The Comparison of the Effects of Caffeine Topical 0.25% and 0.5% as Anti-wrinkle Therapy

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Abstract: This 4-weeks, double-blind, randomized, controlled clinical study was conducted to compare the effects of topical caffeine 0.25% with 0.5% on barrier function and elasticity in the skin. A total of 41 healthy subjects consisted of male and female aged 20-60 y.o. The subjects were grouped into two. Each group received a topical caffeine with different concentrations of 0.25% and 0.5%. Hydroxyethylcellulose (HEC) gel as the placebo has 97.5% water content. Physical stability test was conducted at the preparation. The treatment was performed on the forehead and periorbital by applying a topical caffeine 0.25% on one forehead and periorbital and 0.5% on the others. Application of gels was performed 2 times daily for 4 weeks. Measurement of Transepidermal Water Loss (TEWL) using Tewameter® TM300 and elasticity using Elastometer® EM25 were performed before and after treatment. Clinical evaluations for efficacy were made at baseline and after two and 4 weeks of gel use. The measurements results were analyzed using one-way Annova. Overall, the results of the study showed that topical caffeine applications can improve skin barrier function and increase the elasticity the skin especially as anti wrinkle.

1 INTRODUCTION

The process of aging or aging is a natural process and will affect every individual. Aging is a gradual process of organ decadence and its function associated with aging after undergoing a maturation process characterized by decreased ability, gradual deterioration of organs and functions that eventually will experience the tendency of death (Saghrani & Baumann, 2002). The aging process begins when the growth ends, where the process is characterized by gradual negative effects of age in the organ system, decreased organ function, degeneration and changes in the structure of proteins and enzymes. The main features are organ and tissue dysfunction and decreased ability or total loss of adaptation to environmental changes. There are many factors that interact in this aging process, whether social, economic, diseases, nutrition, hereditary, lifestyle and others (Brandner et al., 2008).

There are two main processes that trigger aging of the skin or skin aging. They are intrinsic and extrinsic factors. Stochastic processes implicate random cell damage as a result of mutations during the metabolic process due to free radical production.

While extrinsic aging is caused by environmental factors such as exposure to sunlight, air pollution, smoking, alcohol abuse and poor nutrition. Intrinsic aging refers to a genetic and time-dependent background. Various expressions on intrinsic aging include smoothing and thinning of the skin that exacerbate the appearance of expression lines. In aging skin is extrinsically characterized by photodamage such as wrinkles, pigmented lesions, hypopigmented patches and actinic keratosis (Zegarska et al., 2010).

Caffeine is one of the alkaloids which can be found in coffee, tea and some soft drinks. Caffeine which has the name of chemical compound 1,3,7-trimethylxanthine has been widely used in making various kinds of cosmetic products (Herman & Herman, 2013). Topical caffeine has been produced in the form of creams and lotions since it is known to have many effects on the skin as it can slow the aging process due to ultraviolet light, absorb ultraviolet radiation, prevent skin cancer, an active component in anti-cellulite preparations, potent antioxidants, increase blood microcirculation in skin and also stimulates the growth of hair through inhibition of the 5-α-reductase activity (Fischer et al., 2008; Kawasumi et al., 2011 Kim et al., 2002; Krutmann &

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Gilchrest, 2014; Salminen & Kaarniranta, 2010). The use of caffeine in cosmetic products with concentrations up to 3% is still considered safe, not toxic, and easily absorbed into human skin (Brandner et al., 2006). Caffeine's ability to augment elimination of UV-damaged cells via apoptosis may be relevant for its protective effects on UV-induced skin tumor development (Kawasumi et al., 2011).

This study is expected to show the effects of caffeine in inhibiting the effects of ultraviolet radiation on the skin by measuring the elasticity of the skin. The mechanism of action of caffeine in the cosmetic field is not fully known, thus it needs a lot of studies to prove whether caffeine is proven to improve skin appearance. The ability to penetrate caffeine through the skin barrier is a basic principle that must be known before (Kim et al., 2002). The objective of this study was to determine the efficacy of topical caffeine with concentrations of 0.25% and 0.5% to skin elasticity so that it can be as anti-wrinkle therapy.

