Original Article

A personalized nutrition plan based on genetic profile improves outcomes of facial regeneration with Platelet-Rich Fibrin liquid matrixes

Cleopatra Nacopoulos[1,2], Ioannis Vlastos[3], Anna-Maria Vesala[1], Evgenia Lazou[4,5], Dimitrios Chaniotis[5], Kalliopi Gkouskou[4,6]

[1]Facial Aesthetics and Dental Clinic, Kifissias Ave, Athens 11527, Greece.
[2]Laboratory of Research for the Musculoskeletal System (LRMS), School of Medicine, University of Athens, Kifissia 14561, Greece.
[3]Aghia Sophia children's hospital, Athens 11527, Greece.
[4]Embiodiagnostics, Heraklion 71500, Greece.
[5]University of West Attika, Athens 12243, Greece.
[6]Laboratory of Molecular Medicine, University of Athens, Medical School, Athens 11527, Greece.

Correspondence to: Prof. Cleopatra Nacopoulos, Facial aesthetics and Dental Clinic, 103, Kifissias Ave, Athens 11527, Greece. E-mail:cleopatra.nacopoulos@gmail.com

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Abstract

Aim: The importance of nutrition in the prevention of skin ageing has been shown by large observational studies. Despite this fact, there are no studies assessing dietary

changes as adjunct procedures to aesthetic interventions. The objective of this manuscript is to study whether a personalized nutritional plan conveys additional benefits to Platelet-Rich Fibrin (PRF) facial regeneration.

Methods: Forty seven healthy women (mean age 52.5years old, SD = 7.7) were offered minimally invasive facial regeneration with the use of PRF liquid matrixes, as well as a personalized nutritional plan. The nutritional plan was informed by a nutrigenetic test based on 128 polymorphisms. Horizontal forehead lines, zygomatic wrinkles or mid-cheek furrows, nasolabial folds, perioral expression wrinkles, and marionette line were assessed separately with the use of the Facial Wrinkles Assessment Scale (FWAS).

Results: Total FWAS scores change was statistically significantly better in women who reported an at least partially adaptation of nutritional recommendations for a 3-month period or longer ($z = 2.4$, $P = 0.008$).

Conclusion: Personalized nutritional recommendations based on individual needs as well as on generally accepted dietary guidelines can improve treatment outcomes of minimally invasive facial skin aesthetics interventions.

Keywords: PRF, Nutrigenetics, facial skin aesthetics

INTRODUCTION

Over the last decade, the use of autologous blood concentrates, such as platelet-rich plasma (PRP) and platelet-rich fibrin (PRF), has gained importance in aesthetic medicine for dermal stimulation, augmentation, and rejuvenation[1-3]. Platelet-rich fibrin liquid matrices based on the low speed centrifugation concept have shown effectiveness in facial regeneration[4,5] and are being increasingly applied in facial aesthetics either alone or in combination with other techniques.

At the same time, studies of cells in the laboratory, animal models and human trials also

support roles for a variety of nutrients in preventing skin ageing[6]. Large observational studies have suggested associations of vitamin C, linoleic acid, green and yellow vegetables with younger-looking skin[7,8] indicating the need of more holistic approaches that incorporate nutritional advices into aesthetic treatments.

Personalized nutrition plans informed by knowledge of an individual's DNA are increasingly being utilized for health as well as general well-being purposes. There are numerous studies, particularly in the fields of preventive medicine and cardiovascular diseases, showing that the specification of general dietary recommendation bythe inclusion of genetic variants can have a significant impact in health parameters. At the same time there are thousands of publications based on large cohort or other retrospective studies indicating that the exact amounts of the various nutrients can be specified among others by genotype results. Adherence to a nutritional plan that conforms to standard dietary guidelines and at the same time take into account the various individual needs may improve healthy skin parameters.In this study we sought to investigate whether a personalized nutrition plan convey additional benefits to a minimally invasive technique for facial regeneration.

