Biophysical and ultrasonographic changes in pityriasis rosea compared with uninvolved skin

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Background: 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 (Pope et al., 2019). The rashes of PR are usually asymptomatic but occasionally may be pruritic (Van Ravenstein 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 lesions (Lallas et al., 2012). The most common dermoscopic features of PR lesions are...
are pigmented 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 (Català-Péday 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, and temperature of the skin as the main markers of inflammation (Curto et al., 2014; Kwon et al., 2014). 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.

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 during 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 \( p = .001 \), 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
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 (Polanka et al., 2013), these findings are compatible with the pathophysiologic 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 in 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 sono- graphic properties of PR lesions (Gay and Gross, 2020), 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 (Gay and Gross, 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 (Urban, 2017).

When considering abnormalities in the biophysical and sono- graphic properties of PR lesions, 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 sono- graphic characteristics vary with sex and age (Firooz et al., 2017; Urbina et al., 2017), noninvolved skin must serve as a control for assessment of skin biophysical characteristics.

**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/m²/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 (µg/cm²)                          | 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.

**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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