Chapter 12
The Role of Capsaicin in Dermatology

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Abstract Neurogenic pain and pruritus are the common chief complaints at dermatology office visits. Unfortunately, they are also notoriously difficult conditions to treat. Topical capsaicin used as a single therapy or as an adjuvant offers a low-risk option for patients who do not achieve control on other therapies. This chapter presents the evidence behind topical capsaicin use in dermatologic conditions characterized by neurogenic pain or pruritus, including postherpetic neuralgia, notalgia paresthetica, brachioradial pruritus, lichen simplex chronicus, prurigo nodularis, pruritus ani, pruritus of hemodialysis, aquagenic pruritus, apocrine chromhidrosis, lipodermatosclerosis, alopecia areata, and psoriasis. It presents the most common capsaicin formulations, dosages, and durations of treatment for each condition. Additionally, the chapter addresses various adverse effects and limitations in the use of topical capsaicin in dermatology.

12.1 Introduction

In a 2006 study by McDermott et al., patients who experienced neuropathic pain had greater unemployment status, reported missing from work more than 5 days per month, and had decreased daily functioning as a result of their pain (McDermott et al. 2006; Tolle et al. 2006). This occurred despite more frequent visits to their physician and management with a variety of prescription medications (McDermott et al. 2006; Tolle et al. 2006). A more recent study from Europe demonstrated that neuropathic pain is associated with increased rates of insomnia, anxiety, and depression (Langley et al. 2013). Neuropathic pain and itch are common reasons for dermatology office visits, and the burden that results from these

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conditions may be due in part to suboptimal treatment. Capsaicin represents a viable topical treatment option for patients experiencing neuropathic pain and itch who may fail to achieve relief from more commonly prescribed analgesics, antidepressants, antiepileptics, and other sedatives (Tolle et al. 2006).

While capsaicin has been used for medicinal purposes for centuries, its early documented use as a topical analgesic for treatment of neuropathic pain or itch is sparse. Native Americans used pepper pods as topical relief on their gums for toothaches, in addition to topical use as an aphrodisiac (Szallasi and Blumberg 1999). The analgesic effect of capsaicin was recognized in literature as early as 1850, when it was documented in the Dublin Free Press for relief of sore teeth (Szallasi and Blumberg 1999).

Since that time, topical use of capsaicin in the field of dermatology has expanded to include many conditions with a component of pain or itch. In this chapter, we will discuss the use of capsaicin in each of the following dermatologic conditions (Table 12.1):

- Postherpetic neuralgia
- notalgia paresthetica
- Brachioradial pruritus
- Lichen simplex chronicus and prurigo nodularis
- Pruritus ani, vulvae, and scroti
- Pruritus of hemodialysis
- Aquagenic pruritus
- Apocrine chromhydrosis
- Lipdermatosclerosis
- Alopecia areata
- Psoriasis

12.2 Dermatologic Conditions Responsive to Capsaicin Therapy

12.2.1 Post-Herpetic Neuralgia

Postherpetic neuralgia is defined as pain persisting more than 90 days following the occurrence of herpes zoster infection. It is the most common complication of HZV infection and occurs in 10–30 % of cases. The incidence and severity of herpes zoster infection increases with age, as does the likelihood of postherpetic neuralgia. Trigeminal neuralgia refers to postherpetic neuralgia occurring in the distribution of one of the branches of the trigeminal nerve (Pellissier et al. 2007).

Post-herpetic neuralgia and trigeminal neuralgia are conditions characterized by both neuropathic pain and neuropathic pruritus. As such, these conditions are particularly challenging to treat. Traditional treatment regimens include early high dose antiviral medications, oral analgesics such as nonsteroidal anti-inflammatory

