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Deeper Wrinkle Formation and Less Melanin Production in Aged Korean Women with B Blood Type

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Dear Editor:

ABO blood type was found from coagulation phenomenon during the blood transfusion, resulted from the individual expression of blood group antigens on the red blood cell (RBC) surface that is decided by individual's ABO gene polymorphism[1]. The antigen for O blood type (H antigen), synthesized by α-1,2-fucosyltransferase (FUT) 1 or 2, is a precursor for A and B blood type antigens which are synthesized by A transferase or B transferase translated from sub-alleles of ABO genes[2,3]. O alleles are non-functional sub-alleles of ABO genes[3]. Therefore, ABO blood type is decided by combination of two ABO alleles of individual[1,3].

In addition to the RBCs, the blood group antigen expression was also found on many other tissues or secretions, including the granular layer of the epidermis[2,4]. However, still little evidence for their physiological roles has not been accumulated yet. Therefore, in this study, blood type-specific difference in skin photoaging-related phenotypes, including wrinkle, elasticity, and skin color, were investigated from aged healthy Korean women (age range, 66~84 years; mean age±standard error of mean, 72.9±0.41 years; total n=99; n=29 for blood type A; n=26 for B, n=31 for O, n=13 for AB). Wrinkle depth and elasticity at the skin near eyes (1.5 cm-away area) were measured using Skin-Visiometer® SV 600 and Cutometer® MPA 580 (Courage & Khazaka Electronic, Köln, Germany), respectively. Facial facultative skin color was determined by measuring erythema index (EI) and melanin index (MI) in normal areas and hyperpigmented areas using Mexameter® MX16 (Courage & Khazaka Electronic)[5]. Detailed experimental methods and information were described in Supplementary material. This study was approved by the institutional review board of Seoul National University Hospital, and all of the subjects gave written informed consent, which was reviewed by the board (IRB no. H-1205-035-409).

As a result, B blood type individuals showed the highest mean values among the four blood types for all eye wrinkle depth parameters (R1~R5), and R3 and R4 showed significantly higher measurements in B blood type individuals than non-B blood type individuals by Student t-test (p=0.020 for R3, p=0.0499 for R4) (Fig. 1A). In addition, correlation of individuals' R3 values with age was not observed in other blood types, probably because individuals involved in this study are highly aged (>65 years); however, significant correlation of R3 with age (R^2=0.3209, p=0.003) was only observed in B blood type individuals (Fig. 1B). These results imply that individuals with B blood type in aged Korean women may have deeper eye wrinkles than non-B blood type individuals and may have a little bit more sensitive skin to solar ultraviolet (UV) irradiation than other blood types.

