Treatment of Androgenic Alopecia with Autologous Skin Micrografts
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Abstract:

Key words: Stem Cells, Re-cell, Adipose-Derived Stem Cells, Micrografts, Rigenera.

Introduction

Life expectancy for humans has increased significantly in recent years. This has deepened the issue of the deleterious effects of aging, due to the high incidence of age-related conditions. The possibility of curing or improving certain conditions using biological materials developed based on the patient's own tissues has always been a very interesting idea. Regenerative medicine is now a reality, with treatments applied on an increasing number of patients and with various purposes.

Skin is a very attractive tissue for regenerative medicine applied to aesthetic medicine. There are several reasons for this. First, it can be accessed easily and immediately: all materials necessary to start certain procedures can be obtained by means of a conventional biopsy. Second, most aesthetic treatments are applied on the skin itself. The fact that donor biological material comes from the same tissue where it will be later injected is not trivial, since it lowers the legal classification of procedures and makes application easier. However, if skin was processed and injected into different tissue, some of these treatments may be classified as "cell treatments" or "advanced therapies", subject to much stricter and more restrictive legislation.

It was first believed that the future of regenerative medicine applied to aesthetic medicine would be based on cell cultures. The ability to select a certain type of cell, such as fibroblasts, and culture them to replace later at the target site was of course very attractive. Not only the ability to expand the clone or increase the number of cells, but also the possibility of using their derived products was promising. That is -following the example above-, those cells could be made to
synthesize certain proteins (such as collagen), and those proteins, rather than the entire cell, would be reinjected. However, isolating certain cells was not all that easy, not to mention culturing them.

Practically the same thing happened with stem cells (SCs). First scientists and then doctors stumbled upon the problems of working with SCs. Controlling cell division and directing cell differentiation toward a certain lineage proved to be titanic tasks. Not to mention dedifferentiation, which involved retracing the steps of the cell back to the crossroads where it was forced to pick a development path toward a different cell lineage. This sounded like science fiction. In 2012, Yamanaka and Gurdon\(^3\) showed that all this was possible by reprogramming adult cells into SCs. For the world of high-complexity and high-budget medicine, SCs became a reality with enormous potential and some treatment usefulness, and complications for application became mainly normative, economic, ethical, and regulatory. However, the circumstances of SCs related to aesthetic medicine are quite different.

In the context of aesthetic medicine, a series of treatments have opened their way with great success: procedures with mechanical disintegration of donor tissue. These treatments are particularly interesting because no chemicals, enzymes or complex processing are used. Devices are available which work by breaking up tissue structure and concentrating, but not isolating, certain cells. It is worth noting that manufacturers are beginning to understand the specific needs of regenerative medicine protocols applied to aesthetic medicine. These new devices are very easy to use, automate virtually all parameters and steps in the processes and, most importantly, are enclosed. They prevent graft contamination at any step of the process and prevent dependency on the doctor processing the graft. This means that they are not operator-dependent. This ensures the quality of the product injected, regardless of who processes the tissue, which in turn makes it easier to standardize protocols and compare results.

The Rigenera\(^\text{®}\) method uses a special microdermatome that breaks up the structure of skin obtained by means of 2.5 mm biopsies and filters elements smaller than 50 microns,\(^4\) such as cells. The processed material is reinjected into the patient’s skin, at the site of the condition to be treated. Fiber proteins and the stratum corneum are naturally excluded, since the cell fraction obtained is the biological product desired with therapeutic action. No added chemicals or any other physical processing medium is used. This method is not used only in the treatment of androgenic alopecia. It has been used for several years in the treatment of chronic wounds and ulcers\(^5\) of various etiologies, in the management of acute wounds and subsequent scars,\(^6\) in the treatment of joint conditions and associated pain, in bone regeneration,\(^7\) and in dental conditions.\(^8\)

The purpose of this work is to assess the results obtained during one year in the treatment of patients with alopecia using a skin micrograft technique with the Rigenera\(^\text{®}\) system.
Materials and Methods

Subjects were recruited consecutively between June 1, 2015, and December 15, 2016, among people who visited MediEstetic in Madrid, Valdemoro and Toledo and satisfied the following inclusion criteria: i) different stages of alopecia as motive for consultation, ii) tests including PSA and hormone profile, iii) androgenic alopecia diagnosis, iv) no concomitant conditions of the scalp, and v) no systemic conditions. The treatment protocol was the following:

