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Original Research

Biophysical and ultrasonographic changes in pityriasis rosea compared with uninvolved skin

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ABSTRACT

Background: Pityriasis rosea (PR) is a common, self-limited, inflammatory papulosquamous skin disease with a possible viral etiology.
Objective: The goal of this study was to evaluate skin biophysical properties in patients with PR compared with uninvolved skin to better understand the pathogenesis of PR.
Methods: Stratum corneum hydration, transepidermal water loss, surface friction, pH, sebum, melanin, erythema, temperature, elasticity parameters (R0, R2, R5), thickness, and echodensity of the epidermis and dermis were measured on lesions of classic PR in 21 patients and compared with control sites (average of uninvolved perilesional and symmetrical skin) with a paired *t* test.
Results: Stratum corneum hydration ($p < .001$), R0 ($p = .003$), R2 ($p = .001$), R5 ($p = .003$), and echodensity of the dermis ($p = .006$) were significantly lower, whereas transepidermal water loss ($p = .001$), pH ($p < .001$), and erythema ($p < .001$) were significantly higher in PR lesions. There was no significant difference in friction index, sebum, melanin content, temperature, thickness of the epidermis and dermis, and echodensity of the epidermis between PR and normal skin.
Conclusion: PR skin is characterized by certain alterations in biophysical properties, which are mostly correlated with histologic changes. These changes may be helpful in early, noninvasive diagnosis of PR.

Introduction

Pityriasis rosea (PR) is a common, self-limited, inflammatory papulosquamous skin disease that may have a negative impact on quality of life in patients (Nwako-Mohamadi et al., 2019). The incidence of this disease in the United States is 1.31%. PR is more prevalent in the age group of 10 to 35 years.

Although some authors have not been able to demonstrate the exact pathogenesis of PR, many recent studies have established a causal role for systemic active human herpesvirus (HHV) 6 and HHV-7 infection in the pathogenesis of PR based on the detection of HHV-6 and HHV-7 DNA in plasma and expression of mRNA and specific antigens in skin lesions of patients with PR. In addition, herpesvirus virions in various stages of morphogenesis were detected by electron microscopy in skin lesions and in the supernatant of cocultured peripheral blood mononuclear cells from patients with PR (Drago et al., 2009; 2016).

Histologic findings of PR lesions include parakeratosis, epidermal hyperplasia and spongiosis, exocytosis of lymphocytes, and extravasation of erythrocytes, along with a moderately dense perivascular lymphocytic infiltrate in the superficial dermis (Gay and Gross, 2020). Parakeratosis is the most common stratum corneum (SC) abnormality of PR, which results from abnormal keratinocyte maturation and is defined by the persistence of nucleated cells in the SC (Pople et al., 2019). The rashes of PR are usually asymptomatic but occasionally may be pruritic (VanRavenstein and Edlund, 2017).

The most valid tool for diagnosis of PR is history and clinical examination, and sometimes skin biopsy is needed to confirm the diagnosis (Dasgeb et al., 2013). Dermoscopy is a simple and noninvasive method that also can confirm the diagnosis of papulosquamous disorders, including PR (Alinda et al., 2014), but few studies are available on the dermoscopic features of PR (Lallas et al., 2012). The most common dermoscopic features of PR lesions

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are pigmentary changes, a dull red background, white scale color, and patchy/peripheral scale distribution (Nwako-Mohamadi et al., 2019). Some of these features, such as red dots, may be observed in other inflammatory skin disorders, such as lichen planus and pityriasis rubra pilaris (Lacarrubba et al., 2015).

Recently, different noninvasive methods for evaluating the condition of skin have been used to evaluate physical properties of skin in dermatologic diseases, such as dermatitis, lichen planus, and psoriasis (Yazdanparast et al., 2018; 2019a; 2019b), as well as in some systemic diseases (Catala-Pétavy et al., 2009; Seirafi et al., 2009; Szepetiuk et al., 2008). These measurements are precise, noninvasive, and quantitative tools in dermatology that can be used to give valuable information about diseases and may be helpful in the differential diagnosis of papulosquamous disorders, including PR (Yazdanparast et al., 2019a).