For elasticity at the skin near eyes, the tendency of the

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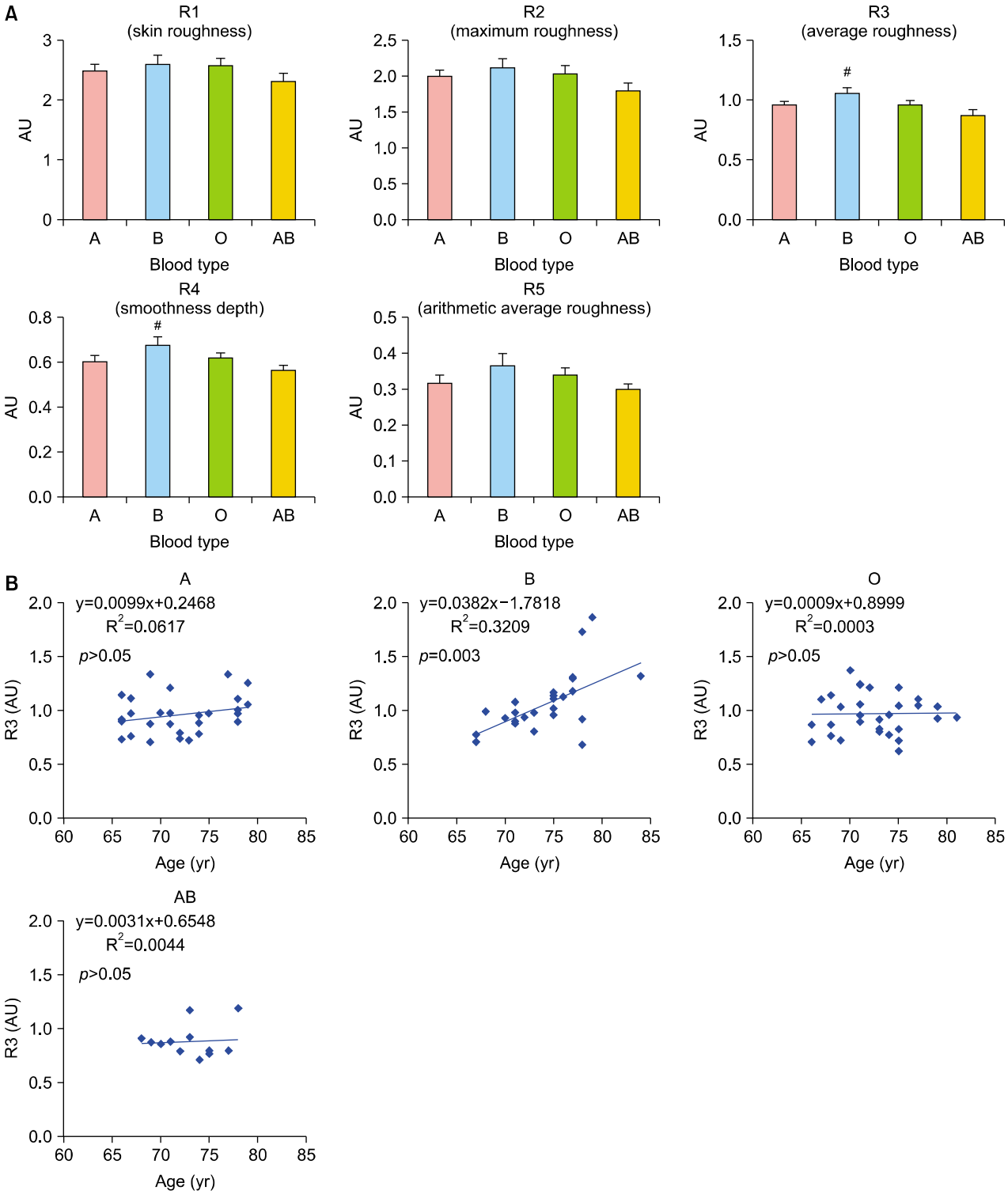

Fig. 1. Deeper eye wrinkle depth in aged Korean women with B blood type. (A) Wrinkle depth at skin near eyes (1.5 cm-away area) of aged Korean women (age range, 66∼84 years; mean age±standard error of mean (SEM), 72.9±0.41 years; total n=99) were measured using Skin-Visiometer® SV 600 (Courage & Khazaka Electronic, Köln, Germany), and analyzed according to the blood type. Measured R1∼R5 values (parameters from Skin-Visiometer) were shown as mean values±SEM for each blood type group (n=29 for A, n=26 for B, n=31 for O, and n=13 for AB). $^{\#}p<0.05$, vs. non-B blood type (A) by Student t-test. AU: arbitrary unit. (B) Correlation of age and R3 (average roughness) values in aged Korean women were shown for each blood type group, and analyzed by regression analysis. The *p*-values below 0.05 were considered as significant from regression analysis. All the measurements were performed in a controlled environment room with a constant room temperature (20°C to 25°C) and humidity (45% to 55%).

lowest measurement in B blood type individuals was also observed in R5 (net elasticity), R6 (viscoelastic/elastic ratio), and R7 (elastic portion), while other parameters did not show B blood type-specific tendency (Supplementary Fig. 1). These results also imply that individuals with B blood type may have the worse elasticity in several parameters; however, increasing sample number may provide more accurate observation for the relationship between blood type and skin elasticity.

For skin color in normal and hyperpigmented areas, EI did not show any blood type-dependent difference; however, MI in normal areas showed significantly lower mean values in B blood type individuals than non-B blood types by Student t-test ($p=0.014$), but not in hyperpigmented areas ($p=0.258$) (Fig. 2). These results imply that B blood type individuals may have brighter facultative skin color than non-B blood type with less melanin production. In addition, ratio of hyperpigmentation occurrence in our data was similar among the blood types (Supplementary material), suggesting that less melanin production may not be caused by less exposure to UV.

Therefore, it can be suggested that less melanin production in B blood type individuals may provide less protection from chronic sun exposure, which possibly results in further facial wrinkle formation than other blood types; however, more evidence should be gathered.

Nonetheless, many studies have reported the correlation between ABO blood type and incidence of several types of cancers, microbial infectious diseases, and cardiovascular diseases, and a chronic pancreatitis[1,6,7], suggesting that there should be underlying mechanisms for these ABO blood type-specific phenotypes.

