Pruritus in Psoriasis

Beni Amatya
Dermatology and Venereology Unit, Department of Medicine, Karolinska Institutet, Solna, SE-171 76 Stockholm, Sweden. E-mail: beni.amatya@ki.se

Beni Amatya defended her PhD thesis on 13 February 2009 at Karolinska University Hospital, Solna, Stockholm, Sweden with the title: "Study of Pruritus in Psoriasis Vulgaris: Role of Tachykinins" (Supervisor: Professor Klas Nordlind, Dermatology and Venereology unit, Karolinska University Hospital, Solna; Opponent: Professor Jacek Szepietowski, Department of Dermatology, Venereology and Allergology, University of Medicine, Wroclaw, Poland). Below you can read her minireview on "Pruritus in Psoriasis".

Introduction

Psoriasis is a common chronic inflammatory skin disease. Although the word "*psora*", derived from the Greek, means "itch" (1), pruritus has never been considered an important symptom in psoriasis. Studies of pruritus in psoriasis are sparse.

Epidemiology

The prevalence of pruritus in psoriasis has been reported from different parts of the world, ranging from 64% to 84% (2–6). Among the clinical variants of psoriasis, pruritus is more common in plaque-type psoriasis compared with other variants such as guttate, pustular or erythrodermic (4, 6).

Characteristics of pruritus

Few studies have been conducted to investigate the features of pruritus in psoriasis. Patients have described pruritus as "painful", "like pins and needles", and as other sensations, such as stinging, tickling and crawling (6, 7). Pruritus intensity in psoriasis, measured using the 10-cm visual analogue scale (VAS) can be categorized into two groups, with lower intensity in the range 2–4 cm and higher intensity in the range 5–7 cm (2, 6, 8, 9). The mean pruritus intensity score, however, is lower in patients with psoriasis compared with other diseases such as atopic dermatitis (10) and uraemic pruritus (11). Interestingly, higher pruritus intensity, as well as the symptoms heat sensation, pain, stinging, tickling and crawling are more common in women than in men (2, 4). The most common reported sites of pruritus are the lower back and lower legs, followed by the scalp, while very few patients report generalized itch (2, 3, 6, 12).

Stress is considered by patients to be a major aggravating factor for itch in psoriasis (2, 6, 7, 13). Other aggravating factors are dry and cold weather, hot showers, chlorinated baths, clothes such as woollen and synthetic textiles, foods (chocolate, dairy products, nuts) and irregular meals (2, 6). Sweating and physical exercises have been reported to be important worsening factors for pruritus (6), whereas in another study patients did not report any association for these factors (2). Several methods are used by patients to relieve pruritus, such as scratching until the skin bleeds, using a wet towel or pinching the affected area. Sunbathing, cold showers, holidays and climate journeys have been reported to relieve pruritus in most patients (2, 6).

Patients with higher ratings of pruritus notice more psychosocial stress caused by the disease affecting their quality of life (6). Mood, concentration, sleep, appetite and sexual desire are negatively affected by pruritus (2, 3, 6, 7).

Treatment

Currently available effective treatment modalities for pruritus in psoriasis are limited; the treatment options are similar to the treatment for psoriasis *per se*. Anti-pruritic therapies used are coal-tar products, topical corticosteroids, salicylates, menthol, pramoxine, capsaicin, vitamin D analogues and topical immunomodulators and emollients (2, 14). Sedating antihistamines, mirtazapine, and biologicals, such as efalizumab, are other treatment options for pruritus in psoriasis (15, 16). Phototherapy has been reported as an effective treatment of pruritus in psoriasis in some studies (17–19). However, other studies have indicated that it is less effective (2, 6).

Mediators of pruritus in psoriasis

The mechanism of pruritus and the involvement of mediators in psoriasis are still not clear. Various peripherally acting possible mediators associated with pruritus have been suggested, including substance P, calcitonin gene-related peptide (CGRP),

vasoactive intestinal peptide (VIP) and neuropeptide Y (NPY) (3, 9, 20–22).

Substance P, a tachykinin member is thought to play a role in the pathogenesis of pruritus in psoriasis. When comparing non-itching and itching psoriasis, there was an increase in substance P-containing nerve fibres in the perivascular area in the skin of subjects with itching psoriasis, a down-regulation of neutral endopeptidase basally in the epidermis and within the endothelium, as well as many degranulating mast cells (20). The number of substance P immunoreactive nerve fibres was higher in lesional pruritic psoriasis than in non-lesional and normal healthy control skin (Fig. 1). There was a strong tendency towards correlation of pruritus intensity with the number of substance P immunoreactive nerve fibres in the lesional skin (21). Intradermally injected substance P-induced pruritus was more intense in psoriatic skin than in healthy controls. It also evoked a tendency to a higher intensity of pruritus in lesional than in non-lesional psoriatic skin. A positive correlation was also observed with clinical itch assessed with VAS and pruritus intensity induced with substance P (23).

