Prospective Study

Effectiveness and Impact of Capsaicin 8% Patch on Quality of Life in Patients with Lumbosacral Pain: An Open-label Study

Panagiotis Zis, PhD, Nikolitsa Bernali, MD, Erifili Argira, PhD, Ioanna Siafaka, PhD, and Athina Vadalouca, PhD

From: Evangelismos General Hospital, Athens, Greece

Address Correspondence:
Panagiotis Zis, MD, PhD
Evangelismos General Hospital
Neurology
45-47 Ipsilantou Str
Athens, 11526
Greece
E-mail: takiszis@gmail.com

Disclaimer: There was no external funding in the preparation of this manuscript.
Conflict of interest: Each author certifies that he or she, or a member of his or her immediate family, has no commercial association (i.e., consultancies, stock ownership, equity interest, patent/licensing arrangements, etc.) that might pose a conflict of interest in connection with the submitted manuscript.

Manuscript received: 12-26-2015
Revised manuscript received: 03-08-2016
Accepted for publication: 03-15-2016

Free full manuscript: www.painphysicianjournal.com

Background: Capsaicin 8% patch (Qutenza™) is mainly used to treat postherpetic neuralgia and HIV-associated neuropathy. Evidence of the efficacy of Qutenza in other forms of neuropathic pain is lacking.

Objective: To evaluate the analgesic effect and the impact on quality of life after a single application of the capsaicin 8% cutaneous patch in patients with lumbosacral pain.

Study Design: Prospective open-label study of capsaicin 8% patch in patients with lumbosacral pain.

Setting: Outpatient Pain and Palliative Care Center.

Methods: All recruited patients were evaluated prior to capsaicin 8% patch administration and were followed-up at 2 weeks, at 8 weeks, and at 12 weeks post administration. Visual analog scale (VAS) was used to record pain intensity and EQ-5D was used to assess the quality of life of the participants.

Results: Ninety patients met our inclusion criteria (54.4% men, mean age 59.1 ± 9.2 years). At baseline the mean VAS score of the participants was 7.6 ± 0.7. A statistically significant reduction of the VAS score between baseline and week 2 (mean VAS score 5.6 ± 1.1, $P < 0.001$) was observed. The therapeutic effect further continued between week 2 and week 8 (mean VAS score 3.2 ± 1.2, $P < 0.001$) and between week 8 and at endpoint at week 12 (mean VAS score 2.6 ± 1.1, $P < 0.001$).

Between baseline and weeks 2, 8, and 12 (end-point) a significant improvement in all 5 dimensions of EQ-5D (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) was observed ($P < 0.001$)

Limitations: As it is an open-label study, a prospective randomized placebo-controlled study should be designed to confirm the effectiveness of capsaicin 8% patch in patients with lumbosacral pain.

Conclusions: Administration of the capsaicin 8% patch resulted in a significant relief of neuropathic pain and a significant improvement of the quality of life of patients with lumbosacral neuropathic pain.

Key words: Lumbosacral pain, peripheral pain, Qutenza, neuropathic pain, capsaicin, patch, quality of life, effectiveness

Pain Physician 2016; 19:E1049-E1053

Capsaicin is an alkaloid found in the Capsicum family and is the main ingredient responsible for the hot pungent taste of chili peppers (1). Topical capsaicin formulations are widely used to manage pain. Since 1980, low-concentration capsaicin creams, lotions, and patches intended for daily skin application have become available (2). QutenzaTM, a high-concentration single administration capsaicin 8% patch, is mainly used to treat post-herpetic neuralgia and human immunodeficiency virus (HIV) associated neuropathy (3).

Our clinical experience in a limited number of patients with lumbosacral pain who tried capsaicin 8% patch supported that the latter may have a beneficial effect in the pain management of such patients.

Therefore, we designed a prospective open-label study with a twofold aim: to assess the effectiveness of capsaicin 8% patch and its impact on life quality in patients with lumbosacral pain.

Methods

Participants

Following the approval of the Institutional Ethical Committee of General Hospital of Thiva, all consecutive patients suffering from lumbosacral pain who visited the Outpatient Pain and Palliative Care Center were invited to participate in the study.

Inclusion Criteria

1. Confirmed diagnosis of lumbosacral pain according to the International Association for the Study of Pain (IASP). IASP defines lumbosacral pain as pain perceived as arising from a region encompassing or centered over the lower third of the lumbar region and the upper third of the sacral region (4). All of our study patients suffered from lumbar discogenic pain or internal disc disruption as defined by IASP (4).
2. Age equal to or greater than 18 years.
3. Visual analog scale (VAS) score equal to or greater than 5 out of a maximum 10.
4. Douleur Neuropathique 4 Questionnaire (DN4) score equal to or greater than 4 out of a maximum 10 (5,6).
5. Duration of pain of at least 3 months.
6. Willing to provide a written informed consent to undergo the experimental procedures.

Exclusion Criteria

1. History of allergy to capsaicin.
2. History of substance abuse.
3. History of severe psychiatric diseases. A clinical psychologist assessed all patients. Patients with history of a psychotic disorder and severe depression were not invited to participate to the study.
4. Being pregnant or lactating.
5. Previous use of capsaicin 8% patch.
6. Surgical operation in the affected area within the last 6 months.

