with a number of receptors, activating a cascade of signals that influence gene migration, proliferation, and expression at the extracellular matrix level.15

Hyaluronic acid and its sodium salts are used for wound healing. One explanation for its positive effect is that collagen deposited by fibroblasts is a key factor in tissue reconstruction, and hyaluronic acid has been found to stimulate fibroblast proliferation in both in vivo and in vitro studies.16 There is also evidence of an increase in extracellular matrix remodeling and an improved organization of collagen deposits after the application of hyaluronic acid.17 Moreover, the degradation products of hyaluronic acid are proangiogenic and can modulate the production of hyaluronic acid by fibroblasts, which is regulated by a large number of growth factors.18 Finally, hyaluronic acid also favors tissue regeneration by increasing keratinocyte proliferation and mobility.19,20

A major advantage in the clinical setting of hyaluronic acid and its salts is that it has very few adverse effects, with only isolated reports of inflammation and hypersensitivity.21-23 Hyaluronic acid is currently considered a useful resource in tissue regeneration.5

Pressure ulcers. Pressure ulcers are lesions of ischemic origin on the skin and underlying tissue with loss of cutaneous substance. They are produced by prolonged pressure or friction between a hard surface of the patient and a hard surface in contact with the patient. Care guidelines in numerous institutions classify 3 primary types of risk factors for PU formation: pressure, friction, and shear.24 Pressure ulcers are most frequently observed at bone protuberances, when the soft tissue has been compressed against an external surface. Tissue hypoxia produces rapid tissue degeneration in the area, which can range widely between a mild skin reddening and deep ulcers involving muscle or even bone.1,3

The prevalence of PUs in Spain increased between the first National PU Survey in 200125 and the second in

Keypoints

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2005 from to 8.34% to 9.11% of primary care patients receiving home care; 8.81% to 8.91% of hospitalized patients; and 7.6% to 10.9% of patients in residences for the elderly. This high prevalence is associated with major economic repercussions, as detailed in numerous studies worldwide.

The moist healing procedure has demonstrated the best outcomes to date. However, there have been wide investigations on alternative treatments to deliver more rapid tissue regeneration, including the utilization of growth factors and platelets and of autologous growth factor- and platelet-rich plasma.

Pressure ulcers and hyaluronic acid. Hyaluronic acid has long been used to regenerate damaged tissue, but few data are available on its use to treat PUs. A biopsy study found significantly lower hyaluronic acid levels in tissue samples from chronic PUs than in samples from open skin wounds, and lower levels in both compared to healthy tissue samples. This may be related to depolymerization of hyaluronic acid due to the higher hyaluronidase activity and presence of reactive oxygen species (free radicals) in the inflammatory response. Further studies reported the use of sodium hyaluronate and iodine complex in patients with diabetic foot problems. This treatment was effective in the majority of the patients with diabetes. The local treatment did not produce side effects or allergic reaction. Barrois et al investigated the efficacy and tolerability of hyaluronic acid (lysine-hyaluronate) treatment over 3 weeks in 21 patients with PUs. The results showed tolerability and efficacy of this treatment was good or very good, depending on the reduction of surface area, the presence of granulation tissue, and the decrease of fibrous tissue. A recent study determined the usefulness of combining hyaluronic acid and argentic sulphadiazine in the treatment of PUs. Paggetti et al found that improvement or complete healing of PUs was observed in 67% of patients at early follow-up (10 days), increasing to 76% and 87% at 20 and 35 days, respectively.

Hyaluronic acid has also been used as an active wound dressing. Zavan et al described the utility of porous nanoparticles of hyaluronan enriched with growth factors in the treatment of PUs. Other studies showed the efficacy of a 3-dimensional, polymerized hyaluronic acid as a biologic medicated dressing. Recently, a new formulation of hyaluronic acid (lysine-hyaluronate) has been studied to treat decubitus ulcers. The results obtained in a double-blind randomized study showed a greater reduction of the ulcer size treated with lysine-hyaluronate vs the commonly used sodium hyaluronate.

Conclusion

More effective treatment options are required for PUs due to their elevated prevalence, negative impact on quality of life of patients, and high associated costs. There is wide scientific evidence on the positive role of hyaluronic acid and its sodium salts in tissue regeneration and wound healing. It maintains wound hydration and may neutralize the excess hyaluronidase in lesions and eliminate free radicals. High efficacy of hyaluronic acid was proven, particularly in the treatment of diabetic ulcers. Its use when treating PUs resulted in reduction of the ulcer size and a good tolerability and efficacy, but few data are available on its use to treat these wounds. Further research is warranted into the utilization of hyaluronic acid and related substances for PUs.

References


Keypoints

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- A major advantage in the clinical setting of hyaluronic acid and its salts is that it has very few adverse effects, with only isolated reports of inflammation and hypersensitivity.