Table 12.1 Dermatologic conditions responsive to capsaicin therapy

Dermatologic condition	Clinical manifestations
Post-herpetic neuralgia	Pain persisting more than 90 days following the occurrence of herpes zoster infection
Notalgia paresthetica	Focal pruritus typically located unilaterally on the mid- or upper back
	No primary lesion can be identified
	Often there is evidence of chronic rubbing or scratching seen as hyperpigmentation or mild lichenification in the area where the patient experiences the itch
Brachioradial pruritus	Unilateral or bilateral pruritus of the distal, and less commonly, proximal arms
	No primary lesion can be identified
	Often there is evidence of chronic rubbing or scratching seen as hyperpigmentation or mild lichenification in the area where the patient experiences the itch
Lichen simplex chronicus and prurigo nodularis	Thickened, erythematous or hyperpigmented scaly plaques that may also show evidence of excoriation
	Distribution is variable, and depends on the underlying source of pruritus. Lesions are in areas that the patient can reach
Pruritus ani, vulvae, and scroti	Intractable itching in the perianal or genital area, often with secondary lichenification
Pruritus of hemodialysis	Systemic pruritus
	May be associated with underlying neuropathy
Aquagenic pruritus	Rare condition characterized by itching sensation of the skin following exposure to water of any temperature or salinity
Apocrine chromhidrosis	Apocrine sweat is pigmented, usually yellow, green, or black
Lipodermatosclerosis	A manifestation of chronic venous insufficiency
	Painful panniculitis that typically presents on the medial lower legs in women over 40 years of age, as a result of chronic venous insufficiency
	Erythema progressing to hyperpigmentation, warmth, and induration
Alopecia areata	Most commonly, discrete round to oval areas of non-scarring hair loss
	Other, more rare forms include loss all scalp hair (alopecia totalis) or all of body hair (alopecia universalis)
Psoriasis	Classic form: variably sized erythematous and scaly plaques distributed on the extensor extremities, buttocks, and scalp
	Other forms: • Gutatte: eruptive, small plaques • Erythrodermic: total body erythema • Pustular: eruptive form, often in patients with unstable chronic psoriasis, may be associated with systemic symptoms

drugs, and high dose anti-epileptics, particularly gabapentin. Additionally, oral corticosteroids are often given to decrease inflammation-related pain. Topical analgesics, specifically lidocaine and capsaicin have also shown efficacy in pain and itch amelioration (Watson et al. 1993).

A 6-week randomized, double-blinded, vehicle-controlled study with 2-year open label follow-up demonstrated some amount of pain relief in 64 % of patients with postherpetic neuralgia treated with 0.075 % capsaicin cream compared to only 25 % of patients on placebo. A more recent Phase III trial of topical synthetic capsaicin (8 % transcapsaicin patch) documented a 30 % decrease in pain scores after 2–12 weeks when compared with placebo after 1 h exposure (Backonja et al. 2008). Although effect on pruritus was not mentioned, it may be speculated that itch was relieved to a similar extent.

The 8 % transdermal patch formulation is relatively new with limited data; however, this higher concentration preparation shows promise as a useful adjuvant therapy for the persistent pain of postherpetic neuralgia, particularly with repeat applications over the course of 2 years (Backonja et al. 2008).

12.2.2 Notalgia Paresthetica

Notalgia paresthetica is a common condition, presenting most frequently in middle-aged or older adults as focal pruritus typically located unilaterally on the mid or upper back. Usually, no primary lesion can be identified on examination, but often there is evidence of chronic rubbing or scratching seen as hyperpigmentation or mild lichenification in the area where the patient experiences the itch. Rare cases may have a bilateral and symmetric presentation. More extensive secondary changes may result from chronic scratching.

The pathogenesis of notalgia paresthetica is related to entrapment of the posterior rami of spinal nerves originating at T2–T6. Patients may have a history of back injury or complain of back and/or neck pain. Additionally, there is often evidence of spinal column degeneration or other vertebral pathology on imaging. Although pruritus may improve in many of these patients with surgical correction of their vertebral disease, a less invasive method for treating itch is preferred for patients who do not otherwise require surgery. Systemic therapy with gabapentin has shown some benefit, but topical therapy may be satisfactory in some cases without the side effects associated with gabapentin. Topical therapies include local anesthetics, corticosteroids, and capsaicin.

Both topical capsaicin cream (0.025 %) and the 8 % capsaicin patch have been shown to be efficacious in this condition. In a double-blind, vehicle-controlled crossover study with topical capsaicin, 20 patients with notalgia paresthetica were randomized to capsaicin 0.025 % cream or vehicle control group with crossover after 4 weeks of treatment and a 2 week washout period. Overall, 70 % of patients experienced improvement in their symptoms with capsaicin therapy while 30 % of patients had improvement with vehicle. While most patients experienced

some relapse after 1 month of no treatment, repeat use of topical capsaicin cream 0.025 % again resulted in remission of their pruritus (Wallengren and Klinker 1995).

