

A Case of Wasp-induced Pain Treated with Topical Phenytoin Cream

Jan M keppel Hesselink

Institute for Neuropathic Pain, Spoorlaan 2a, 3735 MV Bosch en Duin, The Netherlands

*Corresponding author: Jan M Keppel Hesselink, Institute for Neuropathic Pain, Spoorlaan 2a, 3735 MV Bosch en Duin, The Netherlands; Email: jan@neuropathie.nu

Abstract

Phenytoin cream has been evaluated in many patients suffering from peripheral neuropathic pain. Its onset of action has been documented to be within 30 minutes. Its mechanism of action is via the inhibition of sodium channels of the nociceptors in the skin, as well as the inhibition of a number of secondary targets in the skin, such as the keratinocytes and possibly immune-competent cells. Here we describe for the first time the successful treatment of lingering neuralgiformic pains after a wasp sting. Within 20 minutes after application of 10% phenytoin cream, the pain vanished completely. Phenytoin cream might therefore also be of use in the treatment of pain induced by stinging insects.

Keywords: *Sting; Analgesia; Topical; Treatment*

Received Date: July 19, 2018; **Accepted Date:** August 01, 2018; **Published Date:** August 08, 2018

Introduction

Phenytoin cream in the Netherlands is available since 2015 as a compounded cream in the concentration range 5-20%. Most clinical evidence is gathered by applying 10% phenytoin cream to patients suffering from various peripheral neuropathic pain syndromes [1]. Here, we describe for the first time the successful treatment of lingering neuralgiform pain following a wasp sting by 10% phenytoin cream.

Family practitioners see frequently patients suffering from the sequela after a sting by a hymenopteran insect (wasps, bees, hornets, yellow jackets) each summer and autumn. Mostly patients present with local reactions, such as pain, swelling and itching, erythema.

The circumstances of the stinging incident, in the morning after walking bare-feet in the grass, while watering the plants, and the absence of a stinger in a toe of the person stung suggest the stinging insect was a vespid (wasp). Vespids never leave stingers behind, in contrast to bees. It is estimated that wasps release about 17 µg of venom after one stinging action [2]. The results are rarely complicated, and mostly pain and swelling disappear within few hours. In this case, pain lingered on during the day and impaired sleep, till the application of topical phenytoin cream.

Case Report

A 64-old healthy male was watering the plants in the garden, and suddenly experienced a sting in his toe. At first, he thought it was an irritation by a nettle, but in the following hours, pain, swelling and redness occurred, and the pain intensified to 8 on

Citation: Jan M keppel Hesselink, A Case of Wasp-induced Pain Treated with Topical Phenytoin Cream. J Clin Cases Rep 1(3): 106-108. © 2018 Tridha Scholars.

the 11 points NRS. The pain had some neuralgic characteristics, lancinating and burning, and during the day and the subsequent night the pain become more nagging too. After going to bed he woke up after 3 hrs due to pain which apparently intensified, and the pain was 5-6. Phenytoin 10% cream was applied, less than a fingertip-unit (ca 0.5 g), containing around 50 mg of phenytoin. Within 10 min the pain decreased to a score of 3 and after 20 min the pain was vanished and sleep was resumed. The next morning all complaints were vanished.

Discussion

Although in general the prognosis for most people suffering from a wasp sting is good, and episodes of pain, swelling and erythema are self-limiting resolving within the first hours, sometimes, as in this case pain remains after a sting and can even result in sleep disturbances. Treatment in general is simple, cooling the area of the sting, and anti-histamines. Topical corticosteroids, camphor and menthol or lidocaine formulations have been suggested [3]. According to a search in PubMed, only one study is available evaluating in a randomized controlled way the efficacy of an intervention against sting pain and swelling by topical treatment aspirin paste. This topical treatment appeared not to effective in reducing the duration of swelling or pain in bee and wasp stings [4]. It is therefore of interest to report this case, as it is the first case in literature presenting the fast pain reduction after a wasp sting by application of 10% phenytoin cream on the sting area. Phenytoin cream has been developed as compounded cream since 2014-2015 and to date in our Institute for Neuropathic Pain in the Netherlands, we have gathered detailed information in 100 patients, and for a number of these patients, follow-up data for more than a year are available. In general, patients like to rub-in cream there where it hurts. In our current data pool, we have monitored a relative fast onset of perceptible pain relief after applying 10% phenytoin cream, mostly within 30 min. It seems that the duration of action of 10% is nearly double (around 8 hrs) compared to that of 5% phenytoin cream, suggesting a dose-response curve [1]. In a separate crossover n=1 design we found that in one particular patient the pain reduction using a high concentration of phenytoin cream was again better compared to 10% phenytoin cream [5].