Procedures

After eligibility assessment, a 2.5% lignocaine and 2.5% prilocaine cream (EMLA cream) was used to anesthetize the skin where the capsaicin 8% patch would be applied. The capsaicin 8% patch was applied to intact, non-irritated, dry skin of the most painful area, and remained in place for 60 minutes according to the manufacturer's guidelines (7).

During the treatment with capsaicin 8% patch no other treatment was allowed.

The patient was followed up at 2 weeks, at 8 weeks, and at 12 weeks after treatment. At each visit, the patient completed the VAS. At week 2 and week 12 the patient completed the EQ-5D descriptive system (8), which is a health-related quality of life instrument. The EQ-5D descriptive system comprises 5 dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression), each of which has 3 levels: no problems, some problems, extreme problems.

Statistical Analyses

A database was developed using the Statistical Package for Social Science (version 16.0 for Mac; SPSS). Frequencies and descriptive statistics were examined for each variable. Comparisons of VAS scores between visits and comparison of the change in VAS score at 12 weeks compared to baseline (percentage) were made using the paired t-test. Comparisons of EQ-5D responses between visits were made using the chi-square test.

Correlations between the change in VAS score at 12 weeks compared to baseline (percentage) and age, body mass index (BMI), and DN4 total score were examined using Spearman's correlations.

A multiple linear regression model was constructed with change in VAS score at 12 weeks compared to baseline (percentage) being the dependent variable.

A value of $P < 0.05$ was considered to be statistically significant.

Results

Study Population

In total, 90 individuals fulfilled the above mentioned inclusion criteria. Clinical and demographic characteristics of the study total population are summarized in Table 1. All patients completed the study.

Effectiveness

Figure 1 summarizes the VAS scores at each visit. At baseline the mean VAS score of the participants was 7.6 ± 0.7. A statistically significant reduction of the VAS score between baseline and week 2 (mean VAS score 5.6 ± 1.1, $P < 0.001$) was observed. The therapeutic effect further continued between week 2 and week 8 (mean VAS score 3.2 ± 1.2, $P < 0.001$) and between week 8 and at endpoint at week 12 (mean VAS score 2.6 ± 1.1, $P < 0.001$). The mean relative reduction of pain intensity between baseline and week 12 was 66.0%.

Comparison between genders did not show any significant difference regarding the change (percentage) in VAS score at 12 weeks compared to baseline (men 66.0 ± 7.4 vs women 66.1 ± 17.1, $P = 0.936$). Change in VAS score at 12 weeks compared to baseline was negatively correlated with BMI (Spearman's rho -0.294, $P = 0.005$) and age (Spearman's rho -0.329, $P = 0.002$) but not correlated to DN4 total score (Spearman's rho -0.047, $P = 0.659$).

Age, gender, and BMI were entered in a linear regression model with change in VAS score at 12 weeks compared to baseline being the dependent variable. Linear regression analysis showed that, after adjusting for gender, only BMI is negatively associated with the change in VAS score (beta -0.271, $P = 0.013$) when age is not (beta -0.157, $P = 0.137$).

Table 1. *Characteristics of the study population (n=90).*

Demographic characteristics	
Male sex (%)	49 (54.4)
Age in years (SD)	59.1 (9.2)
Age range	43 - 78
Clinical Characteristics	
BMI (SD)	29.6 (2.7)
VAS score at baseline (SD)	7.6 (0.7)
DN4 score at baseline (SD)	6.0 (0.7)

SD, standard deviation; BMI, body mass index; VAS, visual analogue scale; DN4, Douleur Neuropathique 4 Questionnaire