Additionally, a report of two cases of notalgia paresthetica treated with a 8 % capsaicin patch resulted in complete remission of itch in both patients immediately following removal of the patch. The patient who was able to tolerate the complete goal duration of therapy (60 min) remained symptom-free at 12 weeks. The other patient was able to tolerate the patch for only 20 min and experienced recurrence of pruritus after few days. While the authors admit that data for use of the capsaicin patch for neuropathic itch is currently limited, their experience does show efficacy of this formulation in the treatment of notalgia paresthetica with ease and convenience of application as a benefit over the cream (Metz et al. 2011).

12.2.3 Brachioradial Pruritus

Patients with brachioradial pruritus present with unilateral or bilateral pruritus of the distal, and less commonly, proximal arms. The pruritus is often felt to be worse during the summer months or after prolonged sun exposure and is most common in middle-aged or older patients with fair skin. As with notalgia paresthetica, there is no identifiable primary lesion, though secondary changes associated with chronic scratching and rubbing may be present.

The etiology of brachioradial pruritus is not completely understood. Because it apparently worsens with sun exposure in many patients, one theory suggests that brachioradial pruritus is a result of sun damage to peripheral nerve fibers in the sun-exposed skin of the arm. One study demonstrated a decrease of sensory nerve fibers in the distal arms of patients with brachioradial pruritus at the end of the summer season compared to number of nerve fibers during a symptom-free period (Wallengren and Sundler 2005). A second theory proposes that cervical spine disease causing entrapment of cervical nerve rami results in neuropathic itch in the distal arm distribution, analogous to the theoretical cause of notalgia paresthetica. Indeed, many patients complain of neck pain and have evidence of spinal column disease in the C5–C6 distribution on imaging. Current thinking is that cervical vertebral disease may predispose patients to brachioradial pruritus while ultraviolet light is an eliciting factor (Wallengren and Sundler 2005).

As with notalgia paresthetica, surgical treatment of cervical vertebral disease may result in amelioration of pruritus in some patients with brachioradial pruritus. Gabapentin has also been used with some success in treatment of this condition. Unfortunately, brachioradial pruritus is often resistant to topical or oral corticosteroids and antihistamines.

Topical capsaicin has been used successfully in some cases. Two studies done in tropical latitudes demonstrated 12 of 15 (80 %) patients experienced improvement of symptoms when treated with topical capsaicin (Knight and Hayashi 1994; Goodless and Eaglstein 1993). In another study carried out in a temperate climate,

all patients experienced relief of itch during the treatment period but found that capsaicin 0.025 % cream was no better than vehicle. The authors postulate that one reason for this outcome is the difficulty in distinguishing laterality in pruritus. They also considered the possibility of spontaneous improvement as the weather changed to cooler temperatures (Wallengren and Sundler 2005). Regardless; capsaicin remains a safe alternative for treatment of brachioradial pruritus.

12.2.4 Lichen Simplex Chronicus and Prurigo Nodularis

Lichen simplex chronicus (LSC) and prurigo nodularis are dermatologic conditions that present in patients who chronically scratch or rub their skin due to intractable pruritus from a variety of primary sources. The causative source may be a dermatologic condition such as atopic dermatitis, scabies, or pemphigoid, or it may be related to pruritus associated with systemic illness or malignancy. Lichen simplex chronicus and prurigo nodularis are not uncommon findings in patients with diabetes mellitus, obstructive biliary disease, chronic kidney disease, liver failure, endocrine dysfunction, or malignancies such as leukemia and lymphoma. Additionally, pruritus and secondary changes of lichen simplex chronicus and prurigo nodularis can be seen in patients with severe emotional stress or anxiety.

Lichen simplex chronicus presents as thickened, erythematous or hyperpigmented scaly plaques that may also show evidence of excoriation. Distribution is variable, and depends on the underlying source of pruritus. Regardless of the source, the lesions are usually located on easy-to-reach skin; that is, areas that the patient has access to rub or scratch repeatedly.

Prurigo nodularis is a similar condition in that it results from chronic mechanical irritation of the skin, however, it presents as discrete nodules of lichenification and excoriation rather than confluent plaques.

