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Original article

Two ethnicities one hyaluronic skin booster comparative: A case series

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Abstract. *Aim:* to assess the safety and efficacy of Viscoderm® Hydrobooster (VH) in treating skin ageing signs on the face of 10 female subjects from Italy and Oman with diverse features in terms of phenotype, genetics and anthropometry. *Methods:* two specialists in aesthetic medicine, one from Italy and one from Oman, recruited 5 patients each between 35-65 years old. 1.1 ml of VH were injected during 2 sessions at 60-day intervals, with 0.02 to 0.05 ml of product at each point. Post-treatment evaluation was scheduled at 4 months from baseline, photos were taken before, after each session and at final visit. VAS score ranging from 0 to 10 was recorded after each treatment, physician's and patient's GAIS scores ranging from -3 to +3 were provided at second and final visit. *Results:* GAIS score at second treatment was 2 for 4 patients out of 10 and in 5 out of 10 physicians reports, and 1 in 5 patients and 5 clinicians' reports, with an average value of 1.3 and 1.5 as to patients and specialists, respectively. As for GAIS evaluations at final visit, 8 patients and 8 clinical reports indicate the maximum positive score, with an average value of 2.8 for both patients and specialists, with strong agreement and great satisfaction. Average VAS value reported at baseline was 5.3 (SD 0.94), average VAS score at second treatment decreased at 5 (SD 0.66). *Conclusions:* in all the cases presented in this study, despite the different ethnicity and ageing features, VH provided deep hydration, increased elasticity, and tissue restructuring, stretching both dynamic and superficial wrinkles, along with improvement of skin defects, such as acne scars, with an early clinical benefit.

Key words: hyaluronic acid, skin aging, dermal fillers, skin hydration, wrinkle correction, ethnicity

Introduction

Art shows how physical beauty has always represented a recurring concept in human history, but with different standards in distinct eras and locations around the World. Nefertiti's bust and Botticelli's Venus represent two well-characterized and extremely different models of beauty, far apart in time and space. On one side, the iconic statue of the wife of Pharaoh Akhenaton, whose name means precisely "The Beautiful One", shows a woman with a typical Middle Eastern face, with olive skin-complexion, straight nose, large almond-shaped eyes emphasized by kajal and framed by well-defined, arched eyebrows and a wide upper-lid margin area, full lips with a barely noticeable regal smile, the high cheekbones and the hair pulled up in the royal headpiece to emphasize the oval of the face, the full cheeks, the well-defined jawlines and the spacious forehead[1]; on the other hand, the voluptuous body of Simonetta Vespucci, the alleged model of Botticelli's Greek goddess rising from the waters of the Aegean Sea, who embodies Italian Renaissance beauty with a sensual body, small rosy lips, round face, heavenly eyes, long blond hair and an ethereal almost angelic expression. Although antithetical, these two images have preserved for the eternal contemplation of the beholder two women that have one point in common, that of being depicted in the fullness of their

youth, a concept that is inevitably found associated with that of beauty, as human beings perceive them as inextricably linked and both precious and ephemeral. Despite a time jump of 500 years from Botticelli and a few millennia from Queen Nefertiti, modern society's consideration of the concept of youthful and fresh beauty has not only not changed, but is even more pronounced, with social-media platforms communicating a perpetually youthful appearance as successful in life and work, thus creating the paradox of a society that ages, yet does not accept a face that loses tone, volume and on which wrinkles and discolorations appear as years go by.

Women who possess a youthful appearance are consistently rated as more attractive than older-appearing women. In a cross-cultural study, women were perceived as more attractive to the extent that their predicted ages were less than their actual ones[2]. Studies on skin colour and texture have demonstrated that humans have a preference for younger-appearing skin that is viewed as both healthier and more attractive[3-7]. As evidence of this, aesthetic medicine (AM) is seeing exponential growth in numbers, and rejuvenation treatments are precisely those in greatest demand. The International Society of Aesthetic Plastic Surgery (ISAPS) 2020 Global Survey reported 10,129,528 surgical procedures and 14,400,347 nonsurgical ones, with HA-based treatments accounting for 3,558,511[8].

