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Effication of amniotic membrane topical stem cell-conditioned medium combined with YAG erbium fractional laser 2940 nm in photoaging skin



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I Gusti Ayu Agung Praharsini¹, I Gusti Ayu Agung Elis Indira¹, Cita Rosita Sigit Prakoeswa^{2*},
Made Swastika Adiguna¹, Luh Mas Rusyati¹, Menul Ayu Umborowati²,
Irmadita Citrashanty², Maylita Sari²

ABSTRACT

Background: Skin ageing is a natural process in humans that is influenced by endogenous and exogenous factors. Nowadays, many people have the concept of health and skin beauty considered as one of the main factors that represent the perception of health in human wellness. Therefore, various anti-ageing therapy strategies that have been developed over the past few years include stem cell therapy. Amniotic Membrane Stem Cells (AMSC) are stem cell products taken from amniotic membranes that contain various proteins and have low immunogenicity. Objective: Proving that Amniotic Membrane Stem Cell (AMSC) metabolite products can improve the clinical picture of photoaging.

Method: Study design using one group pre and post-test design model. Samples were obtained by consecutive sampling and the number of samples was 33 people. Clinical examination of patients with the Glogou scale followed by an one smart skin analyzer. Application of AMSC products 3 times daily at intervals of 2 weeks

after the Erbium YAG Fractional 2940 nm laser and evaluation were carried out at weeks 0, 4, and 8.

Results: Pore diameter showed significant improvement ($p < 0.001$) from first to fifth visit (6.52 ± 0.57 vs 5.79 ± 0.7), wrinkles showed significant improvement ($p < 0.001$) from baseline compared to fifth visit (4.28 ± 0.38 vs 4.09 ± 0.20), pigment, moisture, and skin elasticity showed significant improvement ($p < 0.001$) from the (baseline) compared to fifth consecutive visits (4.35 ± 1.41 vs 3.09 ± 0.68), (42.2 ± 7.64 vs 59.1 ± 7.94), (48.2 ± 14.1 vs 61.7 ± 13.1) respectively. Sebum T Zone and U zone showed significant improvement ($p < 0.001$) from (baseline) and compared to fifth consecutive visit (12325 ± 10616.8 vs 2047.5 ± 1887.9) and (8529.8 ± 9026.8 vs 1560.6 ± 895.7). Side effects of urticaria were found in 1 person.

Conclusion: AMSC product therapy can be used as a potential for anti-ageing therapy.

Keywords: anti ageing, stem cell, treatment, rejuvenation

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¹Dermatology and Venereology Department, Faculty of Medicine, Universitas Udayana-Sanglah General Hospital, Bali-Indonesia

²Dermatology and Venereology Department, Faculty of Medicine, Universitas Airlangga-Dr. Soetomo Hospital, Surabaya, Indonesia

INTRODUCTION

Ageing of the skin is a complex biological process caused by intrinsic factors (genetic, hormonal) and extrinsic factors such as ultraviolet radiation.¹ Photoaging is a change in the aging of the skin due to external factors (chronic exposure to sunlight repeatedly).² Physiological changes in ageing skin manifest like xerosis, loss of skin barrier elasticity and function, wrinkles, thinning of the skin, atrophy of malar fat and changes in pigmentation. In ageing skin also has a decreased skin regenerative ability and this ability is regulated by stem cells. These ageing skin changes cause the patient to be insecure and do skin rejuvenation therapy. Various modalities of skin rejuvenation therapy are available and stem cells are one of the therapeutic options

used as anti-ageing.^{1,3}

Stem cell research has been proven to be a skin rejuvenation therapy because of the ability to renewal and cell differentiation. In the field of mesenchymal stromal cell dermatology (MSCs) it is often used. Many studies have examined the effects of conditioned media with stem cells which contain various proteins and growth factors. Amniotic Membrane Stem Cells (AMSC) are stem cell products taken from amnion membranes that have low immunogenicity. Stem cell therapy can be combined with laser therapy to enhance the effects of skin rejuvenation therapy.⁴ Based on the description above, a study was conducted to evaluate the efficacy of AMSC combined with the fractional Erbium YAG 2940 nm laser.