METHODS

A total of 47 otherwise healthy women offered PRF facial regeneration based on the low-speed centrifugation concept were included in the study. An ethical approval was granted (acknowledgments No 1/26/09/2016), and the patients signed an informed consent prior to their treatment. All patients were treated by the same experienced physician (CN) using a standard protocol described in more detail in previous publications[4,5]. Briefly, four sessions of PRF treatments were offered with 2- to 3-week intervals. In each session, 60 mL of venous blood was collected in 10 mL PRF tubes (Orange tubes, Process for PRF, Nice, France) and centrifuged according to the following protocols.

• 40 mL (4 tubes) 5 minutes at 1300 rpm (208 g) that results in10-11 mL of PRF

• 20 mL (2 tubes) 3 minutes at 700 rpm (60 g) that results in 2 mL of PRF.

Using a preprogramed centrifuge with a radius of 110 mm (Process for PRF, Nice France) producing a total of 12-13 mL PRF of reduced density. PRF liquid matrixes produced by the two abovementioned centrifugation protocols were mixed and a full face injection technique was applied as described previously[5].

A personalized nutritional plan was offered by a specialized nutritionist during the treatment. A nutrigenetic test was utilized to aid personalized nutritional recommendations. In more detail, prior to the first PRF session, additional 5 mL of vein blood was collected for genomic DNA analysis using a Pure Link Genomic DNA Mini Kit Assay (Life Technologies), according to the manufacturer's instructions.

The nutrigenetic test offered to the health professional personalized recommendations based on the genotyping of 128 single nucleotide polymorphisms **[Table 1]**. Among others, this test examines polymorphisms related to macronutrient daily intake, e.g. *GIPR* SNP rs2287019[9], *IRS1* SNP rs294364[10], APOA5 SNP rs964184[11], *PCSK7* SNP rs236918[12], TCF7L2 SNP rs7903146, *TFAP2B* SNP rs987237[13], fatty acid needs, e.g., *.APOE* SNPs rs429358 and rs7412[14], *CET*P SNP rs708272[15], *PPARγ2* SNP rs1801282[16],aging,e.g., *FTO* SNP rs9939609[17], supplement response and special supplemental needs, e.g., *CYP2R1* SNP rs10741657[18], *VDR*SNP rs7968585[19,20], *MTHFR* SNP rs1801133, rs1801131[21],special antioxidant needs e.g., COMTSNP rs4680, oxidative stress, e.g., *MTHFR* SNP rs1801133[22],micronutrient responses, e.g., *GPX*1 SNP rs1050450[23],inflammation response, e.g., *IL-6* SNP rs1800795[24],FTO SNP rs9939609, *MC4R*SNP rs17782313, and T*MEM18*SNP, rs6548238[25],choline needs, e.g., PEMT SNP rs12325817[26, 27],susceptibility to injury, e.g ACTN3 SNP rs1815739[28-30],*WNT16* SNP, rs2908004 and rs2707466[31,32],telomere length, e.g., SNPs, rs2736100, rs7675998, rs9420907, rs8105767, rs755017, rs11125529, rs894160, rs4293393[33,34].

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Pathology or health issue	SNP	Genotype related health effect	**Recommendation**
Folate deficiency	MTHFR rs1801133	Increased susceptibility to depression	Increase folate intake
Hypertension	MTHFR rs1801133	Elevated blood pressure	Supplementation with dietary riboflavin
Prediabetes, hyperglycemia, risk of developing T2DM	MTNR1B rs10830963	Reduction in the release of insulin rate	Morning melatonin supplementation
Difficulty in weight loss/ control	COMT rs4680	Reduction in COMT enzymatic activity	Increase catechin intake in order to increase energy expenditure
Cognitive impairment, dementia, AD	APOE (rs7412, rs429358) risk haplotype e4e4	Inefficient and/or delayed response to fatty acid intake and ketogenic therapy	Supplementation with DHA in the form of lysoPC121 because it induces ameliorated cognition outcomes when applied prior to the onset of AD dementia.
Difficulty in weight loss/ control	FTO rs1558902 AA	Diet high in protein	Improved weight loss

	FTO rs9939609 A / AA allele	Diet low in saturated fat Diet high in protein Improvement of aerobic fitness Every day physical ativity Vitamin D supplementation	

Table 1. Examples of Single nucleotide polymorphisms (SNPs) and related recommendations. Of note is that a personalized approach should be focused on the needs and expectations of the patients which means that recommendations cannot be universally applied each time a specific SNP is[35-37] found

SNPs

SNPs were genotyped using the TaqMan assays, provided by Life Technologies (https://www.lifetechnologies.com/es/en/home/life-science/pcr/real-time-pcr/real-time-pcrassays.html). We performed genotyping on the Open Array™ SNP Genotyping System (Life Technologies, Carlsbad, CA, USA) using microscope slide-sized plates and the OpenArray Accufill autoloader (Life Technologies, Carlsbad, CA, USA), following the manufacturer's instructions.

