There are an ever-increasing number of medications that can be used to help patients with neuropathic-based oral and perioral pain problems. Advancements in the delivery of medications include the development of vehicles (Pluronic lecithin organogel [PLO]) that can penetrate the mucosa and cutaneous tissues, carrying active medication to the affected site.

Systemic administration of medication for patients with regional or local conditions poses several disadvantages over the preferred oral route. Most notable include hepatic first-pass metabolism, enzymatic degradation, and presystemic elimination within the gastrointestinal (GI) tract. In contrast, administration of a medication directly to a target area, including local injection and transdermal application at the affected site, offers distinct advantages over systemic administration including more rapid onset of action and lower side-effect profile. The oral mucosa, specifically, has a rich blood supply, is relatively permeable, demonstrates short recovery times after stress or damage, and is tolerant to potential allergens due to the virtual lack of Langerhans cells. For orofacial disorders that are regional, near the surface or chronic, topical medications offer a clear advantage over systemic treatment options.

For the clinician, an understanding of the various drug delivery mechanisms available for topical, transdermal, intraoral, and extraoral use can be of great benefit in the management of neuropathic orofacial pain. Orofacial Drug Delivery

Transdermal delivery of medication in the oral and perioral region is dependent upon the agent’s ability to penetrate the stratum corneum of the extraoral skin or the oral mucosa, which can be affected by the patient’s skin integrity, age, the presence of any dermal conditions and natural variations in thickness, and keratinization of the epithelial tissue.

The barrier capabilities of the oral mucosa are greater than that of the intestinal mucosa, but in general are far less effective than the skin. The results are dependent upon the patient’s age, salivary lubrication, the presence of inflammatory conditions, and physical damage to the oral mucosa.

Orofacial Neupathies

Chronic neurologic pain, including diabetic peripheral neuropathy, postherpetic neuralgia, and orofacial pain syndrome is the result of multiple, often unknown etiologies sharing a single pathophysiologic pathway. An understanding of both the peripheral and central changes that occur in neuropathic pain syndromes, as well as the relationships between the various neurotransmitters and nociceptors, which as of yet are not completely understood, is vital to the development of customized treatment protocols. Chronic peripheral nociceptor irritability, as a result of neuronal injury, denervation, or vascular compression occurs subsequent to a release of excitatory and inflammatory mediators as well as functional changes in the peripherally located sodium channels. Central neuronal changes and the activation of N-methyl-D-aspartate (NMDA) receptors start a chain of events that...
TOPICAL FORMULATIONS FOR THE TREATMENT OF OROFACIAL NEUROPATHIC PAIN

Rx
Capsaicin 0.05% and Ketamine Hydrochloride 2% in Pluronic Lecithin Organogel

Rx
Ketoprofen 10% and Lidocaine Hydrochloride 5% in Pluronic Lecithin Organogel

caine in tetracaine, benzocaine, carbamazepine, amitriptyline, and baclofen. Capsaicin has dem-
strated efficacy in traumatic neuropathy, trigeminal neuralgia, postherpetic neuralgia, and che-
mo-therapy or radiation-induced oral mucositis.1 While NSAIDs can cause serious GI side effects when taken orally, transdermal formu-
lations avoid GI tract ir-
titation and first pass metabolism. Few if any systemic side effects and improved patient compliance have been reported with local ap-
plication of NSAIDs, including ketoprofen, diclofenac, and ibuprofen.8–9

Drug Delivery Systems

Improvements in the delivery options for medications for intra- and extraoral use in-
clude the development of vehicles designed to penetrate the mucosa and cutaneous tissues, carrying active ingredient to the affected site, as well as mucoadhesive dosage forms devised to prolong the time in which an active moiety can remain at the site.

The ability of an agent to penetrate either the facial skin or the oral mucosa can be increased by the use of delivery vehicles that incorporate the lipid solubility of the medication. The development of oil/water microemulsion systems has provided transdermal vehicles that are bal-
anced for delivery of both hydrophobic and hydrophilic drugs.10 The standard of transdermal delivery systems is PLO, which is composed of Pluronic gel (the water phase) and lecithin/sto-
protyn palmitate (the oil phase). This micro-
emulsion has been shown to have the ability to deliver a multitude of pharmacological agents, including NSAIDs, across the epidermal barrier through either simple diffusion through the lipid intercellular matrix or by the slight disorganization of the skin which allows the drug to pass through the stratum corneum.11–13 Unlike dimethyl sulfoxide (DMSO), which damages the stratum cor-
neum by solubilizing the lipid layers, PLO harmlessly disrupts the layers allowing the medication to slip through.14 PLO has been shown to dissolve, spread, and facilitate the release and permeation of drugs ap-
plicated transdermally.15

Medication impregnated mucoadhesive bases and pastes reduce the inconvenience of repeated reapplication of topical agents for intraoral use. Topical agents without adhesive properties can dissolve, spread throughout the mouth and can ultimately be swallowed. Additional delivery systems for the orofacial region include:

• Adhesive patches and powders
• Aqueous gel
• Dissolving polymeric devices
• Dissolving tablets or lozenges
• Medicated chewing gum, candy and lollipops
• Medicated lip balms
• Mouthwashes
• Tissue adhesives and sutures
• Toothpastes

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