2 METHODS

An analytical observational, randomized control study with clinical test approach, before after design in dermatovenereology outpatient clinic Dr. Moewardi general hospital Surakarta, from November to December 2017. A total of 41 subjects were randomized into 2 groups. The inclusion criteria were age 20-60 y.o, no allergic reaction, no skin lesions or suffering from certain skin diseases, did not have chronic metabolic disease and were willing to follow the study by signing informed consent. Each group received topical caffeine with different concentrations. The concentrations of caffeine gel were 0.25% and 0.5%. Caffeine gel applied on the forehead and periorbital region 2 times a day for 4 weeks and measurements was done every 2 weeks.

The active ingredient of caffeine from anhydrous caffeine crystalline powder with 100% content and no water content. The crystalline powder is dissolved into a hydroxyl cellulose (HES) solvent with a moisture content of 97.5%. Preparation of HES gel by mixing 2.5 mg of HES powder into 1 liter of water (H2O), then stand for 4-5 hours, Topical caffeine is made by adding anhydrous caffeine powder according to the concentration required in HES gel. The process produces topical caffeinated caffeine with a concentration of 0.25%, and 0.5%. Physical stability tests were performed on the material before being applied to the study subjects.

The TEWL measurement using Tewameter® TM300 (Courage & Khazaka electronic GmbH Cologne Germany) was conducted before and after treatment. Measurements were performed in a room with a temperature of 23 - 27^{o}C and humidity of 56 - 62%. The acclimation process is done for 15 minutes. The measurement area is cleaned with water and dried with a tissue, then divided into 3 areas vertically and each area is measured for 30 seconds. The value recorded was the average value of the three measurements.

Elasticity measurement using Elastometer® EM25 (Courage & Khazaka electronic GmbH Cologne Germany) was performed before and after treatment. Prior to measurement, the area is cleaned with water and dried with a tissue and then the probe was vertically mounted and pressed slightly until a sign sounds along with the appearance of the result value on the monitor. The measurements were made 4 times at different locations and then recorded the mean value.

The data were processed and analyzed using a computerized statistical program using the One-Way Annova test.

3 RESULTS

The demographic data in our study showed that the study subjects characteristics of each group based on sex and age had the same ratio of 50%. (Figure 1) After caffeine gel preparation with concentrations of 0.25 and 0.5%, TEWL measurement results in all groups showed a decrease in TEWL. The TEWL measurement in forehead showed that after application 0.25% caffeine gel in the 1st visit 33.60 g hm-2 to 27.05 g hm-2 and the last visit become 33.60 g hm-2 with p-value 0.492 and after 0.5% caffeine gel from 34.9 g hm-2 to 27.10 g hm-2 and 4th week become 29.50 g hm-2 (p-value 0.351). (Figure 2A). While, the 0.25% caffeine group showed a decrease of TEWL at the crow's feet of 19.77± 10.72 (1st visit) to 15.30 ± 6.80 in 2nd week and become 17.34 ± 7.04 g hm-2 (4th week) while the 0.05% caffeine group decreased TEWL which 1st visit was 16.76 ±8.43 g hm-2 to 13.62±6.96 (2nd week) and 12.73 ± 4.69 g hm-2 (3rd visit) with p-value p=0.16 and 0.25 (Figure 2B). In the 0.25% caffeine group showed an increase in elasticity forehead from 64.24 ± 9.64% to 2nd visit become 68.82±9.60% and last visited become 69.09 ± 13.36% with p-value 0.301 and 0.5% caffeine group showed an elasticity increase from 61.35 ± 8.31% to 2nd visit 67.32±6.45 and 3rd visit become 69.54 ± 13.36% with p value 0.024 (significant) (Figure 3.A).

Crow's feet elasticity in 0.25% caffeine group resulted an elasticity increase 62.17±14.7% at 1st visit to 66.98±13.2 % and last visit become 64.22±20.76% with p value =0.656. On the other hand, 0.5% caffeine group showed elasticity at 1st visited 60.85+12% to 67+11.44% and the 3rd visit become 68+17.22% (p value= 0.165) (Figure 3.B).