Many studies have focused on evaluating the erythema and temperature of the skin as the main markers of inflammation (Curto et al., 2014; Kwon et al., 2014). However, a thorough examination of the epidermal barrier status, evaluation of SC hydration, skin surface pH, and transepidermal water loss (TEWL) is also required (Darlenski et al., 2009).

A comprehensive study to evaluate the biophysical and sonographic characteristics of skin in PR has not been performed to date. The purpose of this study was to evaluate the biophysical and sonographic properties in PR skin lesions and to compare involved and uninvolved skin.

Methods

All patients older than 18 years with classic PR who were referred to our clinic between September 2014 and March 2016 and fulfilled the eligibility criteria were recruited by a convenient sampling method. The clinical diagnosis was made by a dermatologist and confirmed with histologic findings for all patients. The exclusion criteria included any systemic diseases that can affect the skin, recent history of any other skin diseases or operations in the previous 3 months, use of any systemic or topical treatment or other interventions to treat PR in the past 2 weeks, and pregnancy.

This study was approved by the institutional review board of our center and the Ethics Committee of Tehran University of Medical Sciences and was carried out in accordance with the Declaration of Helsinki. Oral informed consent was obtained from all participants. Patient data were kept confidential, and all measurements were noninvasive and done free of charge. Baseline characteristics, including age, sex, Fitzpatrick's skin type, locations of the lesions, and duration of the lesions, were recorded. Participants were instructed not to use any topical products on their skin as of the night prior to the biophysical assessments. Before the measurements, participants were asked to rest and relax in the supine position for 20 minutes in standard conditions (25%–30% humidity and 20°–22 °C temperature).

Measurements were done on one of the prominent PR lesions, perilesional uninvolved skin, and symmetrical uninvolved skin. The selection of these three sites for measurement was done by the same dermatologist who confirmed the diagnosis. Generally, the active border of a lesion was selected as lesional skin and the normal-appearing skin on the same location on the other side of the body was selected as symmetrical uninvolved. The normal-appearing skin at least 3 cm away from the active border of the lesion was selected as perilesional uninvolved skin.

The measurements were done with the Multi Probe Adapter system, manufactured by Courage + Khazaka electronic, GmbH and included SC hydration (using Corneometer CM 825), TEWL (using Tewameter TM 300), pH (using Skin-pH-Meter PH 905), erythema and melanin indices (using Mexameter MX 18), sebum (using Sebumeter SM 815), friction value (using Frictiometer FR700), elasticity parameters including R0, R2, and R5 (using Cutometer 580), and skin temperature (using Skin Thermometer ST 500, CK GmbH, Cologne, Germany).

The Frictiometer measures torque as the friction index and is related to skin elasticity and plasticity. R0 (Uf) shows the total elastic and plastic deformation and is the reciprocal of firmness. R2 shows gross elasticity (R2 = Ua/Uf, where Ua = viscoelastic/plastic recovery or final retraction of skin and Uf = total deformation of the skin). R5 shows the net elasticity of the skin (R5 = Ur/Ue, where Ur = immediate elastic recovery or immediate retraction and Ue = immediate extensibility or elastic deformation; Neto et al., 2013). Moreover, high-frequency ultrasonography (HFUS) was performed with 50 MHz and 22 MHz probes of a DUB skin scanner (tpm Company, Germany) to assess the thickness and echodensity of the epidermis and dermis, respectively, on the three sites of measurement.

The statistical analyses were performed using SPSS software, version 18 (SPSS Inc., Chicago, IL). Mean and standard deviation (SD) were used for the description of quantitative data, and a comparison of quantitative data between the two groups was performed by paired sample t test. The statistical significance level was defined as $p < .05$.

