Original paper

Skin biophysical parameters and serum dermokine levels in airline pilots: a comparative study with office workers

Piercarlo Minoretti[1,2], Andrés S. Santiago Sáez[2], Ángel F. García Martín[2], Miryam Liańo Riera[2], Manuel Gómez Serrano[2], Enzo Emanuele[3]

[1]Studio Minoretti, Oggiono, Italy
[2]Department of Legal Medicine, Psychiatry and Pathology, School of Medicine, Complutense University of Madrid, Madrid, Spain
[3]2E Science, Robbio, Italy

Adv Dermatol Allergol 2023; XL (6): 757–761
DOI: https://doi.org/10.5114/ada.2023.132262

Abstract

Introduction: Concerns are growing in the aviation industry about occupational skin diseases like malignant melanoma (MM) among airline pilots (APs), due to the unique working environment that exposes them to various skin stressors.
Aim: To compare five skin biophysical parameters in a group of 40 male APs, each matched in terms of age and service tenure (minimum of 5 years) with a control group of 40 male office workers (OWs). Considering the potential role of dermokine (DMKN) in skin barrier dysfunction and the pathogenesis of MM, we further analyzed the serum levels of this molecule and correlated them with the measured skin parameters.
Material and methods: Stratum corneum skin hydration, transepidermal water loss (TEWL), sebum content, erythema index (EI), and melanin index (MI) were quantified by non-invasive instruments in the cheek region. Serum DMKN levels were measured using a commercially available enzyme-linked immunosorbent assay kit.
Results: Compared with OWs, the skin of APs exhibited a decrease in hydration levels in the stratum corneum, coinciding with a higher TEWL. However, there was no significant variance in sebum content between the groups. MI was notably higher in APs than in OWs, as was EI. In APs, serum DMKN levels were independently associated with MI ($\beta = 0.56$, $p < 0.05$).
Conclusions: We found a significant link between the profession of an airline pilot and changes in skin biophysical parameters. Further research into the interplay between serum DMKN levels and the risk of MM in APs is warranted.

Key words: airline pilots, skin biophysical parameters, dermokine.

Introduction

The aviation environment exposes airline pilots (APs) to numerous direct and indirect skin stressors, leading to the increased medical attention towards occupational skin diseases within the aerospace industry [1]. Exposure to various irritants and allergens, such as jet fuel, aircraft materials, batteries, and chemicals, pose significant occupational risk factors for skin disorders [2]. Additionally, during flight, pilots are exposed to ultraviolet (UV) radiation and low-dose cosmic ionizing radiation [3–5]. Although prior studies have identified APs as a professional group with an increased risk of both malignant melanoma (MM) [6] and non-melanoma skin cancer [7], the degree to which exposure to in-flight radiation contributes to this heightened risk continues to be a subject of debate [5, 8]. In addition to direct skin stressors, there are at least two indirect factors that may negatively impact the skin health of flying personnel. Studies in the general population [9, 10] have shown that poor sleep quality and low sleep efficiency, which are common among APs [11, 12], can lead to an increased transepidermal water loss (TEWL) and decreased skin barrier functionality. Furthermore, psychological stressors, which are prevalent in the aerospace industry [13], may also impair the skin's epidermal barrier, resulting in reduced stratum corneum (SC) hydration and elevated TEWL [14, 15].

When the epidermal barrier is disrupted, the keratinocytes respond by producing a variety of soluble mediators. These include cytokines and chemokines, which

Address for correspondence: Enzo Emanuele MD, PhD, 2E Science, Via Monte Grappa 13, I-27038 Robbio (PV), Italy, phone: +39 3385054463, e-mail: enzo.emanuele@2escience.com
Submitted: 16.07.2023, **accepted:** 8.08.2023.

lead to the activation of resident skin lymphocytes or the recruitment of leukocytes [16]. In recent years, a skin-specific glycoprotein known as dermokine (DMKN), found primarily in the upper layers of the epidermis, has been discovered to play a pivotal role in the interaction between skin barrier dysfunction and inflammation [17]. Significantly, DMKN has been observed to exhibit an approximate ten-fold increase in mesenchymal stem cells cultured under hypoxic conditions [18]. Hypoxia can occur in aviation even in pressurized environments, whether due to life support systems failure or incorrect equipment usage [19]. In a recent study, Ma *et al.* [20] have also shown that DMKN expression might be persistently increased, triggering the epithelial-mesenchymal transition signalling pathway, in human MM – a malignancy whose risk is known to be elevated among APs [6].