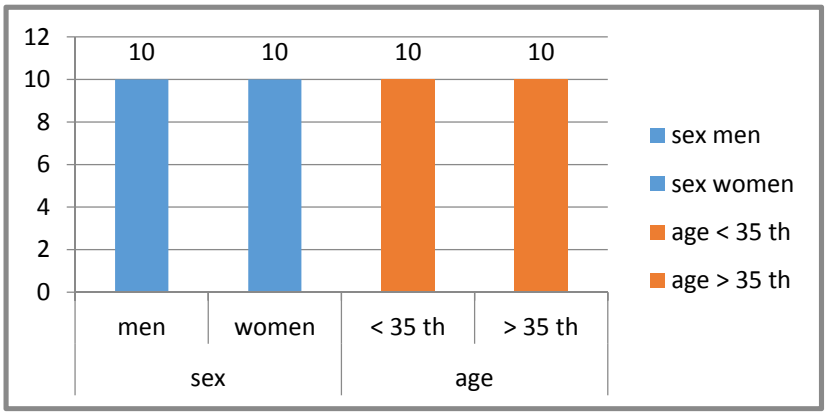

Figure.1 demographic data of research subjects by sex and age have the same distribution

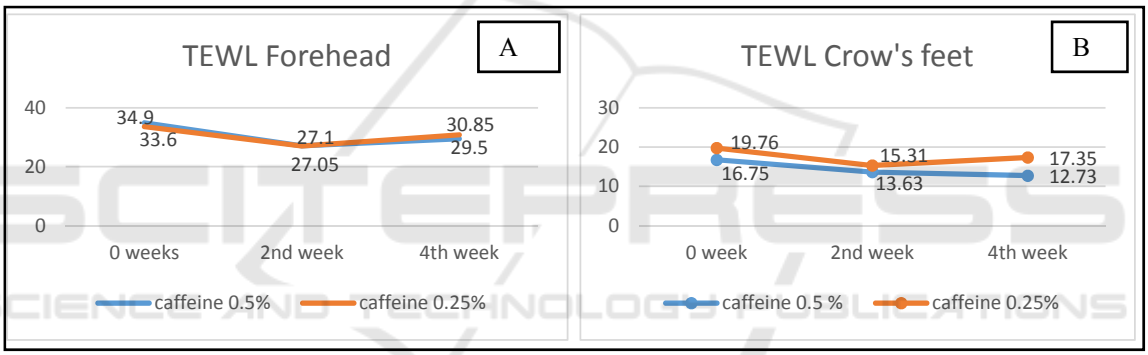

Figure 2. A. Results Measurement of TEWL between caffeine 0.25% and 0.5% on forehead. B. Results measurement of TEWL on crow's feet.