Treatment of both of these conditions is difficult. The pruritus is often intractable and the mechanical irritation caused by scratching or rubbing worsens the lichenification and inflammation, and subsequently, the pruritus. While treatment of the underlying condition can help significantly, often, that condition is not curable and therefore the pruritus persists. Therapeutic regimens aimed at easing the itch include topical medications such as emollients containing menthol and topical corticosteroids. These treatments are often insufficient on their own because as the stratum corneum thickens in these conditions, it inhibits penetration of the medication into the dermis. While intralesional steroids have been used with some success, the size of the plaque of LSC or the number of prurigo nodules may make this modality impractical. Systemic therapies that have been used with some success include antihistamines, ultraviolet light, corticosteroids, cyclosporine, thalidomide, and etretinate. Although these medications have been shown to be successful at ameliorating pruritus, each has side effects that limit the practicality of its use. Capsaicin is a reasonable alternative as it lacks systemic side effects and penetration through a thickened stratum corneum can be enhanced through occlusion.

To evaluate the efficacy of topical capsaicin in the treatment of prurigo nodularis, Stander et al. measured both the clinical and histologic features pre- and posttreatment in 33 patients. Each patient applied capsaicin to the lesional areas 4–6 times daily, starting with a concentration of 0.025 % and increasing as needed, to achieve complete cessation of pruritus. The highest concentration required was 0.3 % by a single patient. Treatment duration was also variable, lasting from 2 weeks to 33 months in one patient with poor compliance. However, all participants achieved complete remission within 12 days and 24 patients experienced flattening of lesions within 2 months. Although there was recurrence of pruritus once the capsaicin application was stopped in about half of the study patients, the majority experienced 2 weeks to 2 months of treatment-free remission. Patients also experienced relief when the medication was reinitiated following cessation and recurrence. The histologic changes accompanying the clinical changes showed thinning of the stratum corneum and epidermis, and decreased inflammation and scarring. Ultrastructurally, decreased reactivity to substance P was noted following treatment with capsaicin. The authors conclude that capsaicin is effective for symptomatic relief as well as clinical resolution of the nodules. They recommend regular application of topical capsaicin 4–6 times daily at a concentration that achieves complete cessation of pruritus with reapplication upon recurrence (Stander et al. 2001).

12.2.5 Pruritus Ani, Vulvae, and Scroti

Pruritus of the anogenital skin and mucosa may be idiopathic or secondary to an underlying disorder. It presents as intractable itching in the perianal or genital area, often with secondary lichenification. In order to diagnose primary or idiopathic pruritus ani, vulvae, or scroti, possible secondary causes should be ruled out. Potential causes of secondary anogenital pruritus include irritant or allergic contact dermatitis, primary cutaneous conditions (psoriasis, atopic dermatitis, seborrheic dermatitis, lichen planus, lichen sclerosus), malignancy (anogenital carcinoma, paget's disease), infection (pinworms, sexually transmitted diseases), hemorrhoids, rectal fistulas, or sinus tracts. In the absence of an underlying condition, idiopathic anogenital pruritus has been attributed to dietary causes such as excessive caffeine intake, personal hygiene, or psychogenic factors (Bolognia and Jorizzo 2012).

In cases of secondary anogenital pruritus, symptoms improve with treatment of the underlying condition. For idiopathic cases, treatment can be more challenging. In patients with a suspected psychogenic component, psychological evaluation, and counseling may be beneficial. Mild cases may respond to frequent sitz baths and mild-potency topical corticosteroids. However, severe cases with secondary lichenification may require more potent topical steroids, leading to increased risk of atrophy (Bolognia and Jorizzo 2012).

A randomized, placebo-controlled crossover study evaluating the efficacy of topical capsaicin use for patients with anogenital pruritus found that 31 of 49 participants experienced relief of symptoms during the treatment period. Participants

applied 0.006 % capsaicin ointment or placebo ointment with menthol to the affected area 3 times daily for 4 weeks followed by a 1-week wash out and 4 week crossover period. Four patients withdrew from the study due to side effects. There was a statistically significant ($p < 0.001$) difference in response rate between the two groups. Responders required consistent treatment of at least one application of capsaicin daily to remain symptom-free (Lysy et al. 2003). For patients who are refractory to topical steroids, or have a risk of atrophy with continued treatment, topical capsaicin appears to be a safe and effective alternative.

12.2.6 Pruritus of Hemodialysis

Pruritus is the most common and most distressing dermatologic condition in patients undergoing chronic hemodialysis. Although prevalence has decreased recently because of improved dialysis techniques, it still occurs in 25–43 % of patients. The most common sites of involvement are the back, head, and abdomen, and frequently 1/3 of the total body surface area is involved (Weisshaar et al. 2003).

