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Research Article

Organic Hair Transplantation: A New Concept in Hair Transplantation

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Abstract

Introduction: Senile aalopecia occurs in all individuals beginning at age 35 regardless of gender due to aging. Androgenic alopecia begins much earlier in life. Standard treatments for alopecia include transplanting existing hair follicles to bald or thinning areas and/or stimulating existing follicles with topical, oral, or injectable medications. These therapies are associated with high costs, adverse side effects, and, in some cases, an inadequate response. Adipose-Derived Mesenchymal Stem Cells (ADMSCs), on the other hand, represent a promising medical breakthrough in the field of skin rejuvenation. ADMSCs secrete several growth factors, cytokines, and exosomes that collectively rejuvenate skin by increasing collagen production and promoting fibroblast migration. In this study, the "Cihantimur Fat Transfer" method is used to mechanically extract adipose-derived stem cells that, upon combination with enzymatically digested adipose tissue, yields an ADMSC-enriched lipograft. These ADMSC-enriched lipografts are then used in conjunction with the Follicular Unit Extraction (FUE) hair transplantation technique to treat alopecia. The results shown herein indicate that this combinatory approach increases the survival rate of grafts and reduces hair loss owing to a more hospitable transplant environment afforded by the growth factor rich ADMSC lipograft. **Materials and Methods:** Eighteen patients (17 male, 1 female) underwent hair transplantation surgeries between 1 January 2013 and 20 March 2015. Approximately 3000-4000 follicular units were transplanted in each case using the FUE technique. Critically, the graft areas for half of the subjects were pre-treated with an ADMSC-enriched lipograft prepared according to following technique. Autologous fat tissue (100 mL) was obtained from the abdominal area. Half of that tissue was processed using the Cihantimur Fat Transfer method, and the remaining half was processed via enzymatic digestion. The two fractions were recombined to produce a lipograft with high concentrations of both ADMSCs and stromal cells, which are important to cell survival. The results of the organic hair transplantation technique were assessed by patient satisfaction questionnaires. **Results:** Patients who received the ADMSC-enriched lipograft pre-treatment demonstrated less edema than those who underwent a standard FUE transplantation by the same surgeon but without the pre-treatment. By five days following surgery, edema was completely resolved in all patients. For the study group, micro wounds were healed, and erythema was no longer significant by two weeks after surgery. All patients indicated that they did not experience significant pain after the procedure, though a mild tenderness was noted. Overall, patient satisfaction was high; the treatment decreased progressive hair loss increased pre-existing hair diameter. **Discussion:** The use of stem cells as a therapeutic has increased substantially, particularly in aesthetics operations, since their regenerative effects were first recognized. We use an aseptic squeezing centrifugation lipotransfer system that removes approximately 30% of aspirate containing unwanted older adipose cells and liquid triglycerides. The result is a product rich in adipose-derived stem cells and interstitial structures. Although several approaches to promote hair growth using ADSCs have evolved, our method is the only

one that combines ADMSCs, autologous fat grafting, and hair transplantation to give superior results. **Conclusion:** Due to the progressive nature of androgenic alopecia, the optimal treatment approach must incorporate preventative hair loss measures with techniques to improve graft survival following surgical intervention. This paper introduces a combinatory ADMSC-FUE treatment to curtail hair loss, improve the quality of existing hair, and increase hair transplant graft survival with a high level of patient satisfaction. Our results are promising, but we recognize that these new methods should be performed on a larger patient population in a randomized trial to confirm the benefits of our combinatory approach to treating androgenic alopecia.

Introduction

Hair loss is evidenced as part of the normal aging process in both men and women. Male pattern hair loss, which affects over 70% of men, may commence before age 35 [1]. The reported incidence of female pattern hair loss varies with age; for females around 30 years old, the incidence is 12%, and for females between 60 and 69, the incidence increases to 30-40% [2,3]. In females, the condition usually manifests after puberty and progresses at variable rates and degrees of clinical severity. Androgens, genetics, and other factors play a significant role in pattern hair loss for both men and women, and an early clinical presentation is generally associated with a more severe progression, regardless of gender.

Hair loss has a significant psychological impact on both sexes and can lead to suppressed self-esteem, depression, introversion, neuroticism, and psychological impairment [4-9]. Hair restoration surgery alone is a highly effective means of restoring hair to bald scalp, but the procedure is limited by donor hair density [10]. Topical and oral medications (i.e., minoxidil and finasteride), along with cell-based injectables from homologous and autologous sources (i.e., mesotherapy and platelet-rich plasma), can improve hair coverage and inhibit hair loss [11]; however, these products cannot induce significant hair growth in advanced stages of alopecia. Moreover, side effects associated with hair loss medications, including unwanted body hair growth and/or sexual dysfunction, often reduce patient compliance which, unfortunately, may accelerate hair loss [12].

