

Case Report

Posttraumatic and Postsurgical Neuropathic Pain Responsive to Treatment with Capsaicin 8% Topical Patch

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Capsaicin 8% patch (Qutenza) is mainly used to treat postherpetic neuralgia and human immunodeficiency virus-associated neuropathy. However, evidence of the efficacy of Qutenza in other forms of neuropathic pain is lacking.

A 24-year old Libyan man, with no previous medical history, sustained multiple wounds in the right side of the chest and back after a bomb explosion. The patient experienced pain, which persisted in a wide location around the surgical intervention for a long time, beyond the usual course of natural healing of an acute pain and was different from that suffered preoperatively. The characteristics of the pain included burning, electric shock-like sensation, tingling, and numbness, and it was paroxysmal. The pain was associated with hyperalgesia and intense allodynia in a wide area, approximately of 1,100 cm².

Our initial treatment strategy included pregabalin, tramadol, and duloxetine. However, our patient's pain responded to treatment with capsaicin 8% patch when the initial treatments showed only minimal effectiveness regarding the intensity of pain. Interestingly, the most important finding was that capsaicin 8% patch showed a more than 80% reduction of the area of allodynia associated with the pain, when other treatments failed. Moreover, although recent data showed that in patients who respond to Qutenza, analgesia starts within a few days of treatment and lasts on average 5 months, our patient showed an initial response within 7 days of treatment but a longer duration of more than 18 months.

Although further controlled studies are needed to explore the efficacy of the capsaicin 8% patch in patients who experience posttraumatic neuropathic pain, we encourage clinicians to try the capsaicin 8% patch when alternative treatments fail.

Key words: Capsaicin, posttraumatic, neuropathic, pain

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Neuropathic pain (NP) is the pain arising as a direct consequence of a lesion or disease affecting the somatosensory system (1). This common type of pain is often underdiagnosed and undertreated, and it is associated with suffering, disability, and impaired quality of life (2). Causes of NP are multiple and include diabetes mellitus, postherpetic neuralgia, stroke, HIV related polyneuropathy cancer, chemotherapy-induced polyneuropathy, and post-

radiotherapy polyneuropathy (3-5). Posttraumatic peripheral nerve pain is also a common cause of NP and occurs after nerve damage due to trauma from accidental injury or surgery.

NP can be very difficult to treat with only approximately half of patients achieving partial relief (6). Several groups, including the International Association for the Study of Pain (IASP) (6) and the European Federation of Neurological Societies (EFNS) (7), have

developed evidence-based guidelines for the treatment of NP.

We describe, for the first time, a case of a patient with resistant posttraumatic and postsurgical neuropathic pain that responded to treatment with capsaicin 8% topical patch.

CASE REPORT

A 24-year old Libyan man, with no previous medical history, gets injured after a bomb explosion during the Libyan Civil War in May 2011. The patient sustained multiple wounds on the right side of the chest and back. He was immediately transferred to the local hospital where he underwent surgery by a trauma surgeon for removal of the bomb pieces and for wound closure (Fig. 1). However, some pieces that were located in the right lung could not be removed (Fig. 2).

The patient experienced pain, which persisted in a wide location around the surgical intervention for a long time, beyond the usual course of natural healing of an acute pain and was different from that suffered

preoperatively. In November 2011, in order to achieve pain relief, the patient was referred to the pain clinic in the Athens Medical Center.

On examination, the patient was diagnosed with posttraumatic neuropathic pain. The characteristics of pain included burning, electric shock-like sensation, tingling, and numbness, and it was paroxysmal. The pain was associated with hyperalgesia and intense allodynia in a wide area, approximately of 1,100 cm², around the surgical trauma and the smaller healed wounds of the bomb pieces (Figs. 3-4). In a visual analog scale (VAS) the patient rated the pain as 10/10 (with 5/10 being his maximum accepted score). Using the Douleur Neuropathique 4 (DN4) Questionnaire (8) the patient scored 9/10, when the cutoff for diagnosis of neuropathic pain is 4/10. He has also reported poor sleep and poor quality of life to the point that he could not even put on clothes without causing pain exacerbation.