Phenytoin acts as a broad-acting sodium-channel blocker, and its mechanism of action resides in the skin, where it functionally downregulates overactive nociceptors and cross-talking other cell populations, like the keratinocytes, and the immune-competent cells [6]. The quick onset of action is important for patients, as direct pain-reducing effects are a high motivator for patients to continue therapy, and thus it increases patient-compliance [7]. The positive effects on disturbed sleep due to chronic pain has been documented before [8]. Also, in this case, a fast onset of action was clear, within 10 min, pain was reduced for around 50%, and within 20 min, pain subsided. Phenytoin however is not only a broad acting sodium channel; additional mechanisms of action have been described. It is of course unclear how off main target effects of phenytoin might contribute to the reported results. Recently a new mechanism of action was published, based on its blocking the upstream necrosome formation steps in cells undergoing necroptosis [9]. In fact, venomous spiders, snakes and wasps may induce necroptosis and our findings might help to create a mechanistic hypothesis as to why this cream might have been beneficial [10]. It is remarkable, that a molecule which has been in clinical use for over 80 years, still can surprise us with new indications and putative new mechanisms of action [11].

Conflict of Interest

The author is patent holder of two patents related to the topical formulations of phenytoin in the treatment of pain: 1) Topical phenytoin for the use in the treatment of peripheral neuropathic pain and 2) Topical pharmaceutical composition containing phenytoin and a (co-) analgesic for the treatment of chronic pain.

References

1. Kopsky DJ, Keppel Hesselink JM (2018) Phenytoin cream for the treatment of neuropathic pain: case series. *Pharmaceuticals (Basel)* 11(2): E53.
2. Winkler B, Bolwig C, Seppala U, et al. (2003) Allergen specific immunosuppression by mucosal treatment with recombinant Ves v 5, a major allergen of *Vespula vulgaris* venom, in a murine model of wasp venom allergy. *Immunology* 110: 376-385.
3. Fitzgerald KT and Flood AA (2006) Hymenoptera stings. *Clinical Techniques in Small Animal Practice* 21(4): 194-204.
4. Balit CR, Isbister GK, Buckley NA (2003) Randomized controlled trial of topical aspirin in the treatment of bee and wasp stings. *Journal of Toxicology: Clinical Toxicology* 41(6): 801-808.
5. Keppel Hesselink JM and Kopsky DJ (2018) The individualized N-of-1 trial: dose-response in a single-blind cross-over response test of phenytoin 10% and 30% cream in neuropathic pain. *EC Anaesthesia* 4(6): 1-6.
6. Keppel Hesselink JM (2017) Rethinking peripheral sensitization, peripheral neuropathic pain and the putative value of topical analgesics. *Journal of Pharmacology and Clinical Research* 4(2): 555631.
7. Keppel Hesselink JM and Kopsky DJ (2017) Topical phenytoin cream in small fiber neuropathic pain: fast onset of perceptible pain relief. *International Journal of Pain & Relief* 1(1): 015-019.
8. Keppel Hesselink JM and Kopsky DJ (2017) Phenytoin cream reduces pain and improves sleep in patients suffering from neuropathic pain. *Austin Journal of Anesthesia and Analgesia* 5(2): 1061.
9. Von Mässenhausen A, Tonnus W, Himmerkus N, et al. (2018) Phenytoin inhibits necroptosis. *Cell Death & Disease* 9(3): 359.
10. Ardisson-Araújo DMP, Da Silva Morgado F, Schwartz EF, et al. (2013) A new theraphosid spider toxin causes early insect cell death by necrosis when expressed in vitro during recombinant baculovirus infection. *PLoS One* 8(12): e84404.
11. Keppel Hesselink JM (2017) Phenytoin: a step by step insight into its multiple mechanisms of action-80 years of mechanistic studies in neuropharmacology. *Journal of Neurology* 264(9): 2043-2047.