Skin aging can be described clinically as features of wrinkles, sunspots, uneven skin colour, and sagging skin. These cutaneous effects are influenced by both intrinsic and extrinsic factors and often are varied based on ethnic origin given underlying structural and functional differences[3]. Chronological (i.e., intrinsic) aging reflects the unique genetic background of an individual, and it is affected by extrinsic aging which is related to lifestyle and individual habits, such as sun exposure, tobacco use, diet, and exercise, in a relationship that is not fully clarified. However, there appears to be an increasingly crucial key role played by molecular damage induced by oxidative stress that results in the formation of reactive oxygen species (ROS) and subsequent DNA damage and alteration in the composition of the dermis, which loses its structural proteins (i.e., collagen and elastin), hyaluronic acid (HA), and proteoglycans resulting in dryness, decreased elasticity, superficial and deep wrinkles, and pigmentation changes which are typical of the aging skin[9-12].

Depending on the patients' characteristics, needs, and expectations, slowing down aging through AM is possible through surgical methods and others less invasive ones, such as injecting fillers of various types to preserve and restore volume, tone, and elasticity. Among the most popular fillers are those based on hyaluronic acid (HA), an increasingly popular molecule in various areas of medicine (e.g., orthopaedics, ophthalmology, dermatology) for its antioxidant, anti-inflammatory and regenerative abilities. Over the last decades, HA has been gaining increasing popularity especially among AM patients and specialists for its biocompatibility as a normal component of the extracellular matrix, therefore extremely tolerable, and by reason of its efficacy in reducing superficial and deep wrinkles, refreshing the overall appearance of the skin, with results that are maintained over time and that appear to improve with repeated procedures[13-18].

Viscoderm® Hydrobooster (VH) is the HA-based product used in this case series, it is a ready-to-use solution of stabilized, injectable HA with unique rheological properties of high deformability, low stiffness and viscosity. This provides hydrostretching, which is described as a dual function consisting in effective dermal hydration and tissue bio-restructuring, along with a mechanical stretching action on superficial wrinkles. The low stiffness and viscosity, and the high plasticity also promote an optimal tissue integration and enable the product to be injected into different layers of the dermis, up to the most superficial ones, making it particularly effective on the most dynamic facial areas (i.e., perioral, periocular areas, and the forehead)[19].

VH is suitable to improve dry skin, with poor elasticity and/or poor skin texture, and stretch superficial mimic wrinkles. Moreover, it shows effectiveness in ameliorating acne scars. A study on 18 volunteers who had undergone two injections of VH 2 months apart and were followed up for a further 3 months, demonstrated a significant improvement of their wrinkles grade around the eyes and the lip, and severity of nasolabial folds after the first injection. Furthermore, an improvement of the aging/photoaging grade and surface microrelief after 2 months, and a concomitant improvement of instrumental skin profilometry

and optical colorimetry were observed following the second injection[19]. The study also confirmed the good tolerability profile of the product and the long-lasting effect. In another study, 100 consecutive women with Glogau Wrinkle Scale grade 2-3, requiring deep hydration according to medical advice, were administered two injections of VH 2 months apart, with highly satisfactory aesthetic results and an excellent tolerability profile[20].

The purpose of this article is to describe the results of a small case series consisting of 10 clinical cases collected by two AM specialists in Italy and Oman to investigate the safety and efficacy of VH in subjects who are extremely heterogeneous in terms of phenotype, genetic and anthropometric characteristics that may affect aging and treatment outcomes differently.

Methods

Patients' selection

Two AM specialists, one from Italy and one from Oman, were asked to recruit 5 patients each between 35-65 years old, who never had VH before, and who were not administered any other concomitant aesthetic treatment. Patients who presented with skin irritations or any active inflammatory processes in the treatment area, who had received COVID-19 vaccination less than 4 weeks before or after VH treatment, who were affected by autoimmune diseases, pregnant or breast-feeding subjects, who were receiving concomitant aesthetic treatments, or who were not compliant to protocol or post treatment recommendations were excluded.

Treatment protocol

The protocol cycle was indicated as 2 treatment sessions at 60-day intervals with a post treatment evaluation at 4 months from baseline, photos were taken before and after each treatment session and at the final visit (Figure 1). A VAS score was recorded after each treatment, both the physician's and patient's GAIS scores were provided at the second and final visit. Photo release form, data protection policy as well as informed consent were signed by the patient.