Although injectable biologics and autologous preparations present lower risks of side effects, not all preparations are created equal. Indeed, the growth factor profile of Platelet-Rich Plasma (PRP) varies according to the device used to prepare it and differs further still from platelet lysate, which contains a significantly higher concentration of high molecular weight growth factors [13,14]. Quality differences aside, all stem-cell activation therapies become ineffective once the stem cell niche is lost [15]. Since androgenic alopecia is associated with high levels of inflammation that progressively diminish the stem cell niche in the bulge region of the hair follicle, early intervention is critical for a cell-based therapy to be effective.

As previously, noted, surgical intervention is the only method presently recognized to restore hair in patients with advanced alopecia, but even this technique is subject to limitations. As hair counts in the donor and recipient areas continue to recede, the probability of a successful surgical outcome drastically decreases. At some point, hair loss in the donor area precludes surgical intervention, and the absence of stem cells in the recipient area negates the efficacy of a cell-based treatment. Consequently, an alternative approach to treating hair loss in advanced cases of alopecia is necessary.

One such treatment option is evaluated herein. Specifically, this study evaluates the efficacy of a Follicular Unit Extraction (FUE) hair transplant surgery performed on scalps pre-treated with an Adipose-Derived Mesenchymal Stem Cell (ADMSC)-enriched lipograft. ADMSCs are recognized for their immunomodulating and anti-inflammatory capacity; thus, the combination of ADMSCs with an FUE procedure is expected to make the donor scalp more receptive to graft transplantation and promote hair growth (Figure1).

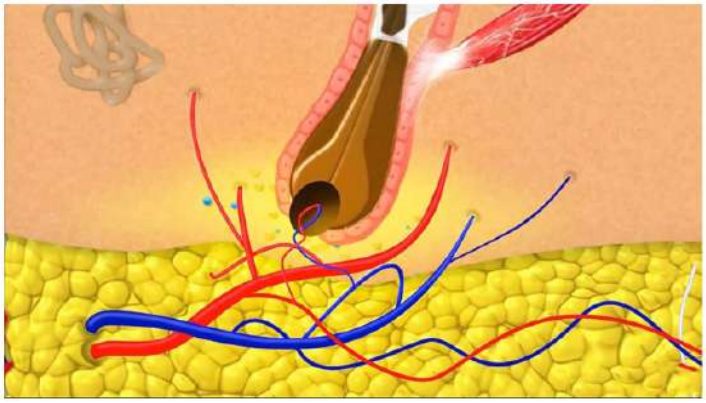

Figure 1: Illustration of a normal hair follicle. Capillaries provide nutritional support to the hair follicle, and the surrounding adipose tissue acts as a paracrine gland by secreting a variety of growth factors that help regulate the normal hair growth cycle.

Materials and Methods

For this study, a total of 18 patients (17 male, 1 female) underwent an FUE hair transplant surgery in which 3000 to 4000 grafts were placed in the donor scalp region. The patient population was divided into a control group and a test group, each consisting of 8 subjects. Patients in the control group were treated

with a classical FUE hair transplant, but patients in the test group received an ADMSC-enriched lipograft injection in the donor scalp before FUE grafts were placed.

ADMSC-enriched lipografts were prepared according to the following protocol. First, a Nutational Infrasonic Liposuction (NIL) device was used to collect 100 mL of autologous adipose tissue from the abdominal area. This technique emulsifies the adipose prior to aspiration, which minimizes tissue damage and facilitates the extraction of stem cells from the walls of adipocytes [16]. The lipoaspirate was then divided into two 50 mL fractions that were further processed using either a mechanical or enzymatic technique. The mechanical technique involved transferring the lipoaspirate to a weight-mesh filter (Lipokit, Medikan International Inc.) to concentrate ADMSCs and remove triglycerides and fluid given during the liposuction process. Removing the triglycerides and excess fluid was particularly important because it prevented the development of oil cysts and edema, respectively. The enzymatic technique consisted of digesting the lipoaspirate with collagenase to obtain ADMSCs [17]. Combination of the NIL procedure and Lipokit sorting process is known as Cihantimur Fat Transfer.