• Preparation. Hair washed and with no hairspray. Application of topical ozone in a bag for 15 minutes.
• Selection of the donor area. Area of the scalp not sensitive to the action of testosterone where greater follicle density is identified. Samples extracted from the occipital region.
• Hair in the extraction area marked and cut.
• Preparation of materials to be used in the intervention: fields, antiseptic, anesthetic, Rigeneracons®, and other perishables.
• Peripheral local anesthetic. Lidocaine 2% without adrenaline in a bleb.
• Micrograft obtained. 4 mm punch.
• Micrograft washed with saline.
• De-epithelization and fragmentation with 11 blade.
• Micrograft placed in the Rigeneracons® device, on the rack. 1.5 ml of saline at room temperature added.
• The Rigeneracons® device is inserted into the machine which performs mechanical disintegration at 80 rpm: One or two 1-minute or 2-minute cycles until no traces of solid biological material can be seen inside.
• Recovery of material obtained with a 2 ml syringe.
• Deep intradermal injection in the receiving area with 29G x 12 mm needles.
• The entire process is repeated with a new ml of saline to obtain a second, lower-concentration cell suspension, which is then injected in the same way.
• Home care instructions, appointment for follow-up one month later, and removal of stitches from the donor area.

The degree of alopecia was rated on the Ludwig scale for women and on the Hamilton-Norwood scale for men, including the A (front) and V (vertex-crown) variants for types III to V. All patients were prescribed supplemental Minoxidil 2% associated with Finasteride 0.15%. In the cases of patients who were already undergoing an established treatment, this was maintained unchanged.

Patient satisfaction was rated on a 7-point scale from -3 to +3: +3 for intense hair growth, +2 for moderate hair growth, +1 for mild hair growth, 0 for no change, -1 for mild hair loss, -2 for moderate hair loss, and -3 for intense hair loss.

A simple scale with only three categories (improvement, no change, and worsening) was developed for subjective results assessment by the physician.

The Rigeneracons® device is a sterile Class I CE medical device manufactured by Human Brain Wave srl in Italy. Technical specifications are according to the insert.

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Results

The sample included 44 subjects (28 men and 16 women), with a mean age of 48.05 years (SD 11.77).

The severity of alopecia on the Hamilton-Norwood scale (from 1 to 7, for men) was a mean of 4.36 (SD 2.33) and a median of 4.

The severity of alopecia on the Ludwig scale (from 1 to 3, for women) was a mean of 2.38 (SD 0.62) and a median of 2. Using both scales jointly, the severity of the cases of androgenic alopecia treated was as follows (Figure 1): 18 severe cases (40.91%), 24 moderate cases (54.54%), and 2 mild cases (4.55%).

Assessment of final results by the physician was +2 (median), in a discrete scale (from -3 to +3). The mean was +1.83 and dispersion was 0.88 (SD).

Assessment of final results by the patient (Figure 2) was: “very good” in 20.46% of cases; “good” in 59.09% of cases; “fair” in 11.36% of cases; and “no change” in 9.09% of cases.

Tolerance to the procedure was considered “very good” by patients in 100% of cases.

Discussion

The results we have obtained are very good in general. From the point of view of the treating physician, the improvement observed in patients has been very significant. On the other hand, the patients themselves confirmed the improvement observed by the physician, since 79.55% of patients rated treatment results as “good” or “very good”, while only 2 patients did not perceive any results. In addition, all patients reported high (“very good”) tolerability and many of them noticed slight darkening of the hair, which was deemed a very positive development.

However, there are certain issues that need addressing for an appropriate development of future research with this product. Firstly, physicians should manage patient expectations adequately. It must be made clear before intervention that expected results are not comparable to the results of FUE or FUSS hair transplant surgery. In fact, joint application with these techniques is reasonable and probably very useful. Future studies should test this hypothesis. Secondly, this work is not valid for an appropriate assessment of the technique's efficacy, since many of the patients were undergoing other related
treatments. Our purpose has been to explore solutions to satisfy the demands of our patients. Another type of study, specifically designed with different aims and methodologies to isolate this variable, are required.

Although the number of patients in this observational study is small (44), after a brief period of time observing our patients we can state the following:

1. No significant adverse effects have been observed.
2. Tolerance has been very good.
3. The treatment is very safe.
4. The results obtained are satisfactory for most patients.

Lastly, it is important to understand how this type of treatment is framed within the current scenario of aesthetic medicine. Virtually all aesthetic medicine treatments are ambulatory, unlike many regenerative medicine treatments, which require sterile conditions and certain infrastructure. Aesthetic physicians should be trained to work under these conditions and to comply with the specific needs and standards of regenerative medicine treatments applied to aesthetic medicine. This is a blooming and fast-growing area, but at the same time it requires reliable, effective, and simple solutions.

Conflicts of interest: None.

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References

2. Svolacchia F, De Francesco F, Trovato L, Graziano A, Ferraro GA. An innovative regenerative treatment of scars with dermal micrografts. Dermal micrografts for pathological scar, 2015;0,1-9