Besides substance P, other members of the tachykinin family, such as neurokinin A (NKA) and B (NKB) immunoreactive nerve fibres were also higher in number in lesional compared with non-lesional psoriatic skin or healthy control skin (Fig. 2) (21). Among the receptors of the tachykinin family neurokinin 2 receptor (NK-2R), which has more affinity for NKA, immunoreactive nerves were more prevalent in lesional skin than in non-lesional or healthy control skin. In addition, there was a correlation between pruritus intensity and number of NK-2R-positive inflammatory cells.

Several studies have shown altered expression of CGRP, VIP and NPY in pruritic psoriasis skin (9, 24). Increased expression of CGRP receptors are found in keratinocytes of pruritic psoriasis skin and increased serum level of CGRP, whereas there is a decreased plasma level of NPY in pruritic psoriatic subjects (5, 9, 24). A negative correlation has been shown between pruritus severity and plasma level of VIP (9).

Although histamine plays an important role in pruritus in many pruritic diseases, it seems that it has little role in psoriasis. Intradermally injected histamine evoked pruritus in fewer psoriasis patients than in healthy controls (22). The maximum intensity of pruritus induced was lower in lesional psoriasis than in healthy control skin. There was no correlation between pruritus intensity and histamine plasma level in psoriasis, and no difference in histamine plasma levels between pruritic and non-pruritic patients with psoriasis (24).

Conclusion

Pruritus should be considered one of the major symptoms of psoriasis. The mechanism of pruritus and the role of mediators in psoriasis are still not clear. A better understanding of such

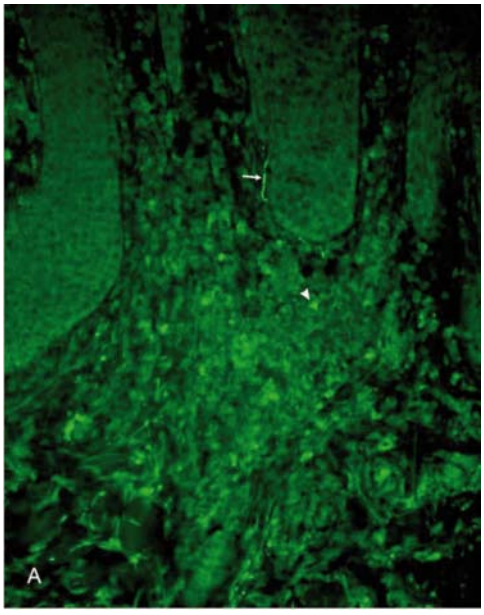

Fig. 1. Substance P-positive nerve (arrow) and inflammatory cells (arrow head) (21).

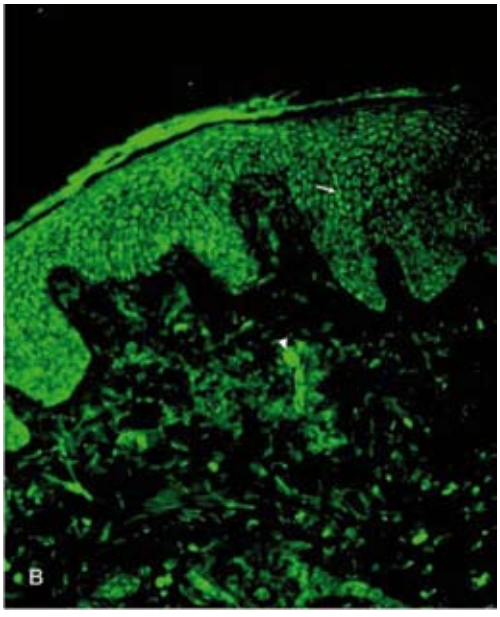

Fig. 2. Neurokinin 2 receptor (NK-2R)-positive intraepidermal nerve (arrow) and inflammatory cells (arrow head) (21).

mechanisms may contribute to the development of improved treatments compared with the traditional systemic and topical therapies currently available for pruritic psoriasis patients, which often have limited effect.