The stem-cell enriched products from the enzymatic and Cihantimur Fat Transfer processes were combined to form an ADMSC-enriched lipograft, which subsequently injected into the donor region of patients in the test group. Incidentally, the injection of adipose tissue increased the volume of the scalp, providing a better working area for the surgeon and avoiding the need to chemicals used during a classical hair transplantation. Next, hair grafts obtained by the FUE method were placed in the scalp, and a surgical dressing was applied. Results of the control and test hair transplantation techniques were assessed using patient satisfaction questionnaires (Figures 2 and 3).

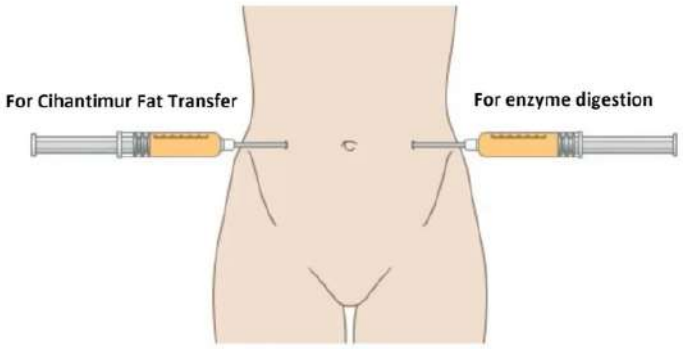

Figure 2: Illustration shows the obtaining the fat tissue from abdominal area in order to prepare stem cell enriched lipograft.

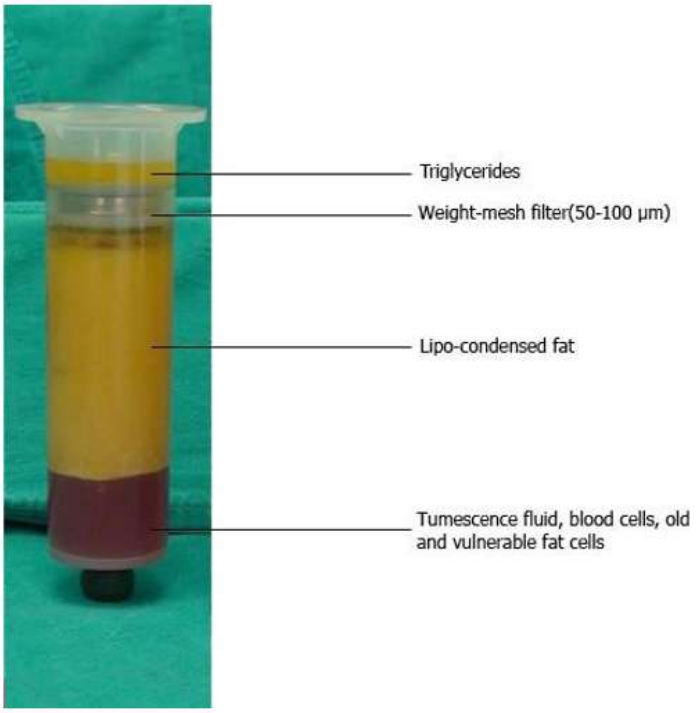

Figure 3: Distribution of the fat aspirate after centrifugation at 3200 rpm for 8 min in Lipokit.

Results

During the patient follow-ups, the level of edema in patients from the test group was notably less than that of patients from the control group. Importantly, the FUE hair transplant in both groups was performed by the same surgeon. Edema was completely resolved in all patients 5 days after surgery. Micro wounds were healed, and erythema was no longer significant two weeks after surgery. All patients indicated that they did not experience pain after the procedure but, rather, a mild tenderness. Overall, patients stated that they were happy with the results. Hair loss decreased, and the diameter of pre-existing hairs visibly increased (Figures 4 and 5).

Figure 4: (a) Before the combinatory hair transplantation, (b) 8 months after the combinatory hair transplantation.

Figure 5: (a) Before the combinatory hair transplantation, (b) 9 months after the combinatory hair transplantation.

Discussion

Androgenic alopecia is characterized by progressive hair loss in a patterned formation. Two factors are recognized as key contributors to this process. The first is a notable decrease in the concentration of growth factors within the scalp extracellular matrix, and the second is a disproportionate number of follicles remaining in the telogen phase of the hair cycle. These factors are interrelated and are both influenced to varying degrees by the underlying adipose tissue. Indeed, adipose tissue plays a regulatory role in the hair cycle through the release of myriad growth factors and proteins that are circulated throughout the scalp by its rich capillary network [18-20]. For example, leptin, a well-known adipokine secreted by mature adipocytes [21], has been shown to induce the anagen phase in hair follicles [22], and immature adipocytes have been shown to induce proliferation of stem cells within the bulge region of the hair follicle [23]. Moreover, Vascular Endothelial Growth Factor (VEGF), which is secreted by ADMSCs [18], is particularly important in stimulating new capillary formation. The secretory profile of cultured ADMSCs has been shown to improve under hypoxic conditions, and conditioned media obtained from the process has been used to improve hair growth as both a stand-alone injectable and in conjunction with surgical intervention [24,25].

