Ongoing treatment with high-concentration capsaicin 8% topical system results in progressive pain reduction for painful diabetic peripheral neuropathy: a retrospective real-world analysis

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Background

- Painful diabetic peripheral neuropathy (PDPN) is a chronic complication of diabetes associated with reduced quality of life and significant morbidity[1,2]
- In PDPN, prolonged hyperglycemia leads to damage to peripheral nerves,[3] including C and Aδ nerve fibers that express transient receptor vanilloid potential 1 (TRPV1) receptors.[4] These receptors play a pivotal role in pain signaling.[4] Patients with diabetes have a reduced epidermal nerve fiber density (ENFD) compared with healthy controls, which can result in dysfunctional TRPV1-expressing fibers and debilitating pain often felt in the extremities[5,6]
- Progression of PDPN is linked to diabetic ulcers, infections, and, in cases of serious injury, foot amputation.[7] PDPN is further complicated by protective sensory loss and an increase in pain, and the disease will continue to progress if left untreated[7]
- Nerve damage is accelerated by poor microcirculation.[8] Glycemic control alone is insufficient to prevent the progression of PDPN and it is necessary to screen all patients with diabetes regularly for PDPN and initiate appropriate treatment in a timely fashion[8]
- In the USA, capsaicin 8% topical system (Figure 1) is approved by the FDA for the treatment of neuropathic pain associated with PDPN of the feet and post-herpetic neuralgia[9]
- Capsaicin is an agonist of TRPV1 receptors expressed on peripheral sensory nerve fibers, and selectively targets the TRPV1 receptors located on C and Aδ nerve fiber terminals.[4] Capsaicin 8% topical system induces reversible neurolysis of sensory nerve fiber terminals, resulting in relief from PDPN as early as 1 week after application (Figure 2). There is evidence that, following capsaicin 8% topical system treatment, the reduced ENFD in PDPN patients regenerates with a more "healthy" phenotype (less spontaneously active and with improved function)[10,11]
- Based on a small subset of biopsy data, the pain-relieving effects of a single application may not persist in the long term, owing to the chronic nature of diabetes and the progressive nature of DPN[10]
- In the PACE trial (NCT01478607), patients treated with repeated applications of 30-min (n=156) capsaicin 8% + standard of care (SOC) demonstrated continual reductions in average daily Numerical Pain Rating Scale (NPRS) scores compared with SOC alone over 12 months[12]
  - The percentage of patients achieving a clinically meaningful response (≥30% reduction from baseline in average daily pain) steadily increased with each subsequent application[12]

Purpose

- In order to better understand the effects of ongoing treatment and patients' response to capsaicin 8%, this retrospective, real-world, single-center case series explored whether patients receiving ongoing treatment with capsaicin 8% topical system for PDPN reported a progressive response in pain reduction, as assessed by NPRS values

Methods

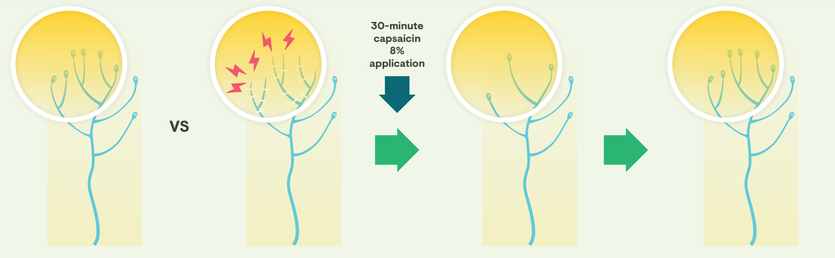
- In our center, 18 patients had received ≥3 applications of capsaicin 8% topical system
- Of these 18 patients, 6 were not included in the final data set owing to missing NPRS scores
- Patients received ongoing treatment with capsaicin 8% topical system with approximately 12–16-week treatment intervals
- Efficacy, defined as a reduction in pain, was measured using the NPRS with values from 0 to 10, with 0 meaning "no pain" and 10 meaning "worst possible pain"
- The pre-application pain intensity score (NPRS) was captured by the clinician, as part of routine practice, prior to each administration of capsaicin 8% topical system
- The post-application pain intensity score (NPRS) was measured during an evaluation preceding the subsequent administration of capsaicin 8% topical system

Conclusions

- In a real-world setting, the majority of patients with PDPN achieved a clinically meaningful response to capsaicin 8% treatment, with significant reduction in average pain scores
- With each successive treatment, pain levels were further reduced. This is consistent with previous findings showing a progressive response in patients with PDPN[9,11]
- We hypothesize that this apparent progressive response is due to capsaicin-induced regeneration and restoration of more normal nerve fiber phenotypes. Other mechanisms that may be involved include gradual sensitization of the TRPV1 receptors, decreases in central sensitization, and/or increased patient activity, leading to beneficial effects on pain
- In PDPN, the peripheral nerves are under continued attack from hyperglycemia, leading to aberrant sensory nerve fiber terminals.[9] This persistent damage may underlie the return of pain and other changes commonly reported in patients with DPN
- As a chronic complication of diabetes, PDPN requires chronic treatment; in the case of capsaicin 8%, this involves timely and repeated re-application

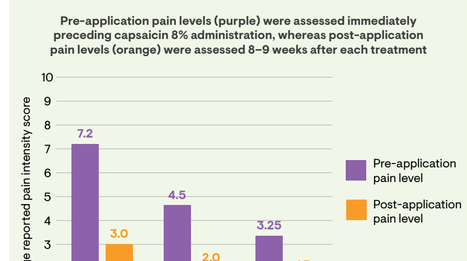
Figure 1: Application of the capsaicin 8% topical system, which must be done by a HCP, in the office

Figure 2: Hypothesized changes in nerve fiber anatomy following capsaicin 8% topical system in PDPN



DPN, diabetic peripheral neuropathy; ENFD, epidermal nerve fiber density; PDPN, painful diabetic peripheral neuropathy; TRPV1, transient receptor vanilloid potential 1.

Figure 3. Effect of capsaicin 8% on pain intensity scores in patients receiving repeated treatments



Patient characteristics

- All patients reported an average NPRS score of ≥4 at baseline
- Eleven patients (61.1%) were male, and seven patients (38.9%) were female
- All patients had type 2 diabetes mellitus (T2DM)
  - The mean (standard deviation [SD]) duration of T2DM between diagnosis and treatment was 16.5 (7.70) years
  - The year of T2DM diagnosis was not available for three patients
- The mean (SD) age and body mass index were 66.6 (11.9) years and 33.4 (5.33) kg/m^2, respectively

Results

- The majority of patients (88.9%) reported a ≥50% reduction in pain from baseline on average in response to capsaicin 8% topical system throughout their treatments
  - Fifteen patients (83.3%) had the first response with the first treatment
  - One patient (5.6%) had the first response on the second treatment
  - Two patients (11.1%) did not respond to treatment
- The data show a progressive reduction in average pain intensity following each application with capsaicin 8% topical system (Figure 3)
  - After each treatment, the pain returned, albeit to lower levels than at baseline

Limitations

- This retrospective case series included a small number of patients from a single center and therefore the data cannot be generalized to larger populations

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Disclosures

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