Injection technique

Protocol indicated a full-face treatment with the double indication of deep hydration together with superficial stretching, 1.1 ml of VH were injected in 2 sessions with an interval of two months, 0.02 to 0.05 ml of product were injected in the superficial and deep level using a 29-gauge needle in each point.

For acne scars, VH was injected through the micro bolus technique in the superficial dermis to fill the scar, and linearly in the deep dermis to hydrate the skin.

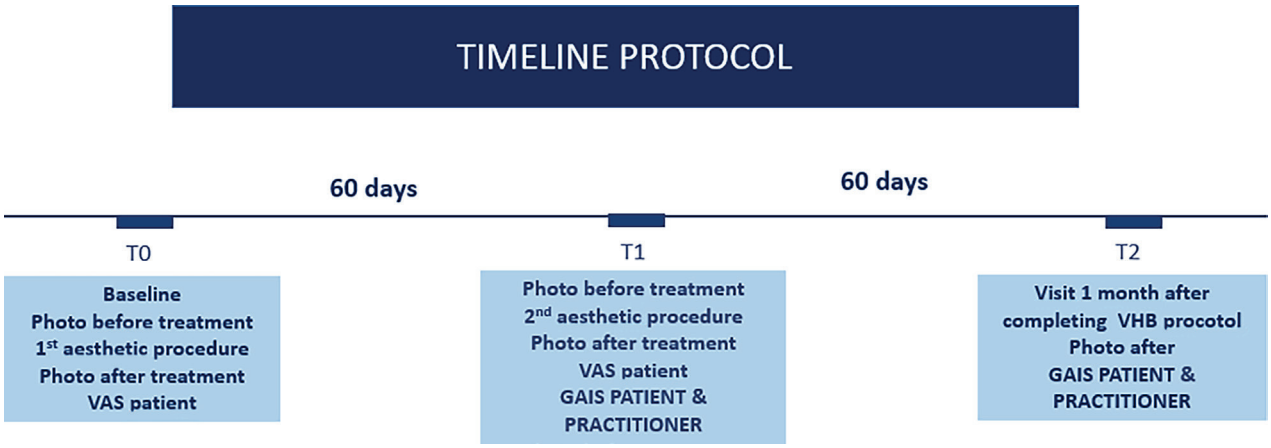

Figure 1. Timeline of treatment sessions and evaluation points.

Results

The Global Aesthetic Improvement Scale (GAIS) was rated from -3 to +3 with the lowest score corresponding to "much worse", the highest one to "very much improved", while 0 indicated "no change".

As to GAIS evaluations from patients and practitioners at 2nd treatment 8 weeks after baseline (T1), 4 patients out of 10 and 5 out of 10 reports from physicians indicate a score of 2 (i.e., much improved), while 5 patients and 5 clinicians' reports indicate a score of 1 (i.e., improved), with an average value of 1.3 and 1.5 as to patients and specialists, respectively. As to GAIS evaluations from patients and practitioners at final visit 16 weeks after baseline (T2), 8 out of 10 patients and 8 out of 10 reports from clinicians indicate the maximum positive score, while 2 patients and 2 reports from physicians indicate a score of 2, with an average value of 2.8 for both patients and specialists (Figure 2).

Comparing the agreement between GAIS values reported by patients and practitioners, there is a discrepancy of one point in 5 cases in T1 and 4 cases in T2 (Figures 3 and 4).

These results describe a strong agreement between doctors' and patients' ratings with a great level of satisfaction, as shown by the scores that increase to the highest GAIS value in 16 out of 20 ratings in T2.

A Visual Analogue Scale (VAS) was rated from 0 to 10 with the lowest score corresponding to "no pain", and the highest described as "the most intense pain sensation imaginable".

The average VAS value reported at baseline (T0) was 5.3 with a standard deviation (SD) of 0.94, average VAS score reported at T1 decreased at 5 with 0.66 SD, indicating that the pain was described as mild and less intense at the second session overall (Figure 5).