In our speculation, because ABO blood type antigen expression is observed only in keratinocytes at the granular layer and upper spinous layers, but not in while fibroblasts or melanocytes[4], the blood type-specific regulation of wrinkle formation and melanin production may be mediated via some indirect regulations finally targeting for the ABO antigen-absent cells. Or, it is possibly because of the association of ABO blood type and personality trait-related genes, i.e., catecholamine activity-related enzymes, including dopamine beta hydroxylase (DBH), catechol-O-methyltransferase (COMT), and monoamine oxidase A (MAOA)[8]. DBH catalyzes the conversion of dopamine to norepinephrine COMT and MAOA catalyze the degradation of neurotransmitters, primarily dopamine and norepinephrine[8]. That association between ABO and DBH genes is from the linkage disequilibrium due to their close position (9q34), and the association between ABO and COMT is also possibly explained by the close position of calcium voltage-gated channel subunit alpha1 B (CACNA1B, 9q34) to DBH, which is involved in regulation of COMT expression[8].

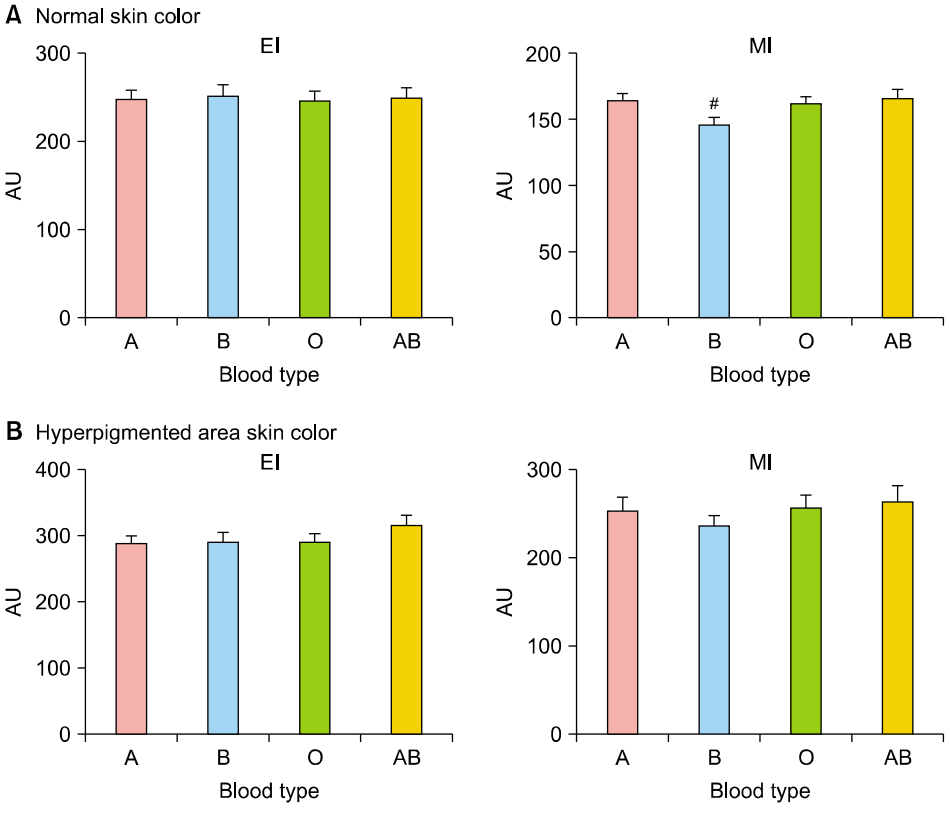

Fig. 2. Less melanin production in aged Korean women with B blood type. Erythema index (EI) and melanin index (MI) were measured using Mexameter® MX16 (Courage & Khazaka Electronic, Köln, Germany) at the normal-looking area (A) and hyperpigmented area (B) in face of aged Korean women (66~84 years, 72.9±0.41 years, n=99), and analyzed according to the blood type. All the measurements were performed in a controlled environment room with a constant room temperature (20°C to 25°C) and humidity (45% to 55%). $^{\#}p<0.05$ vs. non-B blood type by Student t-test. AU: arbitrary unit.

Actually, B blood type individuals are tended to have low activity of DBH and a decreased expression of COMT. In addition, less activity of MAOA gene is tended to be observed in O blood type individuals with unknown mechanism[8].

Catecholamines can be produced by epidermal keratinocytes, and their receptors are expressed in both keratinocytes and melanocytes[9]. In addition, chronic psychological stress is reported to increase wrinkle formation in mice through catecholamines[10]. Therefore, blood type-associated variation of catecholamine regulation possibly has potential to give some clues for our B blood type-related skin phenotype.