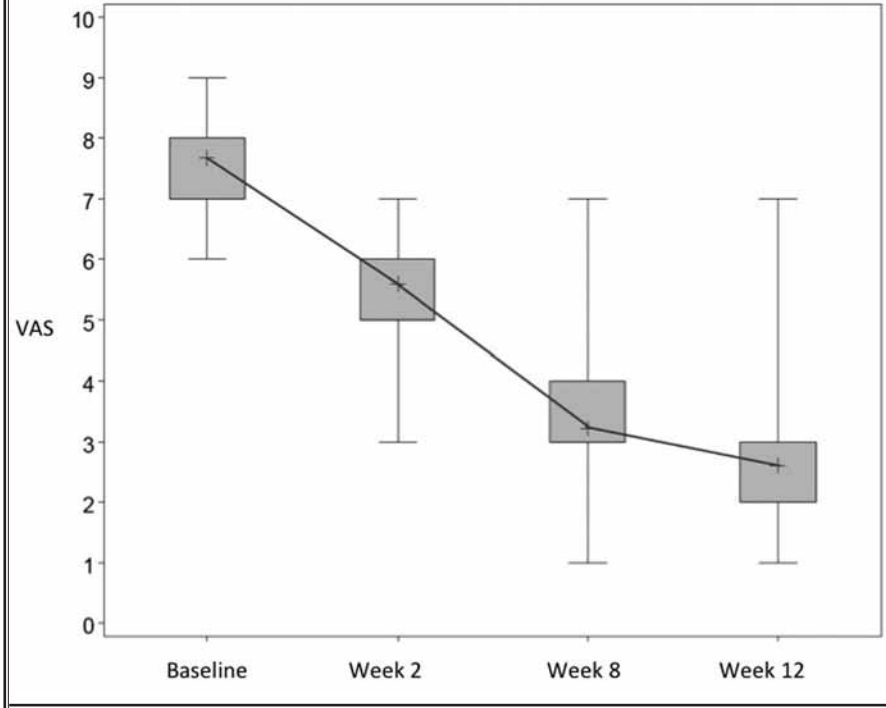

Fig. 1. *Summary of VAS scores at each visit.*

Quality of Life

Table 2 summarizes the EQ-5D responses at each visit. Between baseline and weeks 2, 8, and 12 (endpoint) a significant improvement in all 5 dimensions of the EQ-5D questionnaire was observed ($P < 0.001$), meaning that the quality of life of patients with lumbosacral pain significantly improved after a single administration of the capsaicin 8% patch.

Discussion

The results of our prospective open-label study illustrate that the capsaicin 8% patch is beneficial with regards to pain management as well as improving the life quality of patients with lumbosacral pain.

Apart from post-herpetic neuralgia and HIV-associated neuropathic pain, capsaicin 8% patch has been tried in diabetic painful neuropathy (9), phantom limb pain (10), and peripheral neuropathic pain secondary to chronic inflammatory demyelination neuropathy (CIDP), chemotherapy-induced polyneuropathy and polyneuropathy of unknown etiology (11). Moreover, isolated case reports suggested the possible effectiveness of capsaicin 8% patch in other forms of neuropathic pain, such as post-traumatic and postsurgical pain (12).

To our knowledge, this is the first study of the capsaicin 8% patch in patients with lumbosacral pain. Lumbosacral pain is one of the most common neuropathic pain syndromes. According to IASP classification, lumbosacral pain may be caused by fractures, infections, neoplasms, metabolic bone diseases, arthritis, congenital vertebral anomalies, failed spinal surgery, and prolapsed discs. Our study population included patients suffering from lumbar discogenic pain or internal disc disruption. We chose these patients as the discogenic pain has definite neuropathic characteristics and the capsaicin 8% patch is known to be effective in other neuropathic pain syndromes.

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 in 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 (2). Recent evidence established that capsaicin binds to the transient receptor potential vanilloid 1 (TRPV1) receptor that is expressed predominantly by sensory neurons (1). 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 (2).

The first results of the QUEPP study (13) suggested that the capsaicin 8% cutaneous patch achieved a mean relative reduction of pain intensity between baseline

Table 2. *EQ-5D responses per dimension at each visit*

Dimension	Problems	Baseline	Week 2	Week 8	Week 12	*P*
		%	%	%	%	
Mobility	None	0.0	23.3	92.0	100.0	<0.001
	Some	96.7	76.7	8.0	0.0	
	Extreme	3.3	0.0	0.0	0.0	
Self-care	None	12.2	32.2	95.3	100.0	<0.001
	Some	84.4	67.8	4.7	0.0	
	Extreme	3.3	0.0	0.0	0.0	
Usual activities	None	0.0	11.4	89.8	92.2	<0.001
	Some	93.3	88.6	10.2	7.8	
	Extreme	6.7	0.0	0.0	0.0	
Pain / Discomfort	None	0.0	11.1	90.9	93.3	<0.001
	Some	12.2	86.7	9.1	6.7	
	Extreme	87.8	2.2	0.0	0.0	
Anxiety / Depression	None	0.0	26.7	88.6	100.0	<0.001
	Some	100.0	73.3	11.4	0.0	
	Extreme	0.0	0.0	0.0	0.0	

and week 12 of 24.7%. In our study the mean relative reduction of pain intensity was much higher and estimated to be 66.0%. We believe that this difference is because of the heterogeneity of the populations studied.

In our study we assessed the impact on quality of life of the capsaicin 8% patch in patients with lumbosacral pain. Similarly to all intractable pains, neuropathic lumbosacral pain has devastating consequences on the overall quality of life (14). It has been shown that capsaicin 8% patch, along with the analgesic effect in other types of neuropathic pain, also improves the quality of life of the patients (10,13). Our results support this finding also in patients with lumbosacral pain who received the patch.

Our results should be interpreted with some caution, however, given the fact that this is an open-label study. Therefore a prospective randomized placebo-controlled study should be designed to confirm the effectiveness of the capsaicin 8% patch in patients with lumbosacral pain.

Conclusion

Lumbosacral pain remains a difficult to manage type of neuropathic pain. Non-pharmacological management includes physiotherapy and acupuncture, however the majority of the patients will need pharmacological treatment, which remains the mainstay of treatment. Surgery may be indicated, after a surgical opinion, in patients who have completed an optimal package of care and still suffer from pain. Although, capsaicin 8% patch is not a first line approach for patients with lumbosacral pain, when first line medications fail to help, pain specialists may try it as an option.

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