The pathogenesis of hemodialysis-associated itch is not well understood. Despite the well-established correlation of hyperuricemia and pruritus in patients with chronic renal failure, multiple studies have not shown an association between electrolyte levels and intensity of itch in patients undergoing hemodialysis. In a study involving 167 patients on hemodialysis, the only factor associated with increased pruritus was the presence of a preexisting neuropathy such as restless leg syndrome, paresthesias, decreased sensation, decreased deep tendon reflexes, or decreased muscle strength. The authors suggest that this association confirms the neurogenic origin of the pruritus of hemodialysis (Akhyani et al. 2005).

Multiple treatment modalities have found variable success in the treatment of hemodialysis-associated pruritus. Systemic therapy includes anti-histamines, cholestyramine, erythropoietin, ondansetron, and UVB phototherapy. Topical moisturizers and corticosteroids have also shown some efficacy in select patients. However, no specific therapy has shown consistent efficacy. In a 2003 study, no difference in pruritus was noticed between skin treated with capsaicin 0.05 % and untreated skin. However, topical capsaicin 0.05 % resulted in significantly decreased pruritus in hemodialysis patients compared with healthy controls (Weisshaar et al. 2003). In patients on chronic hemodialysis treatment, pretreatment with capsaicin may be helpful in decreasing dialysis-related pruritus.

12.2.7 Aquagenic Pruritus

Aquagenic pruritus is rare condition characterized by itching sensation of the skin following exposure to water of any temperature or salinity. No primary lesion or skin change is identified. Typically, itching, burning, or stinging sensation will begin within

30 min of exposure to water and last for up to 2 h. The lower extremities are affected first, with migration of symptoms to upper body but with sparing of the head, palms, and soles. While the etiology of idiopathic aquagenic pruritus is unclear, some studies have demonstrated elevated levels of neurotransmitters and peptides implicated in other pruritic conditions, including acetylcholine, histamine, serotonin, and prostaglandin E2 in the dermis and epidermis of affected skin. It is important to evaluate for and exclude underlying conditions that may lead to secondary aquagenic pruritus, such as hematologic malignancy (including Hodgkin disease), polycythemia vera, essential thrombocythemia, or myelodysplastic syndrome (Bolognia and Jorizzo 2012).

Overall, treatment options for idiopathic aquagenic pruritus have been dissatisfying. Systemic medications such as cyproheptadine, cimetidine, and cholestyramine have been used without much success. Ultraviolet light has been more effective with PUVA, demonstrating better results than with broadband UVB.

A study by Lotti et al. evaluated both the clinical and immunofluorescent changes in skin of patients with aquagenic pruritus before and after 4 weeks of treatment with capsaicin cream of three different concentrations (0.025, 0.5, 1.0 %). They found that prior to treatment, neuropeptidergic fibers in skin were filled with neuropeptides when evaluated with direct immunofluorescence and clinically patients experienced pruritus with exposure to water. Following capsaicin treatment, neuropeptidergic fibers were devoid of neuropeptide and water did not evoke pruritus. The authors conclude that aquagenic pruritus is mediated at least in part by neuropeptides, including substance P (Lotti et al. 1994). Thus, capsaicin is a reasonable treatment option for this rare condition. Currently, no standard for dosing or frequency of application exists and either parameter may be adjusted to achieve maximum efficacy while still being tolerable to the patient.

12.2.8 Apocrine Chromhidrosis

Apocrine chromhidrosis is a condition in which apocrine sweat is pigmented, usually yellow, green, or black. This results from the high lipofuscin concentration in apocrine sweat of some patients. One case report demonstrated effective treatment of facial apocrine chromhidrosis with topical capsaicin in a 30-year-old female. The patient applied capsaicin to half of her face 1–2 times daily, and vehicle to the other half. Resolution of her condition occurred only on the half treated with capsaicin and recurred within 2 days of cessation of the therapy (Marks 1989). While treatment options for apocrine chromhidrosis are limited, capsaicin is a valid option with few side effects.

12.2.9 Lipodermatosclerosis

Lipodermatosclerosis, a manifestation of chronic venous insufficiency, is a painful panniculitis that typically presents on the medial lower legs as a result of chronic venous insufficiency. In addition to pain, patients experience erythema

progressing to hyperpigmentation, warmth, and induration of the site. It presents most commonly in women over the age of 40. Clinical manifestations are often bilateral. It is felt that in patients with venous insufficiency, venous hypertension leads to increased leakage of fibrinogen and other blood products from capillaries. Fibrinogen then polymerizes to form fibrin cuffs around vessels, further impairing oxygen exchange and leading to tissue hypoxia. This hypoxia results in the classic changes seen in the subcutaneous tissue in patients with lipodermatosclerosis: septal thickening and sclerosis with hyaline fibrosis and eventually lipomembranous change of fat lobules (Bolognia and Jorizzo 2012).