Aim

In the current study, we hypothesized that the combined effects of direct and indirect occupational skin stressors may deteriorate the skin quality of APs. To gather comprehensive data, we initiated this investigation focusing on five skin biophysical parameters, particularly in the cheek region, selected as a representative of a non-oily and sun-exposed facial area. We examined these characteristics in a group of 40 male APs, each matched in terms of age and service tenure (minimum of 5 years) with a control group of 40 male office workers (OWs). Considering the potential role of DMKN in skin barrier dysfunction [17] and the pathogenesis of MM [20], and its possible regulation by hypoxic conditions, we further analyzed the serum levels of this molecule and correlated them with the observed skin parameters.

Material and methods

Participants

This study utilized a case-control design and recruited 80 male participants from two distinct professional fields – APs and OWs. Each group consisted of 40 individuals, who were selected through convenience sampling. An occupational health physician aided in the voluntary recruitment of participants during routine occupational health evaluations, which were carried out at outpatient clinics (Studio Minoretti, Oggiono, Italy). All participants, with Fitzpatrick skin types II and III, were of Caucasian descent and had no history of skin diseases. To reduce potential confounding variables, we paired each OW with an AP of similar age and tenure, with a minimum of 5 years of service. Women were excluded from the study due to their underrepresentation in the AP population [21, 22]. Additionally, those with a history of infectious, autoimmune, or inflammatory diseases, malignancies, or drug therapy within the previous 90 days were excluded. All participants did not consume dietary supplements and appeared to be in good physical health. Prior to the study, written informed consent was obtained from each subject. To minimize seasonal variations, the research was conducted during the winter months from November to January. The study adhered to ethical standards established by the Declaration of Helsinki and was approved by the local ethics committee (reference number: 2021/08).

Measurement of skin biophysical parameters

In order to guarantee precision in the measurements of skin biophysical parameters, all study participants were strictly advised to abstain from the application of skincare and cosmetic products the evening prior and on the day of the experiment. Measurements were conducted on the left cheek under a tightly controlled environment, maintaining a consistent temperature between 20°C and 22°C and a relative humidity range of 40% to 60%. Before initiating the test, participants were requested to cleanse their face with fresh, running water and then acclimatize to the set conditions by relaxing for a period of 30 min. The MPA10 multi-probe adaptor system (Courage & Khazaka Electronic GmbH, Cologne, Germany) [23] connected to a PC was used to perform all measurements. The Corneometer CM825 was utilized to measure skin hydration in the stratum corneum, expressed in arbitrary units (a.u.) as the mean of at least five readings. Tewameter TM 300 was used to assess TEWL as the mean of at least three readings. Sebumeter SM 815 measured sebum content, while Mexameter MX18 was used to evaluate skin melanin and erythema indices, with the mean of at least three readings.

Quantification of serum DMKN levels

After an overnight fast, venous blood samples were collected into serum collection tubes and centrifuged at 2000 *g* for 15 min. The resulting serum aliquots were then stored at a temperature of –80°C and were thawed only immediately before analysis. Serum DMKN levels were measured using a commercially available enzyme-linked immunosorbent assay kit (Reddot Biotech, Houston, TX, USA) according to the manufacturer's protocol. The detection range for the kit was 0.156–10 ng/ml, with inter- and intra-assay coefficients of variation less than 8% and 6%, respectively. The samples were randomized within different batches, and the laboratory staff was uninformed of the participants' professional status. Every sample from individual subjects was analyzed twice within the same assay.

Statistical analysis

The Kolmogorov-Smirnov test was employed for the purpose of assessing the normality of continuous data. The results indicated that all variables adhered to a normal distribution, thus justifying the exclusive use of parametric statistical methods. Continuous data are expressed as the mean ± standard deviation, whereas categorical data are presented as counts and percentages. A comparative analysis of variables between APs and OWs was conducted using the Student's *t*-test for continuous data, and the χ^2 test for categorical variables. We initially performed correlation analyses, utilizing the Pearson's correlation coefficient, and then proceeded with multivariable linear regression to ascertain the independent associations between skin biophysical parameters and serum DMKN levels in APs. The following potential confounding factors were entered into the multivariable linear regression model: age, length of service, body mass index, total cholesterol, smoking status, and fasting plasma glucose. All calculations were performed using the SPSS software, version 20.0 (IBM, Armonk, NY, USA). Statistical significance was determined by a two-tailed *p*-value of less than 0.05.