*Corresponding to:
Cita Rosita Sigit Prakoeswa;
Dermatology and Venereology Department, Faculty of Medicine, Universitas Udayana-Sanglah General Hospital, Bali-Indonesia;
drcita.rosita@gmail.com

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METHOD

This study uses one group pre-test and post-test design method. Samples are Glagou II-III photoaging patients who seek medical treatment in the outpatient unit of the Sanglah General Hospital cosmetic division and meet the inclusion criteria. Consecutive sampling method was used for sample recruitment. Clinical examination of patients with the Glogou scale for photo-damage classification scale and followed by examination using an a one smart skin analyzer. Evaluations were carried out at weeks 0, 4 and 8. Previously any sample treatment was primed with 0.025% tretinoin cream and SPF 30 sunscreen cream for 2 weeks and tretinoin 0.025% cream was stopped for 3 days before the intervention. In the study subjects, the Erbium YAG 2940 nm fractional laser was performed, followed by the application of metabolite amniotic membrane stem cell (PM-AMSC) products 3 times with intervals of 2 weeks.

The metabolite products used originate from amniotic membranes which are processed in the Stem Cell Institutes of Tropical laboratory at Airlangga University, procedures and processing are carried out according to international standards of human stem cell culture. The amniotic membrane was obtained from a healthy aterm neonatal born using caesarian section method and processed in the Integrated Surgery Center building Dr. Soetomo Hospital, Surabaya, in accordance with the protocol and approval of the Dr. Ethics Committee at the RSUD Dr. Soetomo. The amniotic membrane is processed so that cells are obtained for culture and the final result is a culture medium containing PM-AMSC.

Statistic analysis

Data analysis in this study using SPSS version 24.0 for Windows (IBM Corporation, Armonk, New York, USA). Descriptive analysis for subject characteristics, normality plot with test using Kolmogorov Smirnov, and mean comparison test to measure the improvement of all parameters measured at visits 1, 2, 3, 4 and 5 using repeated Anova test or Friedman test.

RESULT

Total of 33 study participant included in the study, the average age of the sample is 41.3 ± 5.2 years and all sample are female. Government employee constitutes the largest proportion of the work of the study participant. All samples were classified as Glagou scale 3 (Table 1).

Tabel 1. Study characteristics

Variable	n = 33
Age (Years)	
Mean \pm SD	41.3 \pm 5.2
(Min-max)	21-49
Occupation	
Housewife	2 (6.1)
Government employee	30 (90.9)
Private sector employee	1 (3.0)
Glogau scale	
Class III	33 (100)

Clinical improvement of photoaging manifestation after the administration of fractional Erbium YAG 2940 nm and PM-AMSC is shown in table 2. Pore diameter parameters showed significant improvement ($p < 0.001$) from visit I (baseline) and 5th visit (6.52 ± 0.57 vs 5.79 ± 0.7). The mean wrinkle improvement showed a significant improvement ($p < 0.001$) from the first visit (baseline) and the fifth visit (4.28 ± 0.38 vs 4.09 ± 0.20). For the parameters of pigment, moisture and skin elasticity showed significant improvement ($p < 0.001$) from visit I (baseline) and the 5th visit respectively (4.35 ± 1.41 vs 3.09 ± 0.68), (42.2 ± 76.4 vs 59.1 ± 7.94), and (48.2 ± 14.1 vs 61.7 ± 13.1) respectively. Measurement of the sebum variable T zone and U zone showed significant improvement ($p < 0.001$) from first visit (baseline) compared to fifth visit respectively (12325 ± 10616.8 vs 2047.5 ± 1887.9) and (8529.8 ± 9026.8 vs 1560.6 ± 895.7) respectively. Side effects in the form of urticaria were found in 1 sample (Table 2).