Adaptation of the nutritional recommendations was assessed with a simple questionnaire provided at the time of facial reassessment. In more detail, participants were asked whether they adapted any dietary changes ("none", "some" and "all or the majority") and for how long ("1-3weeks", "1-2 months", "3-4 months", "5-6 months"). An at least partially adaptation of recommendations for a 3-month period or longer was regarded as adherence to dietary recommendations [supp table 1]

	1-3 weeks	1-2 months	3-4 months	5-6 months
None				1
Partial	4	9	2	16
Complete	1		1	9

Supp table1. Subjects have been grouped according to the degree of the adaptation of nutritional recommendations. A total of 28 subjects adapted partially or completely the provided recommendations for an at least 3 months period

Horizontal forehead lines, zygomatic wrinkles or mid-cheek furrows, nasolabial folds, perioral expression wrinkles, and marionette line were assessed separately with the use of the Facial Wrinkles Assessment Scale (FWAS), a simple and reliable tool for the assessment of wrinkles[38] **[Figure 1]**.Two authors (CN and AMV) blinded to "adherence on recommended diet" scored the scales prior to initial intervention and at a follow-up visit which took place about 6 months upon the completion of the four PRF sessions.

Statistical analyses

Study participants were divided into two groups: those who reported an at least partial adherence to dietary recommendations for the majority of the time (group A) and the rest (group B). Changes in FWAS scores were compared with Mann-Whitney U Test. Unpaired t-tests were utilized for normally distributed variables and chi-squared test for nominal data.

RESULTS

In all, 43 out of 47 patients completed the study: Two patients ceased treatment; one for financial reasons and the other due to the level of perceived pain associated with treatment. Another was lost in the follow up. The fourth patient reported a health problem (gynaecological cancer) which has not been reported during the PRF treatment and was excluded from the study.

Group A (subjects who reported an at least partial adherence to dietary recommendations for the majority of the time) consisted of 28 women and Group B of the remaining 15 women [**supplementary table 1**]. Demographic characteristics, total FWAS scores and their changes for each group are presented in table 2. An improvement in FWAS scores was recorded in both groups. However, as shown in table 2, improvement in total FWAS scores was statistically more significant in group A (adherent to dietary recommendations) ($z = 2.4$, $p = 0.008$).

	Group A ($n = 28$)	Group B ($n = 15$)	
Mean age (SD)	52 (8.5)	53.4(6.1)	$T = 0.53$, $p = 0.298$
Mean initial total FWAS (SD)	13.7 (3.9)	14.3 (4.6)	$Z = 0.23$, $p = 0.409$
Change of total FWAS (SD)	2.1 (2.4)	0.5 (1.9)	$Z = 2.4$, $p = 0.008$
Smoking	9	6	$X = 0.2655$, $p = 0.606$
Smoking cessation	1	0	
Average weight loss (kg)	0.5	0	

Table 2. Facial Wrinkles Assessment Scales and basic confounding parameters assessed in each group.

DISCUSSION

Blood concentrates are increasingly being utilized as autologous products for aesthetic purposes because they contain platelets for growth factor release, fibrin scaffold for tissue remodelling, plasma proteins for collagen synthesis, white cells for inflammation and recovery, and stem cells for tissue repair and regeneration. Their outcomes

regarding rejuvenation of photo aged facial skin has been shown in small trials[4,39]. This study was not intended to verify previous positive outcomes. In other words, whether surgeons' reported improvement in wrinkles scores is a biased or a true effect is beyond the scope of this observational study. A more appropriately designed study for this purpose has already been reported previously with positive results[4]. Current study was performed with the intention to see whether a personalized nutritional plan has an impact on PRF facial regeneration outcomes. For this reason, scorers were blinded to adherence to this plan. Thus, the additional skin aesthetics benefits conveyed by the dietary recommendations cannot be attributed to observer bias.