Results

Table 1 presents the general characteristics of the 40 APs and 40 OWs who participated in the study. Comparative analysis revealed no statistically significant difference between the two groups concerning age, tenure of service, current smoking habits, body mass index, total cholesterol, and fasting plasma glucose levels.

Skin biophysical parameters

Our analysis revealed significant differences in the biophysical parameters of cheek skin between the two professional categories under consideration (Table 2). In particular, we found that skin hydration within the stratum corneum was markedly lower among APs compared to OWs, with respective readings of 39 ±10 a.u. and 45 ±11 a.u. ($p < 0.001$). Concurrently, TEWL was significantly elevated in APs as compared to OWs, with measurements of 15 ±5 g/m²/h and 12 ±5 g/m²/h, respectively ($p < 0.001$). These findings imply that the occupation of an airline pilot might result in skin barrier impairment. However, there was no significant variance in sebum content between the groups. The melanin index was notably higher in APs than in OWs (181 ±46 a.u. compared to 158 ±34 a.u., respectively, $p < 0.001$), as was the erythema index (299 ±62 a.u. compared to 274 ±57 a.u., respectively, $p < 0.001$). This suggests that the profession of airline pilots could have a more pronounced impact on skin coloration than indoor office work.

Serum dermokine levels and associations with skin biophysical parameters

APs had significantly higher serum DMKN levels (2.0 ±0.8 ng/ml) in comparison to OWs (1.4 ±0.5 ng/ml, $p < 0.001$). A significant positive correlation was observed between the melanin index and serum DMKN levels of APs (Pearson's $r = 0.62$, $p < 0.01$), whereas no other significant correlations with skin biophysical parameters were identified. Notably, the association between APs' serum DMKN levels and their melanin index was found to be independent of potential confounding variables, as indicated by multivariable linear regression analysis ($\beta = 0.56$, $p < 0.05$).

Discussion

In our study, we conducted a comprehensive investigation into the differences in skin biophysical parameters between two occupational groups, namely, APs and OWs, employing non-invasive techniques. Given its continual exposure, the human face is often more susceptible to detrimental environmental elements, such as irritants, allergens, UV radiation, and low-dose cosmic ionizing radiation, compared to other body parts which are predominantly shielded by clothing [23]. Upon examining the skin parameters specifically in the cheek region, we noted significant disparities between APs and OWs. Specifically, the skin of APs exhibited a decrease in hydration levels in the SC, coinciding with a higher level of TEWL – an essential gauge for assessing skin barrier integrity. These observations could potentially be attrib-

Table 1. General characteristics of the study participants

Variable	Airline pilots (*n* = 40)	Office workers (*n* = 40)	*P*-value
Men, *n* (%)	40 (100)	40 (100)	NS
Age [years]	39.2 ±3.3	38.9 ±3.4	NS
Length of service [years]	9.8 ±3.8	10.2 ±4.1	NS
Current smoking, *n* (%)	7 (17.5%)	8 (20.0%)	NS
Body mass index [kg/m²]	24.3 ±2.4	24.6 ±2.7	NS
Total cholesterol [mg/dl]	210 ±11	214 ±10	NS
Fasting plasma glucose [mg/dl]	90 ±9	92 ±11	NS

Data are expressed as means ± standard deviations, unless otherwise indicated; NS – not significant.

Table 2. Skin biophysical parameters and serum dermokine levels in the study participants

Variable	Airline pilots (*n* = 40)	Office workers (*n* = 40)	*P*-value
Skin hydration in the SC [a.u.]	39 ±10	45 ±11	< 0.001
TEWL [g/m²/h]	15 ±5	12 ±4	< 0.001
Sebum content [µg/cm²]	28 ±4	30 ±5	NS
Melanin index [a.u.]	181 ±46	158 ±34	< 0.001
Erythema index [a.u.]	299 ±62	274 ±57	< 0.001
Serum dermokine levels [ng/ml]	2.0 ±0.8	1.4 ±0.5	< 0.001

Data are expressed as means ± standard deviations; SC – stratum corneum, TEWL – transepidermal water loss, a.u. – arbitrary units, NS – not significant.

uted to APs' prolonged professional exposure to harmful UV radiation and low-dose cosmic ionizing radiation, both of which can disrupt skin barrier functionality [24, 25]. Particularly within the SC, UV radiation's impact can instigate modifications in intercellular lipids and provoke abnormal keratinization [24]. These changes, in turn, can lead to an increased TEWL.