A number of therapeutic modalities have been attempted to treat this condition with variable success. Much depends on the stage of the disease. Compression and elevation are helpful in the early stages and are the mainstays of treatment. Anabolic steroids such as stanozolol have been used successfully for their fibrinolytic properties, however, significant side effects that limit its usefulness. Other treatments used in small studies and case reports with varying success include ultrasound, pentoxifylline, fasciotomy, and phlebectomy (Bolognia and Jorizzo 2012).

Typically, the pain associated with early lipodermatosclerosis is the most concerning symptom for patients. Yosipovitch et al. describe two patients with acute lipodermatosclerosis and one with acute lobular panniculitis and venous insufficiency who experienced relief of pain with topical capsaicin. They were each treated for 3 weeks with 0.075 % topical capsaicin 5 times per day, followed by continued treatment 3 times daily for an additional month in two of the cases. Each patient experienced resolution of pain and clinical panniculitis with no recurrence at follow-up of 2–6 months. While little is known about the fibrinolytic activity of capsaicin, Thai people who ingest chili pepper daily do show increased fibrinolytic activity (Visudhiphan et al. 1982). Additionally, capsaicin has been shown to increase bleeding time and inhibit platelet aggregation in mice. The authors postulate that substance P may have fibrinolytic properties, thus making topical capsaicin an useful treatment for early lipodermatosclerosis and other lobular panniculitides (Yosipovitch et al. 2005).

12.2.10 Alopecia Areata

This inflammatory alopecia is characterized by discrete round to oval areas of nonscarring hair loss, most commonly on the scalp. In many cases, the hair will regrow spontaneously, but often the condition recurs in a different area. There are chronic and more extreme forms of alopecia areata where a patient may lose all their scalp hair (alopecia totalis) or all of their body hair (alopecia universalis). The prognosis for complete regrowth in these cases is less promising. Alopecia areata may also affect the fingernails and toenails in a variety of ways, most common of which is pitting of the nail plate. Other nail changes include ridging, trachyonychia, onychomadesis, and red lunulae.

Alopecia areata is considered to be an autoimmune condition wherein T-cells target specific autoantigens on terminal anagen follicles. The histopathologic picture is that of a lymphocytic infiltrate tightly surrounding and sometimes infiltrating the follicular bulb, thus sparing the stem cells in the bulge region of the follicle and, therefore, the follicle's ability to regenerate intact. The main goal of treatment for alopecia areata is the reduction of the inflammatory response. For limited and localized disease, intralesional corticosteroids may speed regrowth of hair. Additional topical treatments include irritants such as azelaic acid and anthralin, or immunotherapy with agents such as squaric acid. For more widespread hair loss, systemic corticosteroids or immunosuppressants like cyclosporine have been used, but these options are limited due to side effects (Bolognia and Jorizzo 2012).

While the role of the immune system is well established in the etiology of alopecia areata, the clinic link between emotional stress and worsening of the condition has led some to search for a neurologic contribution. Previous studies have demonstrated decreased concentrations of substance P and calcitonin gene-related peptide in scalp biopsies of alopecia areata as well as changes in the structure and function of perifollicular nerves (Peters et al. 2001; Rossi et al. 1997). As capsaicin causes release and subsequent depletion of substance P, Ehsani et al. postulated its potential use in treating alopecia areata by transiently increasing the neuropeptide and the neurofollicular interface. They randomized 50 patients with less than 30 % scalp surface area involvement with alopecia areata to a control group or treatment group. The control group applied clobetasol ointment 0.05 % daily for 6 weeks while the treatment group applied capsaicin ointment daily for 2 weeks, then twice daily for 4 weeks. Although there was no statistically significant difference between the control and treatment group in terms of regrowth of terminal hairs, after 4 weeks, the treatment group demonstrated a significantly greater growth of vellus follicles. They concluded that capsaicin has a dual effect on the follicular unit: it inhibits hair shaft elongation and matrix proliferation but promotes vellus hair growth (Ehsani et al. 2009). While this does not appear to be an optimal treatment for alopecia areata, it does highlight a potential role for neuropeptides in the etiology of the condition and a potential target for treatment.