Results

Twenty-one patients with PR were included in this study, of whom 8 patients were male and 13 were female. The age of participants was between 18 and 55 years (mean: 31.33; SD: 10.63). The Fitzpatrick skin types were III in 10 and IV in 11 participants. The duration of the lesions was 7 to 28 days (mean: 15.65; SD: 7.33), and the lesions were located on the upper extremities in 6 patients and the trunk in 15 patients.

There was no statistically significant difference in SC hydration ($p = .599$), TEWL ($p = .580$), pH ($p = .490$), erythema index ($p = .374$), melanin content ($p = .445$), sebum ($p = .403$), friction value ($p = .033$), R0 ($p = .977$), R2 ($p = .114$), R5 ($p = .331$), skin temperature ($p = .115$), thickness of the epidermis ($p = .141$), density of the epidermis ($p = .386$), thickness of the dermis ($p = .890$), and density of the dermis ($p = .827$) between the perilesional uninvolved and symmetrical uninvolved skin. The average of these parameters was used as the control and was compared with lesional skin (Tables 1 and 2).

According to Table 1, SC hydration ($p < .001$), R0 ($p = .003$), R2 ($p = .001$), and R5 ($p = .003$) were significantly lower in PR lesions, whereas TEWL ($p = 0.001$), pH ($p < .001$), and erythema index ($p < .001$) were significantly higher in PR lesions compared with normal skin. No significant differences were found in the friction index ($p = .075$), sebum ($p = .398$), melanin content ($p = .700$), and skin temperature ($p = .461$) between PR and normal skin. The echodensity of the dermis in PR skin was significantly lower than that of normal skin ($p = .006$). No significant difference was found in the thickness of the epidermis ($p = .241$), density of the epidermis ($p = .491$), and thickness of the dermis ($p = .844$) between PR and normal skin (Table 2).

Discussion

According to the results of this study, skin lesions in PR are specified by certain alterations in biophysical and biomechanical properties, including lower SC hydration, gross elasticity, net elasticity, and dermis density, as well as higher TEWL, pH, erythema, and firmness. Furthermore, the biophysical and biomechanical properties of perilesional and symmetrical uninvolved skin were

Table 1
Comparison of biophysical parameters between lesion and control skin in patients with pityriasis rosea.

Parameter (units)	Lesion, mean ± SD	Control (mean of perilesional and symmetrical skin), mean ± SD	*p*-value (paired *t* test)
Hydration (arbitrary)	46.30 ± 18.57	62.816 ± 16.22	<.001
TEWL ($g/m^2/h$)	17.23 ± 10.65	8.88 ± 4.37	.001
Friction (arbitrary)	288.41 ± 237.05	376.827 ± 238.95	.075
pH (arbitrary)	6.30 ± 0.77	5.77 ± 0.71	<.001
Sebum ($\mu g/cm^2$)	14.14 ± 29.89	9.55 ± 18.21	.398
Melanin content (arbitrary)	148.22 ± 43.52	144.68 ± 39.76	.700
Erythema index (arbitrary)	407.63 ± 73.49	219.618 ± 46.38	<.001
Temperature (centigrade)	31.43 ± 1.24	31.29 ± 1.02	.461
R0 (arbitrary)	0.26 ± 0.09	0.30 ± 0.08	.003
R2 (arbitrary)	0.67 ± 0.13	0.79 ± 0.09	.001
R5 (arbitrary)	0.39 ± 0.13	0.51 ± 0.17	.003

SD, standard deviation; TEWL, transepidermal water loss.

Table 2
Comparison of ultrasonographic findings between lesion and control skin in patients with pityriasis rosea.