Despite the negligible differences in sebum content between the two professional groups, our research further revealed that APs demonstrated elevated melanin and erythema indices in comparison to OWs. This observation aligns with the recognized impact of UV radiation exposure, which leads to skin darkening as a result of enhanced melanin production, serving as a defence mechanism [26]. Besides instigating hyperpigmentation, both UV radiation and minor doses of cosmic ionizing radiation have the potential to trigger erythema. This was apparent from the higher erythema index observed on the cheeks of APs. While Cadilhac *et al.* [8] previously discovered no evidence of UVA or UVB radiation in any part of the aircraft cabins they tested, including the cockpit, our studies revealed higher melanin and erythema indices among APs. These findings suggest a possible link to occupational radiation exposure. It is important to note, however, that pilots generally fall into a higher socioeconomic bracket, which could lead to more frequent recreational sun exposure [27] compared to OWs. We acknowledge that this factor cannot be entirely discounted. Whether resulting from work-related or leisure activities, our current research sheds light on previous observations suggesting that APs may be at a higher risk of certain skin diseases, including cutaneous malignancies. These findings highlight the importance of proactive skin care measures for APs, such as regular skin checks and sun protection [28], to help reduce their susceptibility to such conditions.

To elucidate the possible mechanistic foundations behind the noticed skin alterations in APs, we evaluated the associations between the serum concentrations of DMKN and the measured biophysical parameters. DMKN, a protein that is secreted and instrumental in maintaining skin barrier and homeostasis, has previously been identified as a contributing factor in inflammatory dyskeratotic diseases [17]. Additionally, an expanded distribution of DMKN-expressing keratinocytes has been previously reported in inflammatory skin diseases [29]. Intriguingly, we found that serum DMKN levels in APs was independently associated with the melanin index rather than typical skin barrier parameters such as hydration levels in the stratum corneum or TEWL. Although no previous studies have established a link between DMKN and skin pigmentation, it is noteworthy that mutations in the DMKN gene are implicated in the development of MM via the ERK/MAPK signalling pathways [20]. Moreover, DMKN microRNAs have emerged as potentially promising biomarkers for diagnosing and treating MM [30]. Based on these insights, we advocate for further research into the interplay between DMKN and the risk of MM in APs.

Several caveats must be considered when interpreting our findings. The limited sample size introduces an aspect of limited generalizability, making it challenging to arrive at conclusive interpretations. Moreover, our findings' broad applicability may be constrained due to the voluntary participation of APs and OWs, potentially leading to self-selection bias. Although our sample's sex distribution mirrors the larger airline pilot demographic [21, 22], the absence of female participants impedes the applicability of our findings to women. Including a measurable assessment of professional radiation exposure would significantly improve the robustness of our conclusions. Additionally, the observed changes in skin biophysical parameters and serum DMKN levels in APs necessitate a more in-depth, longitudinal, and prospective investigation. This will allow for a more holistic understanding of the observed modifications. Future research could significantly benefit from assessing and comparing serum DMKN levels in APs stratified into two distinct groups: those with a history of MM or non-melanoma skin cancer, and those without such a history. This comparative study may yield consequential insights into the relationship between serum DMKN levels and the prevalence of skin cancer among APs. In light of a recent meta-analysis, there is also compelling evidence to suggest a significant correlation between a higher occurrence of MM and vitamin D insufficiency in the general population [31]. This study further emphasized the less favourable Breslow tumour depth's association with vitamin D's lower levels [31]. Such findings provide an intriguing path for potential studies exploring the correlation between serum vitamin D levels and aviators' risk of skin malignancies. Finally, it would be beneficial for subsequent research to investigate further into the potential variances in evaluated skin biophysical parameters between commercial and military pilots. The unique professional settings in which they operate [32] could potentially exert diverse influences on these variables.

Conclusions

Despite the limitations of a modest sample size, our study proposes a potential link between the profession of an airline pilot and changes in skin biophysical parameters, setting them apart from OWs. To validate these results and the potential role of DMKN, comprehensive studies involving a broader range of workforce demographics are required. Additionally, refining the methods used for exposure assessment, ideally by conducting direct in-flight radiation exposure measurements, could be instrumental in bolstering the validity of our conclusions.

Conflict of interest

The authors declare no conflict of interest.

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