References

1. Glickman FS. Lepra, psora, psoriasis. J Am Acad Dermatol 1986; 14: 863–866.
2. Amatya B, Wennersten G, Nordlind K. Patients' perspective of pruritus in chronic plaque psoriasis: a questionnaire-based study. J Eur Acad Dermatol Venereol 2008; 22: 822–826.
3. Chang SE, Han S-S, Jung H-J, Choi J-H. Neuropeptides and their receptors in psoriatic skin in relation to pruritus. Br J Dermatol 2007; 156: 1272–1277.
4. Sampogna F, Gisondi P, Melchi CF, Amerio P, Girolomoni G, Abeni D. Prevalence of symptoms experienced by patients with different clinical types of psoriasis. Br J Dermatol 2004; 151: 594–599.
5. Szepietowski JC, Reich A, Wisnicka B. Pruritus and psoriasis. Br J Dermatol 2004; 151: 1272–1288.
6. Yosipovitch G, Goon A, Wee J, Chan YH, Goh CL. The prevalence and clinical characteristics of pruritus among patients with extensive psoriasis. Br J Dermatol 2000; 143: 969–973.
7. Amatya B, Nordlind K. Focus groups in Swedish psoriatic patients with pruritus. J Dermatology 2008; 35: 1–5.
8. Reich A, Szepietowski JC, Wi´snicka B, Pacan P. Does stress influence itching in psoriatic patients? Dermatol Psychosomatics 2003; 4: 151–155.
9. Reich A, Orda A, Wisnicka B, Szepietowski JC. Plasma neuropeptides and perception of pruritus in psoriasis. Acta Derm-Venereol 2007; 87: 299–304.
10. Yosipovitch G, Goon ATJ, Wee J, Chan YH, Zucker I, Goh CL. Itch characteristics in Chinese patients with atopic dermatitis using a new questionnaire for the assessment of pruritus. Int J Dermatol 2002; 41: 212–216.
11. Yosipovitch G, Zucker I, Boner G, Grafter U, Shapira Y, David M. A questionnaire for the assessment of pruritus: validation in uremic patients. Acta Derm Venereol 2001; 81: 108–111.
12. Szepietowski JC, Reich A, Wisnicka B. Itching in patients suffering from psoriasis. Acta Dermatovenerol Croat 2002; 10: 221–226.
13. Reich A, Hrehorów E, Szepietowski J.C. Pruritus is a very important factor negatively influencing the well-being of psoriatic patients. Acta Derm Venereol 2010; accepted to be published.
14. Dawn A, Yosipovitch G. Treating itch in psoriasis. Dermatol Nurs 2006; 18: 227–233.
15. Gordon KB, Papp KA, Hamilton TK, Walicke PA, Dummer W, Li N, et al. Efalizumab for patients with moderate to severe plaque psoriasis: a randomized controlled trial. JAMA 2003; 290: 3073–3080.
16. Menter A, Gordon K, Carey W, Hamilton T, Glazer S, Caro I, et al. Efficacy and safety observed during 24 weeks of efalizumab therapy in patients with moderate to severe plaque psoriasis. Arch Dermatol 2005; 141: 31–38.
17. Gupta G, Long J, Tillman DM. The efficacy of narrowband ultraviolet B phototherapy in psoriasis using objective and subjective outcome measures. Br J Dermatol 1999; 140: 887–890.
18. Lebwohl M. Phototherapy of pruritus. In: Bernhard JD, editor. Itch mechanisms and management of pruritus. New York: McGraw-Hill; 1994, p. 300–411.
19. Samson YS, Gielczyk R, Scherschun L, Lim HW. Narrow-band ultraviolet B treatment for vitiligo, pruritus and inflammatory dermatoses. Photodermatol Photoimmunol Photomed 2003; 19: 164–168.
20. Nakamura M, Toyoda M, Morohashi M. Pruritogenic mediators in psoriasis vulgaris: comparative evaluation of itch-associated cutaneous factors. Br J Dermatol 2003; 149: 718–730.
21. Amatya B. Study of pruritus in psoriasis vulgaris: role of tachykinins. Thesis. Stockholm: Karolinska Institutet; 2009.
22. Reich A, Szepietowski JC. Mediators of pruritus in psoriasis. Mediators Inflamm 2007; 64727.
23. Amatya B, Nordlind K, Wahlgren CF. Responses to intradermal injections of substance P in psoriasis patients with pruritus. Skin Pharmacol Physiol 2009; 23: 133–138.
24. Wisnicka B, Szepietowski JC, Reich A, Orda A. Histamine, substance P and calcitonin gene-related peptide plasma concentration and pruritus in patients suffering from psoriasis. Dermatol Psychosomatics 2004; 5: 73–78.