Case 1 - Oman

A 45-year-old patient, with a Fitzpatrick III/IV, presented an overall poor skin quality with dehydration, deep static wrinkles on the frown area, crow's feet, perioral lines (i.e., smoking lines), along with mild post-acne rolling scars. She previously addressed these issues with botulinum toxin and fractional

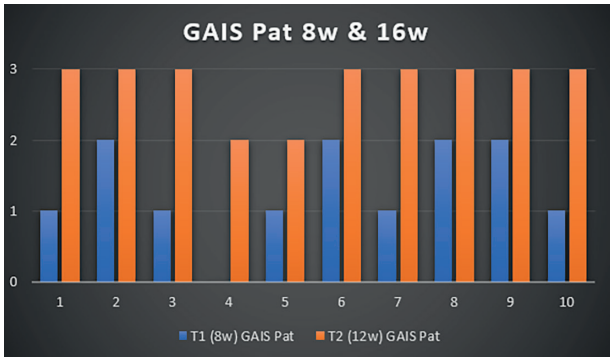

Figure 2. Patients' GAIS at 8 and 16 weeks from baseline. GAIS, Global Aesthetic Improvement Scale; Pat, patient; w, weeks; T1, 8 weeks after baseline/2nd treatment; T2, 16 weeks after baseline/final visit.

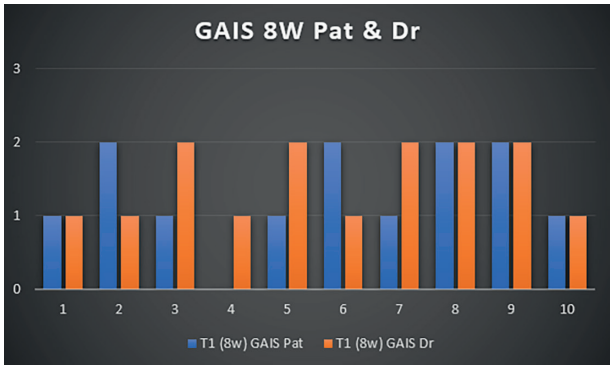

Figure 3. Comparison between physicians' and patients' GAIS at 8 weeks from baseline. GAIS, Global Aesthetic Improvement Scale; Pat, patient; Dr, doctor; w, weeks; T1, 8 weeks after baseline/2nd treatment

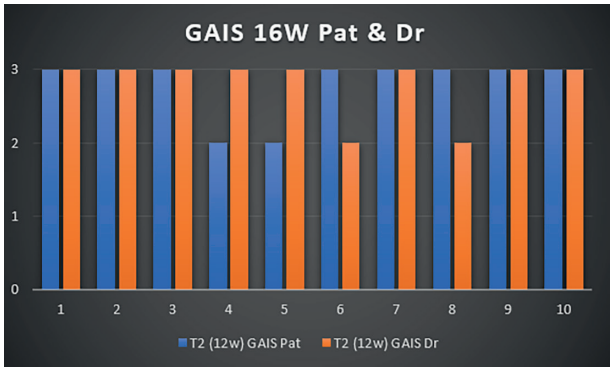

Figure 4. Comparison between physicians' and patients' GAIS at 16 weeks from baseline GAIS, Global Aesthetic Improvement Scale; Pat, patient; Dr, doctor; w, weeks; T1, 8 weeks after baseline/2nd treatment; T2, 16 weeks after baseline/final visit.

erbium YAG laser with bad treatment compliance, and low satisfaction rate. Treatment with VH led to a remarkable improvement in the depth of the wrinkles and of post-acne scars, better skin quality and less dryness. Minimal side effects (i.e., light and short-lasting bruises) and a quick recovery led to a high compliance, with patient reporting satisfaction rate as 8 out of 10, consistent with the 80% improvement reported by the physician, while treatment pain was scored as 4 out of 10 (Figure 6).

Case 2 - Italy

This 53-year-old patient with a Fitzpatrick scale of II/III presented an overall dull skin quality, with deep folds (Glogau III) concentrated in the nasolabial area and around the eyes, along with a general loss of elasticity and irregular texture. Moreover, she complained about dehydration and sagging of the cheeks. She previously had botulinum toxin with little satisfaction. After both treatments with HV she reported minimal side effects, a final satisfaction rate of 9 out of 10, consistent with the 85% improvement as assessed by the physician, a score of 3 out of 10 as for treatment pain, and a better compliance compared to the previous aesthetic procedures she had (Figure 7).

