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Topical Capsaicin for Neuropathic Pain #255

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Background

Derived from *Capsicum* chili peppers, capsaicin has been used as a topical analgesic for centuries. Available in both over-the-counter and prescription strengths, capsaicin preparations have been studied and utilized for management of neuropathic pain. This *Fast Fact* reviews use of capsaicin for topical neuropathic analgesia, including the new 8% single-dose capsaicin patch (Qutenza).

Mechanism of Action

Capsaicin is a highly selective agonist for TRPV1 receptors expressed in afferent neuronal C fibers and some Aδ fibers. Local activation of TRPV1 receptors by heat, pH changes, or endogenous lipids normally leads to nerve depolarization propagated to spinal cord and brain, causing local heat, stinging, and/or itching sensations. Through intracellular enzymatic, cytoskeletal, and osmotic changes, prolonged activation of TRPV1 by capsaicin results in loss of receptor functionality, causing impaired local nociception for extended periods. At higher concentrations, topical capsaicin appears to promote temporary neurolysis, with re-innervation occurring weeks after cessation of drug therapy.[1,2] Capsaicin-induced local depletion of substance P was previously thought to be its mechanism for pain relief. However, this is no longer considered to be the case.[1]

Indications

Topical capsaicin has shown analgesic benefits in postherpetic neuralgia, painful polyneuropathies including diabetic and HIV-related neuropathy, and postmastectomy/surgical neuropathic syndromes.[3] The capsaicin 8% patch is FDA approved for postherpetic neuralgia. Its efficacy in other neuropathies is still being investigated. Generally, these painful areas should involve a discrete area of the body such as a distal extremity or surgical scar. There is no well-defined limit to the body surface area that can be treated with capsaicin cream. The 14×20 cm capsaicin 8% patch is approved for application of up to four patches at a time. Capsaicin creams have been used in children; there are no data about use of the 8% patch.

Clinical Use

Capsaicin is commercially available as 0.025%, 0.075%, and 0.1% creams. Creams are applied by patients or caregivers three to four times per day. The duration of treatment with the cream is empiric. A single-application high-dose capsaicin 8% patch is available. The patch is placed on the skin for 60 minutes by a medical professional in a clinic, then removed. Because the patch application itself is painful, the area is pretreated with lidocaine cream, and residual capsaicin is cleaned afterwards with a special cleansing product. Up to four patches may be applied at one time, and repeated as often as every three months.[4]

Effectiveness

In a recent systematic review, capsaicin 0.075% cream demonstrated statistically significant benefit in postherpetic neuralgia, postsurgical neuropathies, and diabetic neuropathy, compared to placebo.[3] The analgesic effect of capsaicin 0.075% cream has been demonstrated throughout 4–12 weeks of study follow-up, although it may take weeks of application to achieve significant benefit. Although studies demonstrate its effectiveness in musculoskeletal pain, capsaicin 0.025% cream has not been adequately studied for neuropathic pain. The efficacy of the single high-dose capsaicin 8% patch has been observed up to 12 weeks in published data.[5] It is effective for postherpetic neuralgia; however there have been mixed results with the patch for HIV-related neuropathy. To date, no head-to-head trials have compared the capsaicin 8% patch to capsaicin 0.075% cream.

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Toxicity and Precautions

Capsaicin should not be used on open wounds. Major side effects are localized and include erythema and uncomfortable burning, stinging, or itching. Over repeated applications, these burning/stinging sensations decrease, corresponding with progressive neuronal defunctionalization. Inhalation of capsaicin can cause nasopharyngeal or respiratory irritation, sneezing, and tearing. Patients are advised to use gloves while applying the cream, avoid contact with eyes and mucous membranes, and wash hands after application. Transient hypertension associated with increased local pain has been noted. Cessation of capsaicin use due to side effects appears more common with repeated low-dose cream application (15% of patients) compared to the patch (1% of patients in a clinical trial setting).[5]

Cost

Capsaicin 0.025%, 0.075%, 0.1% creams are available over the counter (approximately $8/oz). One capsaicin 8% patch costs approximately $800 (plus clinician fees for application). Costs for three-month supplies of relevant neuropathic pain medications are about $700 for lidocaine 5% patches, one a day; about $900 for pregabalin 100 mg three times a day; about $300 for gabapentin 600 mg three times a day; and about $50 for amitriptyline 100 mg once daily.[6]

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Fever Near the End of Life #256

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Introduction

Clinically significant fever is defined as an increase in body temperature (generally >38.5°C) in conjunction with an elevation of the hypothalamic setpoint. Hyperthermia is an uncontrolled elevation in body temperature without a change in the thermoregulatory center. This *Fast Fact* reviews the key elements in assessment and treatment of fever in patients near the end of life.

Pathophysiology

Fever is mediated by exogenous pyrogens (microbes or their products) and pyrogenic cytokines (i.e., interleukin-1, interleukin-6, interferon alpha, tumor necrosis factor) which induce the synthesis of prostaglandin E2 (PGE2). Centrally, PGE2 increases production of cyclic adenosine monophosphate, which raises the hypothalamic setpoint to febrile levels. Peripherally, this induces myalgias and arthralgias. Pyrogens/pyrogenic cytokines are produced by infection, inflammation, trauma/tissue necrosis, and tumors. Drugs can induce fever through various metabolic and immune responses as well as by mimicking endogenous pyrogens, inflicting direct tissue damage, and interfering with heat loss. Common drugs in palliative care settings that cause fever include antibiotics, antipsychotics (neuroleptic malignant syndrome), and opioid withdrawal. Fever associated with brain injuries is common, perhaps due to direct hypothalamic injury.

Assessment

The extent of evaluation will depend on the patient's condition and overall goals of care. When indicated, a thorough history and physical exam is needed, looking for (1) signs of infection; (2) in cancer patients, evidence of disease progression; and (3) a medication review. A typical infection laboratory and radiographic workup can be pursued if it will affect management. Common etiologies and clinical findings are reviewed below.