Clearly, the regulatory role of adipose on the hair cycle spans the entire cell line from stem cell to mature adipocyte, and the impact of adipose-secreted growth factors has proven effective under both *in vivo* and *ex vivo* conditions [26,27]. Unsurprisingly, ADMSCs are now widely used in aesthetics and plastic surgery practice owing to beneficial effects of their secreted growth factors and the widespread availability of adipose tissue [28]. Obtaining adipose tissue, stromal cells, and ADMSCs through liposuction is straightforward, and there are currently multiple liposuction techniques that may be implemented. However, when the lipoaspirate is to be used for downstream applications, as they are in regenerative medicine, care must be taken to not harm the important cell populations (i.e., ADMSCs and stromal cells). In order to avoid cell damage, this study employed the NIL method. As mentioned previously, this method enables adipose tissue to be obtained smoothly thereby yielding a high concentration of viable cells relative to standard liposuction [16].

The treatment strategy employed in this study aimed to incorporate a high concentration of ADMSCs along with adipose stromal cells to improve the growth factor profile within the scalp Extracellular Matrix (ECM). This strategy was implemented by processing lipoaspirate via mechanical and enzymatic procedures, namely, Cihantimur Fat Transfer and collagenase digestion, to obtain an ADMSC-enriched lipograft. We hypothesized that by making the ECM more hospitable, grafts transplanted to the donor region as well as pre-existing hair within that region would experience increased survival and growth. Our results indicate that the combined approach to treating hair loss does indeed afford an advantage over FUE surgical intervention on its own. All patients reported a high degree of satisfaction with their surgical outcome, and those who received pre-treatment with the ADMSC-enriched lipograft demonstrated less hair loss and thicker follicular diameter in pre-existing hair. Studies demonstrate that dermal papilla proliferation and FGF7 production, a potent initiator of the

cell cycle, are growth factor concentration dependent with adipose culture media supernatant yielding the most impressive response when compared to other growth factor rich media [29]. Although biochemical studies were not performed, we assume that the introduction of ADMSCs and adipose tissue directly contributed to the positive findings owing to the numerous studies that highlight adipose-directed hair growth.

Conclusion

Although the existing hair transplantation techniques yield good results in most patients, they do not address the underlying problems that cause the hair loss. Preventing hair loss while promoting existing hair to grow thicker, along with increasing the success rate of hair transplantation is the overarching goal of all hair transplantation surgeons [30,31]. With the combinatory hair transplantation technique described herein, we define a new approach to hair loss. Our results are promising; nevertheless, these new methods should be performed on larger patient population in randomized trials to realize the full benefits of the method.