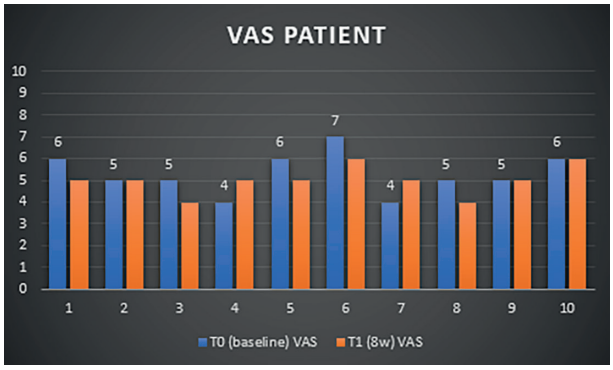

Figure 5. Patients' VAS at T0 and T1. VAS, visual analogue scale; w, weeks; T1, 8 weeks after baseline/2nd treatment.

Case 3 - Oman

This 56-year-old patient, with a Fitzpatrick scale of IV, presented with very deep wrinkles over the forehead, the frown area, around the eyes, with evident nasolabial folds, and an overall loss of skin elasticity. She reported she had never used any sun protection, neither any aesthetic procedure, nor she had been following any skin routine. After 2 treatment sessions with HV, the patient got around 75% improvement as assessed by the physician with very minimal side effects, a high compliance rate, a satisfaction rate of 10 out of 10, while she reported a score of 2 out of 10 as to treatment pain (Figure 8).

Case 4 - Italy

This 67 year-old Italian patient (Figure 9), with Fitzpatrick scale of I/II, and Glogau V, presented with marionetta and bar code wrinkles (*top image, baseline*), appeared improved after VH treatment (*lower image, T2*).

Figure 6. Frontal (a) and side (b) full-face at baseline (left) and T2 (right).

Discussion

Gene mixing among populations is an ongoing process, with somatic differences becoming less and less defined, therefore to make scientific comparisons of any kind among ethnic groups is increasingly challenging. However, it is possible to observe some macroscopic phenotypic and anatomical differences related to the subjects of this study, and make some general biological and physiological considerations related to skin pigmentation that may influence the process of skin aging.

People with lightly pigmented skin (i.e., Fitzpatrick I and II) are generally predisposed to develop earlier signs of photoaging than those with a darker complexion[21]. With ageing, lighter-skin shows a thinner and less cohesive stratum corneum, reduced extensibility, along with loss of collagen and disorganization of the elastic fibers in the dermis. The Italian patients enrolled in this study belong to the Caucasian ethnic group, characterized by specific aging features such as fine perioral and periorbital rhytides with decreased lip volume, skin sagging, jowling of the neck, fine and deep rhytides in the forehead and glabella, laxity of the upper and lower eyelids, pseudo-herniation of the orbital fat pads, increased redundancy of soft tissue, descent of the melo-labial fat pad toward the nasolabial fold, brow ptosis with formation of crow's feet, and lower lid lag also due to bone remodeling[22-24].

Figure 7. Frontal full-face at baseline and T2.

Darker-skin people (i.e., Fitzpatrick III to VI) have a larger amount of non-aggregated and more widely dispersed melanosomes with more melanin which preserves from photoaging. The epidermis contains a thicker stratum corneum, and fibroblasts are more active when compared to lighter skin-types[25]. The increased fibroblast activity leads to compact collagen bundles with a more parallel orientation, conveying more structural integrity and a longer-lasting youthful appearance than in lighter skin types[26].

The 5 Omanis patients belong to the Middle-Eastern ethnic population, in which the Northern African and East Mediterranean genetic heritage is evident in the broad nasal base, decreased nasal projection, bimaxillary protrusion, orbital proptosis, increased soft tissue of the midface, prominent lips, and increased facial convexity[26,27]. This skeletal morphology normally results in a more prominent facial aging in the periorbital region and midface than the upper areas, less brow ptosis, a decreased propensity to lose lip volume and show perioral rhytides, and an overall tendency of the skin to fold, not to wrinkle[27]. These different characteristics justify the varying distribution of wrinkles, laxity, and volume loss in facial regions in the women involved in this study. However, despite the biological differences of chrono-aging depending on skin phototype, atrophy of dermal and epidermal components and in particular the reduction in the number and function of fibroblasts and keratinocytes