Parameter (unit)	Lesion, mean ± SD	Control (mean of perilesional and symmetrical skin), mean ± SD	*p*-value (paired *t* test)
Thickness of epidermis (μm)	132.87 ± 29.91	124.94 ± 19.33	.241
Density of epidermis	78.92 ± 21.26	83.55 ± 25.69	.491
Thickness of dermis (μm)	1413.30 ± 529.15	1430.80 ± 487.93	.844
Density of dermis	31.30 ± 15.47	40.79 ± 18.08	.006

SD, standard deviation.

not very different. SC hydration was significantly lower and TEWL was significantly higher in lesions compared with controls. Because SC hydration and TEWL are indicators of skin barrier function (Polańska et al., 2013), these findings are compatible with the pathophysiology of disease, which includes epidermal hyperplasia and parakeratosis (Gay and Gross, 2020).

Assessment of PR lesions with the Cutometer showed that firmness was significantly higher and gross elasticity and net elasticity were significantly lower in PR lesions. The Cutometer is a reliable device that can determine the viscoelastic properties of human skin (Kawakita et al., 2004). According to previous studies, elasticity is correlated with skin hydration (Baek et al., 2011). In the current study, gross and net elasticity was lower in lesions, which also had lower SC hydration compared with control skin. Moreover, the parameters evaluated by Cutometer correlate with dermal edema and skin induration (Ryu et al., 2008), and the results of the study showed reduced density of the dermis in PR skin, which is an indicator of dermal edema.

Skin pH was significantly higher in PR lesions compared with controls. In fact, no sufficient study on PR skin pH exists yet, and the pathophysiology of PR is still poorly understood (Gay and Gross, 2020). However, skin pH is a central regulator of skin barrier homeostasis and an important innate defense mechanism. Elevated pH levels can change immune responses, and immune responses have been shown to play an important role in the pathogenesis of some other papulosquamous diseases, such as atopic dermatitis (Danby and Cork, 2018). Thus, impaired skin pH could be important to the development of PR.

Studies on the pathogenesis of psoriasis have revealed that changes in barrier defects, skin homeostasis, inflammation, and differentiation play an important role, and skin pH can affect all of these factors. Thus, understanding the role of manipulations of skin pH for topical treatments is essential in the management of psoriasis (Bigliardi, 2018), and this finding can be true for PR as well.

The erythema index was significantly higher in PR lesions compared with normal skin. Erythrocyte extravasation is a histologic feature of PR (Gay and Gross, 2020; Urbina et al., 2017), and so this finding is justifiable.

HFUS is stablished as a noninvasive method that could be used to evaluate treatment response and disease progression in skin lesions (Dasgeb et al., 2013; Polańska et al., 2015), but current developments in the field of noninvasive imaging techniques have shown that HFUS can be included in daily dermatologists' practice as an in vivo assessment tool and may assist in establishing a diagnosis of skin disorders such as psoriasis (Grajdeanu et al., 2019). In PR skin, HFUS has shown an alteration as well in the form of low echodensity of the dermis. Because inflammatory populations are seen in PR lesions (Gay and Gross, 2020) and papillary dermal edema, mild perivascular lymphohistiocytic infiltrate, exocytosis, and extravasated erythrocytes in the papillary dermis are histologic features of PR, low density of the dermis is expected (Urbina et al., 2017).

When considering abnormalities in the biophysical and sonographic properties of PR lesional skin, further comparison studies on other inflammatory skin diseases have been suggested, which may also help differentiate these skin disorders. Of note, for the vast majority of patients, the diagnostician does not need any assistance other than history and clinical presentation, and these studies may mostly have research value rather than practical use. To our knowledge, no paper to date has compared skin biophysical and ultrasonographic characteristics between involved and noninvolved skin of patients with PR. Because skin biophysical and sonographic characteristics vary with sex and age (Firooz et al., 2017; 2012), noninvolved skin must serve as a control for assessment of skin biophysical characteristics.

Conclusion

PR skin is characterized by certain alterations in biophysical, biomechanical, and ultrasonographic properties, which provide valuable information about the disease. These discoveries can help in the development of new medicines, with the goal of correcting and changing skin properties.

Conflicts of Interest

None.

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Study Approval

The author(s) confirm that any aspect of the work covered in this manuscript that has involved human patients has been conducted with the ethical approval of all relevant bodies.

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