12.2.11 Psoriasis

Psoriasis is a common Th1/Th12-mediated inflammatory skin condition that presents in the classic form as variably sized erythematous and scaly plaques distributed on the extensor extremities, buttocks, and scalp. Presentation is variable, with involvement ranging from a few small plaques to complete erythroderma. Patients may have involvement with their hands, feet, scalp, or nails or isolation of disease to those areas. Twenty percent of patients have associated joint pain. While cutaneous pain and itch are not consistent symptoms, many patients experience such discomfort from their psoriatic plaques.

While recent psoriasis therapeutic research has focused on the inflammatory mechanisms involved in the pathogenesis of the disease, there is evidence to suggest that neurogenic pathways may also contribute to or exacerbate the condition. One double-blind study of topical capsaicin in the treatment of psoriasis-related pruritus demonstrated not only significant improvement of itch, but also reduction in combined psoriasis severity scores, as measured by degree of scaling, thickness, erythema, and pruritus, in patients using capsaicin 0.025 % cream for 4–6 weeks when compared to those using a vehicle control. The authors speculate that substance P plays a role not only in the driving the pruritus and pain associated with psoriasis, but also in influencing the inflammatory process by increasing perfusion and thus promoting accumulation of inflammatory markers at the site (Ellis et al. 1993).

An additional study supported the role of neurogenic factors in the pathogenesis of psoriasis. Krogstad, et al. found that lesional psoriatic skin treated with capsaicin showed immediate increase of histamine and overall perfusion. However, when measured at 24 h following application of capsaicin, there was a decrease below baseline of both perfusion and histamine levels (Krogstad et al. 1999). While capsaicin does not target specific inflammatory pathways—the feature that makes many of the new biologic medications and traditional immunosuppressant medications effective in the treatment of , the significant improvement in both pruritus and other psoriatic symptoms shown with topical capsaicin treatment make it a valuable adjuvant therapy in patients for whom systemic therapy is less desirable.

12.3 Treatment Limitations

12.3.1 Adverse Effects

The nature of capsaicin as a derivative of chili peppers and a substance P releaser makes it a powerful skin irritant. This has been known for generations among people who handle chili peppers and develop a contact dermatitis called “Hunan hand” as a result of chronic exposure. Its therapeutic effects are no different. All patients experience skin irritation in the form of burning with the application of even low concentrations of topical capsaicin. In the case of accidental inhalation, capsaicin can induce coughing and burning of the mucosa. This property is exploited in the formulation of personal protection sprays containing capsaicin (Bode and Dong 2011).

Reports of more severe side effects are rare. One report attributes a case of coronary vasospasm and acute myocardial infarction to the use of a topical capsaicin patch in the treatment of lower back pain (Akcay et al. 2009). Multiple studies done in mice also suggest that topical capsaicin may have carcinogenic potential, including skin cancer. The complete blockade of the transient receptor potential

vanilloid subfamily member 1 (TRPV1) in the presence of a tumor promoter resulted in increased skin carcinogenesis in mice. The authors postulate that blockade of TRPV1 through chronic use of topical capsaicin, coupled with a tumor promoter such as ultraviolet light, could result in increased skin cancer (Bode and Dong 2011). Thus, caution should be taken into account when combining topical capsaicin with phototherapy.

12.3.2 Compliance

Perhaps the most significant limitation to using capsaicin to treat dermatologic conditions is compliance with the treatment. Because nearly every patient experiences immediate cutaneous discomfort, many patients are unable to continue treatment for a sufficient length of time to reach a point of therapeutic benefit. In fact, from reported clinical trials and experience, at least 30 % of patients or participants withdraw due to lack of tolerability (Papoiu and Yosipovitch 2010). As response rates for some dermatologic conditions are high, it may be necessary to counsel the patient about the expected transient cutaneous discomfort and the importance of compliance for a meaningful response.

12.4 Summary

Neurogenic pain and pruritus play a role in many dermatologic conditions, making topical capsaicin a viable treatment option that lacks the systemic side effects of the oral alternatives. Additionally, capsaicin is a reasonable alternative for the treatment of other diseases, including apocrine chromhidrosis, lipodermatosclerosis, and alopecia areata. Compliance can be difficult, especially with increased concentrations, as nearly as every patient experiences immediate cutaneous discomfort; however, this can be mitigated with appropriate dose escalation and education.

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