DISCUSSION

The spectrum of sunlight reaching 90% of the earth consists of UVA which can penetrate the epidermis and dermis and play a role in the photoaging process. UVA radiation has the effect of reducing the telomere length of fibroblasts in the skin, inhibiting TGF- β 1 secretion inducing G1 phase arrest, reducing superoxide dismutase (SOD), increasing malate dehydrogenase (MDH) levels and increasing MMP-1.4 expression. On histopathological examination, photoaging skin shows a reduced composition of the extracellular matrix. An extracellular matrix consisting of glycosaminoglycans, collagen and elastin which play a role in skin morphology and growth and elasticity functions.³

Stem cell therapy is one of the promising therapies for overcoming skin ageing.⁵ Stem cells have the ability to regenerate themselves, proliferate and

Table 2. Comparison of parameters of moisture, skin elasticity, pore diameter, pigment, wrinkles, and sebum U zone, and T zone

Variable	Measurement time					p-value
	Visit I	Visit II	Visit III	Visit IV	Visit V	
Pore diameter	6.52 ± 0.57	6.06 ± 0.72	5.97 ± 0.57	5.81 ± 0.70	5.79 ± 0.7	<0.001
Wrinkle	4.28 ± 0.38	4.16 ± 0.39	4.14 ± 0.29	4.09 ± 0.23	4.09 ± 0.21	<0.001
Pigment	4.35 ± 1.41	3.31 ± 0.68	3.10 ± 0.70	3.09 ± 0.69	3.09 ± 0.68	<0.001
Moisture	42.2 ± 7.64	4.99 ± 7.85	54.7 ± 7.24	56.6 ± 7.57	59.2 ± 7.94	<0.001
Skin elasticity	48.2 ± 14.1	49.9 ± 7.85	54.7 ± 7.24	56.6 ± 7.57	61.7 ± 13.1	<0.001
Sebum U zone	8529.8 ± 9026.8	2790.6 ± 2413.4	1879.5 ± 1502.2	1770.2 ± 1229.7	1560.6 ± 895.7	<0.001
Sebum T zone	12324.9 ± 10616.8	4085.8 ± 4619.6	2454.3 ± 2822.3	2405.0 ± 2655.7	2047.5 ± 1887.8	<0.001

differentiate and multiply themselves into various kinds of cells. Adult stem cells are pluripotent and can be explored from a variety of organs, one of which is derived from the amnion membrane.⁶ Amniotic membrane has the advantage of having low immunogenicity, reepithelization effect, anti-inflammatory, antifibrotic, antimicrobial and non-tumorigenic properties, flexible, has easy application and storage, and a source of stem cell.^{7,8} It also has the ability to synthesize and release biologically active substances such as tumor necrosis factor, interferon, transforming growth factor- α , TGF- β , epidermal growth factor, keratinocyte growth factor, hepatic growth factor, interleukin-4, IL-6, IL-8 natural inhibitors of metalloproteases, β -defensins, and prostaglandins, so that the amniotic membrane is good as a candidate for cellular therapy regenerative treatment.⁷ The stem cell amniotic membrane can stimulate the synthesis of extracellular matrix which causes an increase in collagen deposits.⁸

Prakoeswa et al.⁹ study reported 48 female patients with Glogau scale II and III were randomly grouped into group I who received amniotic stem cell membranes and group II who received normal saline, with a frequency topical application 3 times daily and performed micro-needling aimed at increasing penetration. Clinically significant photoaging improvements were found between groups I and II ($p < 0.05$). Meanwhile, Pratiwi et al.¹⁰ study also reported 12 photoaging subjects given topical amniotic membrane stem cell metabolite products, shows clinical photoaging improvements with minimal side effects. Likewise in this study, from 30 subjects with clinical photoaging, PM-

AMSC administration and Erbium YAG 2940 nm fractional laser showed significant clinical improvement in photoaging ($p < 0.001$).

CONCLUSION

The administration of PM-AMSC topically with fractional laser modalities can be used as a skin rejuvenation therapy.

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CONFLICT OF INTEREST

The author declares there is no conflict of interest regarding the publication of current article.

ETHICAL STATEMENT

All of the study protocol has been approved by Ethical Committee Faculty of Medicine, Universitas Udayana-Sanglah General Hospital with ethical clearance reference number 2139/UN14.2.2.VII.14/LP/2018. All participant received written signed informed consent before any data collection and all study procedure in accordance with the declaration of Helsinki.

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