Our treatment strategy included pregabalin (first line adjuvant drug) 75 mgs once daily, which over one week was titrated to 300 mgs twice daily, and tramadol (weak opioid drug) 100 mgs 4 times daily. This regime has led to a reduction in the intensity of pain to 8/10 on VAS and a slight improvement on patient's sleep. However, there were no changes in the pain characteristics and the area of allodynia.

Duloxetine 30 mgs once daily was initiated on week 3 (as an add-on therapy) and was titrated to 30 mgs twice daily over one week. As the patient did not



Fig. 1. Deep wound in the right side of the back, caused by the bomb explosion.



Fig. 2. Chest X-ray, post-surgery, showing the remaining bomb pieces in patient's right lung and soft tissues



Fig. 3. Area of allodynia before application of capsaicin 8% patch (green color) and area of allodynia after 3 patch applications (orange color).



Fig. 4. Area of allodynia before application of capsaicin 8% patch (green color) and area of allodynia after 6 patch applications (orange color).

report any benefit, duloxetine was increased to 60 mg twice daily on week 5. The regime of pregabalin, tramadol, and duloxetine (Table 1) has led to a further reduction of pain intensity to 6/10 on VAS. No further medication adaptations took place.

However, there were still no changes in the pain characteristics, the area of allodynia, and there were no further changes of the pain's impact on the patient's sleep and quality of life. Therefore, after 8 weeks of initial presentation to our clinic and 8 months after the patient's trauma, a capsaicin 8% topical patch was applied, as an add-on treatment, to the area of allodynia. Four patches of capsaicin 8% (280 cm² each) were used to cover the whole area of allodynia. During the patch application, the patient presented redness at the site of application and topical pain that was treated with 40 mg of parecoxib and 100 mg of tramadol administered intravenously. These side effects were resolved

after completion of treatment and patch removal after 60 minutes, as recommended (9).

One week after the first administration of the capsaicin 8% patch, the patient reported further reduction in the intensity of pain to 5/10 on VAS, small reduction in the area of allodynia, and improved sleeping pattern. The treatment with the capsaicin 8% patch was repeated every 12 weeks after the initial application for a total of 6 times. After the third application the patient was rating the pain to be 5/10 on VAS and the area of allodynia was reduced by 50% (Figs. 3-4).

After the sixth application the patient reported similar intensity, however the area of allodynia (area where even touch would provoke pain) was reduced by more than 80% (image 3), achieving thus a better quality of life. Using the Douleur Neuropathique 4 (DN4) Questionnaire the patient achieved a reduction of the total score to 6/10. Since then, the intensity of the pain

Table 1. Basic pharmacodynamic and pharmacokinetic properties of drugs tried prior to the application of capsaicin 8% patch.

Drug	Pharmacodynamics		Pharmacokinetics		
	Mechanism of Action	Half-life	Bioavailability	Metabolism	Excretion
Pregabalin (15)	Binds to the α 2- δ (alpha-2-delta) subunit of the voltage-dependent calcium channel in the central nervous system	~ 6 hours	> 90%	Negligible	Renal
Tramadol (16)	μ -opioid receptor agonist Serotonin releasing agent Norepinephrine reuptake inhibitor NMDA receptor antagonist 5-HT _{2C} receptor antagonist α 7 (alpha-7) nicotinic acetylcholine receptor antagonist TRPV1 receptor agonist M1 and M3 muscarinic acetylcholine receptor antagonist	~ 6 hours	~ 70%	Liver	Renal
Duloxetine (17)	Serotonin-norepinephrine reuptake inhibitor (SNRI)	~ 12 hours	~ 50%	Liver	Renal (> 70%) and intestinal (< 30%)

as well as the area of allodynia have been stabilized and the patient continues to receive pregabalin, tramadol, and duloxetine as described above.

Discussion

Capsaicin, the main ingredient responsible for the hot pungent taste of chili peppers, is an alkaloid found in the Capsicum family. Capsaicin was traditionally used for muscular pain, headaches, to improve circulation, and for its gastrointestinal protective effects. It was also commonly added to herbal formulations because it acts as a catalyst for other herbs and aids in their absorption (10). Topical capsaicin formulations are widely used to manage pain. Since 1980, low-concentration capsaicin creams, lotions, and patches intended for daily skin application have been available in most countries (11). QutenzaTM, a high-concentration single administration capsaicin 8% patch, is mainly used to treat postherpetic neuralgia (PHN) and human immunodeficiency virus-associated neuropathy (12).