Elucidating the underlying mechanisms seems hard, because of many influencing factors, including the unknown blood type antigen-specific molecular actions or responses to exposure to UV, smoking, detergents, cosmetic ingredients, foods, and etc. However, despite small numbers of volunteers, this study may provide some clues for designing further investigating studies for blood type-specific skin phenotypes and their underlying mechanisms.

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SUPPLEMENTARY MATERIALS

Supplementary data can be found via http://anndermatol.org/src/sm/ad-30-364-s001.pdf.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

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Supplementary material

Experimental Methods and supplementary tables

Aged healthy Korean women (age range, 66～84 years, mean age±standard error of mean (SEM), 72.9±0.41 years,;total n=99; n=29 for blood type A; n=26 for B, n=31 for O, n=13 for AB), whose facial wrinkle grade is 3 or more by photographic scale (Grade 0～7)*, were involved in this study. Their blood types were determined by blood typing reagents (Merck Millipore, Darmstadt, Germany), and all measurements by instruments for wrinkle, elasticity, and skin color were performed in a controlled environment room with a constant room temperature (20°C to 25°C) and humidity (45% to 55%). The wrinkle depth and elasticity at the skin near eyes (1.5 cm-away area) were measured using Skin-Visiometer® SV 600 and Cutometer® MPA 580 (Courage & Khazaka Electronic, Köln, Germany), respectively†. Facial facultative skin color was determined by measuring erythema index (EI) and melanin index (MI) in normal areas and hyperpigmented areas using Mexameter® MX16 (Courage & Khazaka Electronic)*. This study was approved by the institutional review board of Seoul National University Hospital, and all of the subjects gave written informed consent, which was reviewed by the board. Detailed sample information of each blood type is shown in Supplementary Table 1. Parameters for the instruments are described in Supplementary Table 2. Ratio of hyperpigmentation occurrence is shown in Supplementary Table 3.

*Chung JH, Lee SH, Youn CS, Park BJ, Kim KH, Park KC, et al. Cutaneous photodamage in Koreans: influence of sex, sun exposure, smoking, and skin color. Arch Dermatol 2001;137:1043-1051.
†Yoon HS, Lee SR, Chung JH. Long-term topical oestrogen treatment of sun-exposed facial skin in post-menopausal women does not improve facial wrinkles or skin elasticity, but induces matrix metalloproteinase-1 expression. Acta Derm Venereol 2014;94:4-8.

Supplementary Table 1. Sample numbers and mean ages of each blood type

Blood type	n	Mean age (yr)
A	29	71.9±0.82
B	26	74.3±0.80
O	31	72.5±0.70
AB	13	73.2±0.88
Total	99	72.9±0.41

Values were shown as mean±standard error.

Supplementary Table 2. Parameters for Cutometer® MPA 580 and Skin-Visiometer® SV 600