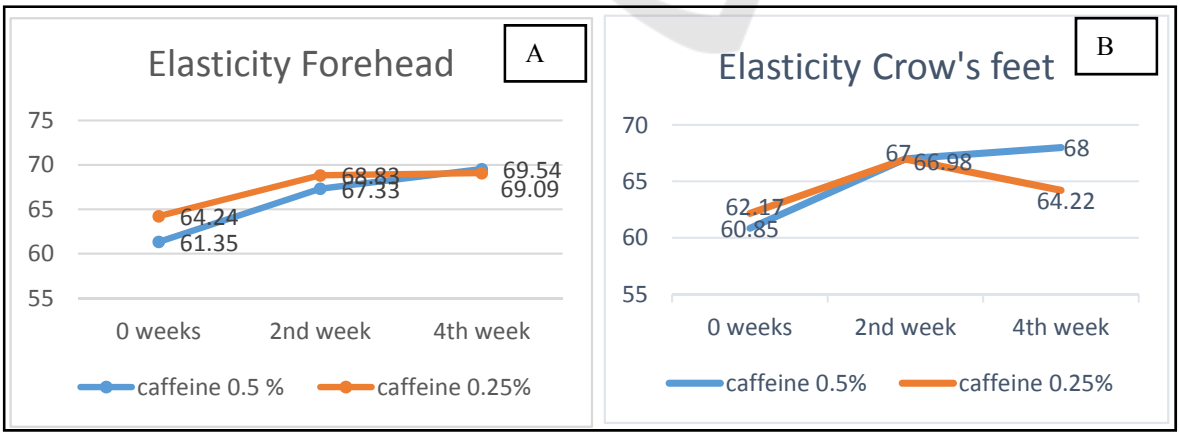

Figure 3. A. Results Measurement of elasticity between caffeine 0.25% and 0.5% on forehead. B. Results measurement of elasticity on crow's feet.

4 DISCUSSION

Aging skin is important because it has a social impact. The skin is a real organ model that represents an aging process. Biological clocks on both skin and internal organs on the same path cause irreversible degeneration processes (Krutmann & Gilchrest, 2014). The aging process begins at the end of growth, which is marked by the gradual negative effect of age in the organ system, decreased organ function, degeneration and changes in the structure of proteins and enzymes. The main features are organ and tissue dysfunction and decreased ability or total loss of adaptation to environmental changes. There are many factors that interact in this aging process, whether social, economic, diseases, nutrition, hereditary, lifestyle, and others (Salminen & Kaarniranta, 2010). Currently caffeine is known to be effective for aging skin care, especially related to cardiovascular disease and cognitive function improvement (Takahashi & Ishigami, 2017).

Coffee and caffeine have been widely used in cosmetic production lately. The use of caffeine in cosmetic products with concentrations of up to 3% is still considered safe, not toxic, and easily absorbed into human skin. Caffeine topically proves safe and does not damage liver cells. In the Gajewska et al. Study, there was no caffeine effect on liver cell survival after peroral and transdermal uptake (up to 5.33mg / kg BW) (Gajewska et al., 2015).

Active compounds in cosmetic ingredients should have the ability affecting cell metabolism and other processes that occur in the skin. It largely depends on the capacity of the molecule to penetrate the skin barrier. Caffeine in the form of hydrophilic preparations is often used in studies of caffeine penetration in the skin (Saghrani & Baumann, 2002). The use of preparations in the form of microemulsions accompanied by higher water concentrations may also increase the absorption of caffeine (Ma et al., 2015). In this study we used HEC in the form of gel and more moisture content high (97.5%) than previous study (87.5%) (Brandner et al., 2006). This study found a decrease in TEWL in the use of caffeine 0.5% compared to 0.25% caffeine. Several studies have suggested that topical caffeine effects will improve the function of epidermal barrier, as indicated by a decrease in TEWL starting in the second week (Brandner et al., 2006).

The role of free radicals is known in the replicative senescens phase, intrinsic and extrinsic aging shown in various biological processes. The role of topical caffeine improves the function of epidermal cellular so as to also play an active role in the aging process (Kochanek et al., 2000). In Magdalena et al study, there is a decrease in the elastin index, indicating that in aging with various wrinkle formations, caffeine decreases collagen synthesis in human fibroblast cultures (Herman & Herman, 2013). Fibroelastic skin can be influenced by many things, such as sun exposure, fat tissue enlargement, decreased circulatory system and lymphatics. The effect of caffeine on this is as lipolytic (Herman & Herman, 2013). By inhibiting phosphodiesterase, there will be an increase in cAMP which stimulates the degradation of triglycerides into free fatty acids by triglyceride lipase, thus inhibiting fat accumulation (Vogelgesang et al.,2011). In addition, caffeine also increases catecholamines in adipose tissue that stimulate peripheral lipolysis by acting on adrenaline-sensitive lipases (Bertin et al., 2001). In this study, topical caffeine in all groups had a decrease effect of TEWL and increased elasticity on the skin especially in the 0.5% caffeine group during the second week.

5 CONCLUSIONS

Our findings proved that topical caffeine administration can improve skin barrier function by decreasing TEWL and increasing skin elasticity index. Further research is needed to prove the efficacy of topical caffeine in wrinkle therapy, using larger samples.

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