Although, the mechanism of action of topical capsaicin has been ascribed to depletion of substance P, experimental and clinical studies show that depletion of substance P from nociceptors is only a correlate of capsaicin treatment and has little, if any, causative role in pain relief. Rather, topical capsaicin acts on the skin to attenuate cutaneous hypersensitivity and reduce pain by a process best described as "defunctionalization" of nociceptor fibers. Defunctionalization is due to a number of effects that include temporary loss of membrane potential, inability to transport neurotrophic factors leading to altered phenotype, and reversible retraction of epidermal and dermal nerve fiber terminals (11). Recent evidence established that capsaicin binds to the

transient receptor potential vanilloid 1 (TRPV1) receptor that is expressed predominantly by sensory neurons (10). Apart from altered expression of the capsaicin receptor TRPV1, peripheral neuropathic hypersensitivity is mediated by other mechanisms, including key ion channels in affected or intact adjacent peripheral nociceptive nerve fibers, aberrant re-innervation, and collateral sprouting, all of which are defunctionalized by topical capsaicin (11).

Capsaicin 8% patch should be applied to intact, non-irritated, dry skin of the most painful area, and allowed to remain in place for 30 minutes for the feet (e.g. HIV-associated neuropathy) and 60 minutes for other locations (e.g. postherpetic neuralgia). A maximum of 4 patches is allowed at each application and treatments may be repeated every 90 days, as warranted by the persistence or return of pain (9).

Advantages of the high-concentration capsaicin patch include longer duration of effect, patient compliance, and low risk for systemic effects or drug-drug interactions (10). On the other hand, the most commonly reported adverse reactions of Qutenza are burning, pain, erythema, and pruritus at the site of application. Adverse reactions are transient, self-limited, and usually mild to moderate in intensity (12).

Despite the well-studied properties of the capsaicin 8% patch in the treatment of postherpetic neuralgia and HIV-related polyneuropathy (13), evidence of the efficacy of Qutenza in other forms of neuropathic pain is lacking. The first results of the QUEPP study of the tolerability and analgesic effectiveness over 12 weeks after a single application of capsaicin 8% cutaneous patch in a group of patients with postherpetic neuralgia, postsurgical neuralgia, posttraumatic neuropathy,

and mixed pain syndromes showed that the capsaicin 8% cutaneous patch is safe and effective. However, the limitation of the study was that it did not include a control group and, therefore, a comparison of the results with that of therapeutic alternatives is not justified (14).

To our knowledge, this is the first case of a patient with postsurgical and posttraumatic pain where capsaicin 8% cutaneous patch has been applied 6 times, with appropriate intervals, and was effective, when all other treatments showed minimal effectiveness. Although recent data showed that in patients who respond to Qutenza, analgesia starts within a few days of treatment and lasts on average 5 months (11), our patient showed initial response within 7 days of treatment but a longer duration of more than 18 months.

Apart from reducing further the intensity of pain by 17% (reduction from VAS 6/10 to VAS 5/10) interestingly, the most important point is that the capsaicin 8% patch showed an impressive reduction of the area of allodynia associated with NP. The reduction of the area was estimated to be more than 80% and this led to a significant change in our patient's quality of life.

Definitely, as this is a single case, further controlled studies are needed to explore the efficacy of capsaicin 8% patch in patients who experience posttraumatic or postsurgical NP.

CONCLUSION

We report a case of a young man with resistant posttraumatic and postsurgical neuropathic pain that responded to treatment with a capsaicin 8% patch when other treatments showed minimal effectiveness regarding the intensity of pain. The most important finding was that the capsaicin 8% patch showed a more than 80% reduction of the area of allodynia associated to the pain, when other treatments failed. Although further controlled studies are needed to explore the efficacy of the capsaicin 8% patch in patients who experience posttraumatic neuropathic pain, we encourage clinicians to try the capsaicin 8% patch when alternative treatments fail.

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