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Measuring the Impact of Vitiligo: Behind the White Spots

Reinhart Speeckaert[1], Jo Lambert[1] and Nanja van Geel[1]

The impact of vitiligo is generally believed to be underestimated. Salzes et al. propose a questionnaire to measure the actual burden of vitiligo. Using a stepwise approach they constructed and validated this instrument taking into account the differences between fair and dark skin phototypes. It is a promising approach that can be implemented on an international scale.

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The impact of a cutaneous disorder on the quality of life is essential for justifying the need for new treatments and attracting additional resources for research. Moreover, from a political point of view, improvement in the quality of life is an objective criterion to determine the cost-effectiveness of treatment. Some general measurement tools have been developed for skin disorders (e.g., dermatology life quality index, Skindex, etc.). However, as the spectrum of dermatological diseases is broad, these more global instruments are often insufficient (Twiss et al., 2012).

Vitiligo has a tendency to develop at visible parts of the body such as the hands and the face, which are socially important. Many studies have shown a reduced quality of life in patients with vitiligo, but other studies have not confirmed a substantial impact of vitiligo on life quality. This may be due to the fact that the generally accepted dermatological questionnaires such as the dermatology life quality index and Skindex-16 lack the sensitivity needed for a disorder without symptoms such as pruritus or pain. The first four questions of the Skindex-16 involve skin itching, burning, hurting, and irritation that are not relevant to vitiligo. Moreover, the dermatology life quality index and Skindex-16 focus in each question on the complaints the patient had last week. Although this is appropriate for patients with skin disorders exhibiting disease flares and remissions, this is not ideal for chronic progressive disorders. In a number of skin disorders (such as psoriasis, atopic dermatitis, and acne), tailored life impact tools have been developed to describe the disease burden more accurately.

Clinical Implications

- The Vitiligo Impact Patient scale is a well-developed and validated instrument to measure the impact of vitiligo.
- Implementation in daily practice could guide treatment decisions and concurs with the concept of personalized medicine.
- This tool contributes to the general awareness of the psychosocial consequences of vitiligo.

Salzes et al. (2016) report the development and validation of a new tool to assess the burden of vitiligo. In contrast to most dermatological disorders, vitiligo lacks clear inflammatory signs such as redness, scaling, and itch. This may lead to the misperception that the impact of the disease on daily life is low. It is rather unfortunate that several different vitiligo impact scores have been published in the last several years with only limited international collaboration. Krishna et al. (2013) proposed a vitiligo impact score—subsequently adapted into a 22-item scale (Vitiligo Impact Scale-22)—that is quite different from the Vitiligo Impact Patient scale (Gupta et al., 2014; Krishna et al., 2013). However, these studies were conducted in India, and they reference issues not relevant to patients in other parts of the world: concerns about contagiousness, people who deliberately avoid contact with patients, and marital issues related to local misperceptions and social stigma toward dermatological disorders. Lilly et al. (2013) validated a vitiligo-specific health-related quality of life instrument, using a study population with mainly dark skin (n = 90; 65% skin type IV–VI). The vitiligo-specific health-related quality of life instrument scale was recently also validated in Brazilian Portuguese patients with vitiligo (Boza et al., 2015). This scale resembles the Vitiligo Impact Patient scale with 12 of 16 questions of the vitiligo-specific health-related quality of life instrument

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overlapping with the Vitiligo Impact Patient scale. As both scales were tested on geographically diverse populations, this supports the validity of the approach. Previously, it has been shown that several items of the dermatology life quality index and Skindex are subject to bias according to cultural differences (Nijsten et al., 2007), suggesting that for vitiligo, a global consensus might best determine the impact score that should be employed in epidemiological studies and in clinical trials. Validation in an international multicenter study would likely be required.

CONFLICT OF INTEREST

The authors state no conflict of interest.

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An Unexpected Role for TRPV4 in Serotonin-Mediated Itch

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Previous studies have revealed that TRPV1 and TRPA1 function downstream of many itch receptors, where they mediate inward current to trigger action potentials in primary afferents. Although other TRP channels, such as TRPV4, are expressed in primary afferents, whether or not they play an analogous role in itch was previously unknown. Now, Akiyama et al. provide evidence that TRPV4 is a key mediator of serotonin-induced itch. This finding is important because it uncovers an unanticipated role for TRPV4 in itch, thereby identifying a novel therapeutic target.

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Clinical relevance of itch

Chronic itch, which is defined as itch lasting more than 6 weeks, is a prevalent problem that occurs in approximately 10% of the population (Mollanazar et al., 2015). Chronic itch conditions negatively affect quality of life, and yet there are no therapies that are both efficacious and selective for itch. The lack of effective treatment is partly attributable to a poor understanding of the mechanisms that underlie it. Although antihistamines are frequently prescribed as a treatment for itch, they are typically ineffective because most types of chronic itch are not histamine-mediated (Mollanazar et al., 2015). Unfortunately, although there are numerous mediators that can cause itch, the factors that are responsible in most circumstances of chronic itch are largely unknown. One candidate mediator is serotonin (5-hydroxytryptamine, 5-HT). Human psychophysical studies have shown that the application of serotonin into the skin causes itch (Weisshaar et al., 2004). In rodents, serotonin is a key component of mast cells, and it is a potent mediator of itch. However, until recently, the mechanisms through which serotonin causes itch have remained uncertain.

TRPs as downstream mediators of itch (pruritogens)

Many pruritogens bind to metabotropic receptors on primary sensory neurons; however, these receptors must be coupled to ionotropic channels via intracellular signaling pathways to allow sufficient current influx to generate action potentials. Several groups have shown that the cation channels TRPV1 and TRPA1 are coupled to different pruritogen receptors and that they are critical for different forms of itch transmission (Ross, 2011). More specifically, TRPV1 is required for histaminergic itch, whereas TRPA1 is required for several types of nonhistaminergic itch, such as that induced by chloroquine, BAM8-22, IL-31, endothelin-1, thymic stromal lymphopoietin, and bile acids. Until recently, whether serotonin receptors were likewise coupled to TRPs remained unknown.

> TRPV4 is a key mediator of serotonin-induced itch, thereby identifying a novel therapeutic target.

Mechanisms of serotonin-induced itch

Understanding serotonin-mediated itch has been complicated by the fact that there are numerous serotonin receptors that are expressed on primary afferents, as well as on immune mediators that

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