In addition, a relatively long-term adherence to a nutritional plan may be related to factors such as age, smoking or smoking sensation. All the patients were initially visited the clinic in order to have a minimally-invasive treatment. Personalized nutrition was offered as an add-on treatment. This may explain the relatively high percentage of the subjects (15/43) who opted not to adhere to a nutritional plan. Since a dietary change of a few days'duration, is unlikely to convey any skin changes in the long term (e.g., after 6 months) we only included those who sustained the recommended diet for at least half the study period. In this context a difference between the aforementioned factors (age, smoking) is possible andcan well influence skin appearance and aesthetic results and need to be tested in pragmatic studies in which predefined strict entry and exclusion criteria are difficult to apply. Nevertheless, a statistically significant difference in relation to these factors were not noticed between our study groups.

An increasing amount of evidence suggests a protective effect of "healthy diet" on skin ageing. Current dietary recommendations promote higher intakes of fruit and vegetables and fish and PUFAs (polyunsaturated fatty acids)[40,41]. Nevertheless, several studies over the past few years have shown that what constitutes a healthy diet for an individual depends to some extent on his or her physiology and lifestyle[42-45]. Individualized nutrition advice, informed by knowledge of genetic variants, are more

and more favoured over standard dietary guidelines based on population-wide averages[46].

Whether a personalized approach based on genotyping results conveys additional benefits over current nutritional recommendations in skin aesthetics, obesity, and other health issues is under study by various teams around the world. Regarding facial skin aesthetics, this study conforms to previous indicating a beneficial middle or long term effect of healthy nutrition[7,8]. In our cases, the inclusion of genetic variants helped the specification of general dietary recommendation that quite often propose a wide range of concentrations regarding macro-and micronutrients. This means that our personalized nutritional plans conformed to "healthy diet" and the proposed optimal nutrition intake to stave off skin ageing. In addition, the exact amounts of the various nutrients were further specified based on the genotype as exemplified above.

Any assessment of all the potential exposure variables, together with the various determinants of skin aging and appearance would require hundreds or thousands of subjects. Despite this, the present study shows that nutritional interventions can be an important element to acknowledge, especially if we consider the fact that our era is characterised by minimally invasive and holistic care in facial aesthetics. In general, the relevant data suggest that when nutritional recommendations are based on individual needs, they can improve the outcome of treatment, and consequently, should be considered as an integral part of any comprehensive care in facial aesthetics.

DECLARATIONS

Authors' contributions

Designed the study: Nacopoulos C, Vlastos I, Gkouskou K

Treated the patients: Nacopoulos C

Performed the molecular biology experiments and provided the nutrigenetic results: Gkouskou K

Offered the individualized nutritional plans: Lazou E

Assisted with data recording: Vesala AM

Supervised the whole process: Chaniotis D, Gkouskou K

Wrote and revised the initial draft: Nacopoulos C, Vlastos I, Gkouskou K, Vesala AM, Chaniotis D

Availability of data and materials

The datasets during and/or analysed during the current study available from the corresponding author on reasonable request.

Financial support and sponsorship

None.

Conflicts of interest

KG is the owner of Embiodiagnostics laboratory that provides a range of comprehensive genomic services to assist individuals to reach decisions on diet and lifestyles based on their DNA profile. The remaining authors disclose no conflict of interest.

Ethical approval and consent to participate

An ethical approval was granted by the Ethical and Scientific Committee of the Plastic and Reconstructive Surgery Department of Agioi Anargyroi General Oncological Hospital of Kifisia, Athens, Greece (No 1/26/09/2016) and the patients signed an informed consent prior to their treatment.

Consent for publication

Manuscript does not contain any individual person’s data.

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Figure 1. Horizontal forehead lines, zygomatic wrinkles or mid-cheek furrows, nasolabial folds, perioral expression wrinkles,and marionette line were scored. The first case had deeper wrinkles with a medium score of 4 and despite her weight loss an improvement can been seen in all but perioral lines. In the second case an improvement from a score of 3 to a score of 2 has been marked only for forehead lines (patients have provided consent for publication of their photos)