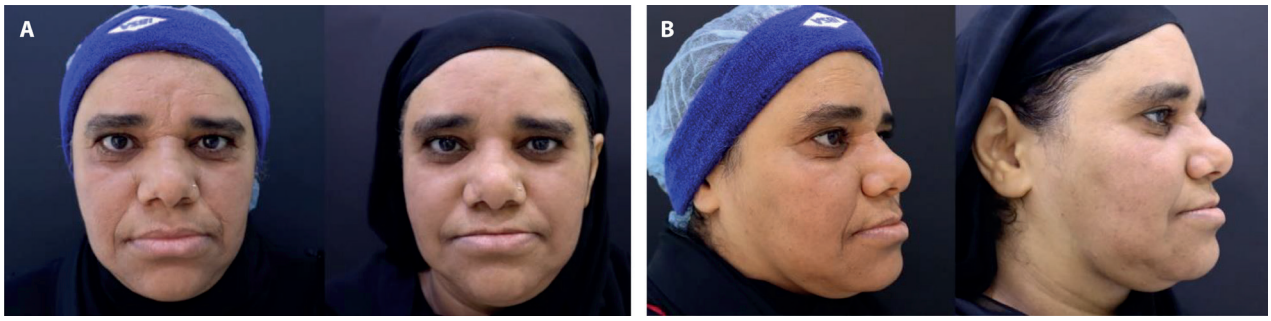

Figure 8. Frontal (a) and side (b) full-face at baseline (left) and T2 (right).

Figure 9. Frontal full-face at baseline (top image) and T2 (bottom image).

occurs in all subjects, with different timing depending on skin pigmentation. Alterations in these cell populations and in the HA which they produce underlie the loss of hydration, tone, volume, elasticity, and the decreased efficiency of antioxidant mechanisms found in the aging skin. Therefore, the use of HA-based products finds a reason in individuals of different ethnicities to restore a younger appearance, despite the different timing in the onset of signs of aging.

VH demonstrates to perform very well in subjects with diverse phenotypic characteristics and different degrees of aging, as it makes it possible to perform a personalized treatment with injections in different areas and at varying levels depending on the patient, since according to the type and depth of wrinkles and skin folds it is possible to calibrate the intervention. Moreover, VH shows not only efficacy against skin lines, but it has also proven to be effective in this case-series against acne scars, decreasing their depth, with a regenerative and healing effect.

By virtue of its peculiar rheological characteristics, VH reveals an interesting aspect that makes it more tolerable right after the procedure, namely its marked hygroscopic capacity at different skin planes without causing any temporary localized oedema in the treated area, or any unpleasant bulging or lumps due to filler injection. This specificity of the product facilitates return to daily routine with little need to cover any post-procedure sign or swelling with any makeup or sunglasses, with undoubted advantages in terms of compliance.

These patients shared a similar need for smoother, hydrated, and toned skin by means of a treatment that was respectful of their unique appearance, painless, minimally demanding, and which allowed an immediate return to daily life activities, and the results show that VH made it possible to achieve these goals. The results of the study show that VH was first and foremost very well-tolerated from the point of view of pain management and the immediate post-procedure period, patients willingly underwent the second treatment, visual improvement was evident with a clear concordance between clinicians and treated subjects in the assessment of the aesthetic outcome.

The main limitation of this study is that skin outcomes were assessed only at a macroscopic-visual level, while there was no evaluation as a tissue-cellular level using ultrasound or microscopes, therefore it is only possible to assume that the clinical outcomes reflect an overall improvement in the epidermal-dermal intimate structure and resident cell population.

Conclusions

The women enrolled in this study, although distant in terms of ethnic, cultural and social characteristics and perhaps with different ideals of beauty (e.g., a proud Egyptian queen, an ethereal and voluptuous Renaissance Venus) share the common need of looking more beautiful and younger. VH treatment has fulfilled this need, by showing a good tolerability and a high degree of satisfaction with strong agreement between patients and physicians, in subjects with different anthropometric, phenotypic, and phototypic characteristics.

In the cases presented in this study, VH has provided deep hydration, increased elasticity, and tissue restructuring, through a mechanical action aimed at stretching both dynamic and superficial wrinkles, along with improvement of skin defects, such as acne scars, with no temporary bulging, but a clinical benefit which was rapidly visible.

These elements suggest that VH can effectively regulate and improve cellular homeostasis, which may be at the basis of early clinical improvement.

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