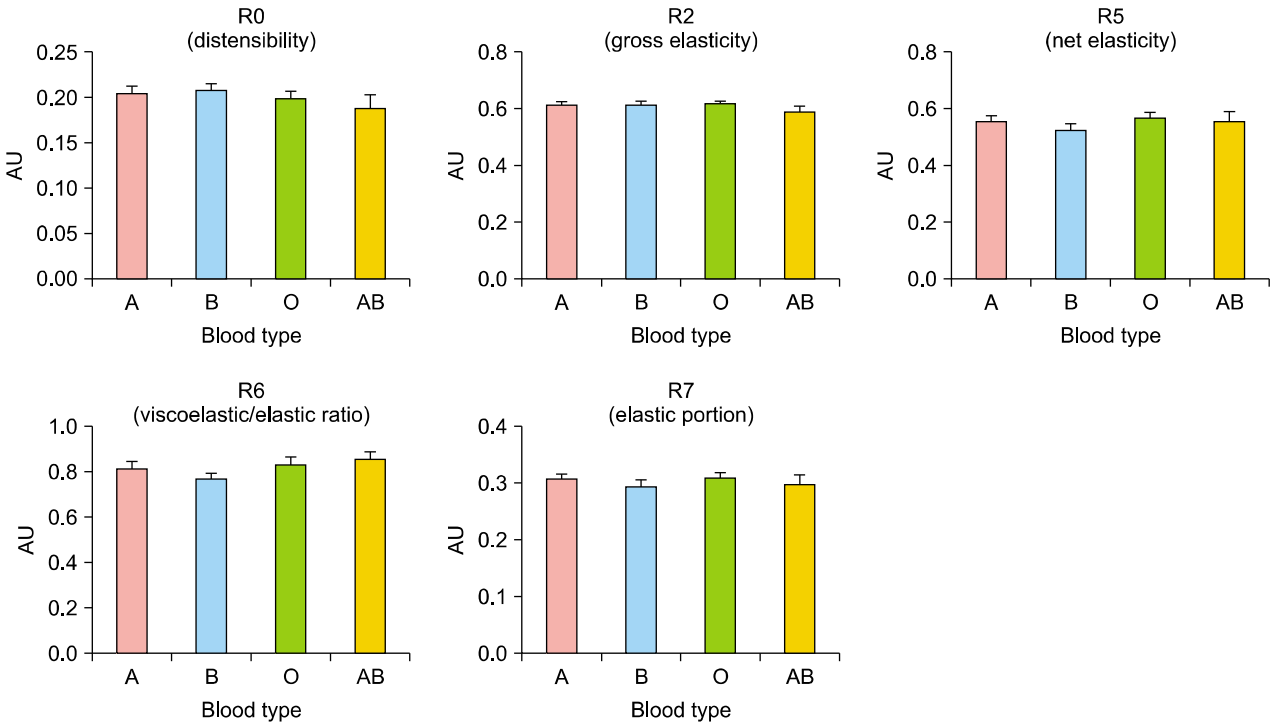
Parameters of Cutometer® MPA 580*	Description
R0	First maximum amplitude after suction (Distensibility)
R1	First minimum amplitude after relaxation
R2	Gross elasticity; (R0-R1)/R0
R3	Last maximum amplitude after repeated suction/relaxation
R4	Last minimum amplitude after repeated suction/relaxation
R5	Net elasticity; elastic portion of relaxation/elastic portion of suction
R6	Viscoelastic/elastic ratio; viscoelastic portion/elastic portion of suction
R7	Elastic portion; elastic portion of relaxation/R0
R8	Complete relaxation; R0-R1
R9	Tiring effect; R3-R0
Parameters of Skin-Visiometer® SV 600†	**Description**
R1	Skin roughness
R2	Maximum roughness
R3	Average roughness
R4	Smoothness Depth
R5	Arithmetic average roughness

*Akhtar N, Zaman SU, Khan BA, Amir MN, Ebrahimzadeh MA. Calendula extract: effects on mechanical parameters of human skin. Acta Pol Pharm 2011;68:693-701.

†Yoon HS, Lee SR, Chung JH. Long-term topical oestrogen treatment of sun-exposed facial skin in post-menopausal women does not improve facial wrinkles or skin elasticity, but induces matrix metalloproteinase-1 expression. Acta Derm Venereol 2014;94:4-8.

Supplementary Table 3. Occurrence of hyperpigmentation according to the blood types

Blood type	N	No hyperpigmentation (n)	Hyperpigmentation (n)	Ratio of hyperpigmentation (%)
A	29	9	20	69.0
B	26	7	19	73.1
O	31	11	20	64.5
AB	13	4	9	69.2
Total	99	31	68	68.7



Supplementary Fig. 1. Measurement of facial skin elastic property in aged Korean women according to the blood types. Skin elasticity at skin near eyes (1.5 cm-away area) of aged Korean women (66～84 years, 72.9±0.41 years, n=99), and were measured using Cutometer® MPA 580 (Courage & Khazaka Electronic, Köln, Germany), and analyzed according to the blood types. Among the parameters from Cutometer for skin elasticity (R0-R9), mean values±standard error of mean (SEM) of average values of R0 (distensibility), R2 (gross elasticity), R5 (net elasticity), R6 (viscoelastic/elastic ratio), and R7 (elastic portion) were shown for each blood type group. Amon 10 parameters of Cutometer, the tendency of the lowest measurement in B blood type individuals was also observed in R5 (net elasticity), R6 (viscoelastic/elastic ratio), and R7 (elastic portion), while other parameters did not show B blood type-specific tendency. Their differences were not significant by Student *t*-test (B vs. non-B, $p=0.197$ for R5, $p=0.100$ for R6, $p=0.341$ for R7). These results imply that individuals with B blood type may have the worse elasticity in several parameters; however, increasing sample number may provide more accurate observation for the relationship between blood type and skin elasticity. All the measurements were performed in a controlled environment room with a constant room temperature (20°C to 25°C) and humidity (45% to 55%). AU, arbitrary unit.