References

1. Sontos Z, Avci P, Hamblin MR (2015) Drug discovery for alopecia: gone today, hair tomorrow. Expert Opin Drug Discov 10: 269-292.
2. Birch MP, Messenger JF, Messenger AG (2001) Hair density, hair diameter and the prevalence of female pattern hair loss. Br J Dermatol 144: 297-304.
3. Norwood OT (2001) Incidence of female androgenetic alopecia (female pattern alopecia). Dermatol Surg 27: 53-54.
4. Connors J, Casey P (2006) Sex, body-esteem and self-esteem. Psychol Rep 98: 699-704.
5. Cash TF (1999) The psychosocial consequences of androgenetic alopecia: a review of the research literature. Br J Dermatol 141: 398-405.
6. Cash TF, Price VH, Savin RC (1993) Psychological effects of androgenetic alopecia on women: comparisons with balding men and with female control subjects. J Am Acad Dermatol 29: 568-575.
7. Alfonso M, Richter-Appelt H, Tosti A, Viera MS, Garcia M (2005) The psychosocial impact of hair loss among men: a multinational European study. Curr Med Res Opin 21: 1829-1836.
8. Budd D, Himmelberger D, Rhodes T, Cash TE, Girman CJ (2000) The effects of hair loss in European men: a survey in four countries. Eur J Dermatol 10: 122-127.
9. Irwig MS (2012) Depressive symptoms and suicidal thoughts among former users of finasteride with persistent sexual side effects. J Clin Psychiatry 73: 1220-1223.
10. Cole JP (2013) An analysis of follicular punches, mechanics, and dynamics in follicular unit extraction. Facial Plast Surg Clin N Am 21: 437-447.
11. Zhang P, Kling RE, Ravuri SK, Kokai LE, Rubin JP, et al. (2014) A review of adipocyte lineage cells and dermal papilla cells in hair follicle regeneration. J Tissue Eng 5: 2041731414556850.
12. Rossi A, Cantisani C, Melis L, Iorio A, Scali E, et al. (2012) Minoxidil use in dermatology, side effects and recent patents. Recent Pat Inflamm Allergy Drug Discov 6: 130-136.
13. Gentile P, Cole JP, Cole MA, Garcovich S, Bielli A, et al. (2017) Evaluation of not-activated and activated PRP in hair loss treatment: role of growth factor and cytokine concentrations obtained by different collection systems. Int J Mol Sci 18: 408.
14. Cole JP, Cole MA, Insalaco C, Cervelli V, Gentile P, et al. (2017) Alopecia and platelet-derived therapies. Stem Cell Investig 4: 88.
15. Toyoshima KE, Asakawa K, Ishibashi N, Toki H, Ogawa M, et al. (2012) Fully functional hair follicle regeneration through the rearrangement of stem cells and their niches. Nat Commun 3: 784.
16. Baptista LS, do Amaral R, Carias R, Aniceto M, Claudio-da-Silva C, et al. (2009) An alternative method for the isolation of mesenchymal stromal cells derived from lipoaspirate samples. Cytotherapy 11: 706-715.
17. Sterodimas A, de Faria J, Nicaretta B, Boriani F (2011) Autologous fat transplantation versus adipose-derived stem cell-enriched lipografts: a study. Aesthet Surg J 31: 682-693.
18. Park BS, Jang KA, Sung JH, Park JS, Kwon YH, et al. (2008) Adipose-derived stem cells and their secretory factors as a promising therapy for skin aging. Dermatol Surg 34: 1323-1326.
19. Won CH, Yoo GH, Kwon OS, Sung MY, Kang YJ, et al. (2010) Hair growth promoting effects of adipose tissue-derived stem cells. J Dermatol Sci 57:134-137.
20. Kim WS, Park SH, Ahn SJ, Kim HK, Park JS, et al. (2008) Whitening effect of adipose-derived stem cells: a critical role of TGF-beta 1. Biol Pharm Bull 31: 606-610.
21. Cammisotto PG, Bukowiecki LJ (2002) Mechanisms of leptin secretion from white adipocytes. Am J Physiol 283: C244-C250.
22. Sumikawa Y, Inui S, Nakajima T, Itami S (2014) Hair cycle control by leptin as a new anagen inducer. Exp Dermatol 23: 27-32.
23. Festa E, Fretz J, Berry R, Schmidt B, Rodeheffer M, et al. (2011) Adipocyte lineage cells contribute to the skin stem cell niche to drive hair cycling. Cell 146: 761-771.
24. Park BS, Kim WS, Choi JS, Kim HK, Won JH, et al. (2010) Hair growth stimulated by conditioned medium of adipose-derived stem cells is enhanced by hypoxia: evidence of increased growth factor secretion. Biomed Res 31: 27-34.
25. Moon KM, Park YH, Lee JS, Chae YB, Kim MM, et al. (2012) The effect of secretory factors of adipose-derived stem cells on human keratinocytes. Int J Mol Sci 13: 1239-1257.
26. Yano, K, Brown LF, Detmar M (2001) Control of hair growth and follicle size by VEGF-mediated angiogenesis. J Clin Invest 107: 409-417.
27. Tomita Y, Akiyama M, Shimizu H (2006) PDGF isoforms induce and maintain anagen phase of murine hair follicles. J Dermatol Sci 43: 105-115.
28. Yamamoto T, Gotoh M, Hattori R, Toriyama K, Kamei Y, et al. (2010) Periurethral injection of autologous adipose-derived stem cells for the treatment of stress urinary incontinence in patients undergoing radical prostatectomy: report of two initial cases. Int J Urol 17: 75-82.
29. Cole J, Cole M (2019) Dermal papilla response to growth factor rich mediums, a comparative trial. FUE Europe 2019.
30. Dawson T (2014) Keynote address, ISHRS annual conference Malaysia, September 2014.
31. Trüeb RM, Rezende HD, Dias MFRG (2018) A Comment on the Science of Hair Aging. Int J Trichology 10: 245-254.