PALLIATIVE PEARLS
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Topical Analgesics for Local Pain
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Acute and chronic pain are significant sources of suffering for patients with advanced illnesses. Adverse effects from systemic (oral, rectal, parenteral, transdermal) analgesics contribute to and often exacerbate suffering and limit dose titration thus hindering effectiveness. Topical analgesics offer a solution to limit systemic adverse effects and should be considered whenever the location and level of pain allow for achievable pain relief with topical application.[1]

There are a number of considerations to make prior to initiating topical therapy including the source, extent and severity of localized pain, class and formulation of topical medication, and patient-specific guidance.

SOURCES OF LOCALIZED PAIN[2]

Acute pain

- Strains
- Sprains
- Tendonitis
- Acute back pain
- Muscle aches

Chronic pain

- Arthralgia (e.g., osteoarthritis, rheumatoid arthritis)
- Low back pain
- Types of neuropathic pain (e.g., diabetic neuropathy, localized peripheral neuropathic pain, post-herpetic neuralgia)
- Skin structure and mucous membranes (e.g., cutaneous ulcers, wounds, stomatitis, painful pruritus)

COMMERCIAL ANESTHETICS

Lidocaine/Lidocaine Hydrochloride

According to a 2014 systematic review, while there is little evidence to support the use of topical lidocaine to treat neuropathic pain, results from case studies and expert opinion suggest that it can be effective in some patients. It is most appropriate for well localized neuropathic pain and although useful as monotherapy, it is most often used as an adjunct to systemic therapy.[3]

Products & Formulations:[4]

Lidocaine

- Prescription only (Rx) *transdermal* patch – 24 hour: Lidoderm® 5%, ZTlido® 1.8%
- Rx ointment: Lidocaine 5%

- Over-the-counter (OTC) *topical* patch: Lidocare® 4%, Aspercreme® 4%
- OTC cream: Lidocaine 3%, AneCream® 4%, LMX® 4%, AneCream® 5%, LMX® 5%, RectiCare® 5%

Lidocaine hydrochloride

- Rx cream: CidalEaze® 3%, Lidotral® 3.88%
- Rx gel/jelly: 7T Lido® 2%, Glydo® 2%, Xylocaine® 2%, LidoRx® 3%, Astero® 4%, Tranzarel® 4%
- Rx solution: Aspercreme® 4%, Xylocaine® 4%
- Rx oromucosal solution: Lidocaine 2% viscous solution
- OTC cream: Aspercreme® 4%
- OTC gel/jelly: Burn relief 0.5%
- OTC lotion: Anastia® 2.75%, Numbonex® 2.75%, LIDO-K® 3%, LIDO-SORB® 3%, LIDOZION® 3%
- OTC topical patch: Aspercreme® 4%
- OTC spray: Burn relief 0.5%
- OTC oromucosal solution: Zilactin L Cold Sore® 4% liquid

Indications:[4]

- Anesthesia of skin and mucous membranes
- Stomatitis
- Pain associated with postherpetic neuralgia

Capsaicin

According to 2004 systematic review, capsaicin has moderate to poor efficacy for relief of chronic musculoskeletal or neuropathic pain however may be useful as an adjunctive therapy or for patients not responsive to other therapies.[3]

Products & Formulations:[4]

- OTC topical patch: Capsaicin 0.025%
- OTC cream: Zostrix® 0.025%, Capsaicin-P® 0.035%, Zostrix HP® 0.075%, Capsaicin-HP® 0.1%, Zostrix Neuropathy® 0.25% (Capzasin®)
- OTC lotion: Capstiva Warming® 0.035%
- OTC solution: Capsaicin 0.15%

Indications:

- Rheumatoid arthritis or osteoarthritis-related pain, myalgia, and arthralgia associated with bruises, simple backache, sprains, or strains
- Diabetic neuropathy, including diabetic foot pain
- Pain associated with postherpetic neuralgia

COMMERCIAL NON-STEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS)

Diclofenac and Ketoprofen

Evidence of effectiveness of topical NSAIDs for chronic low back pain, extensive musculoskeletal pain, and peripheral neuropathic pain is weaker than for acute pain. "A systematic review of four randomized trials found that a topical 1.5 percent solution of diclofenac was more effective than a control vehicle in the relief of knee osteoarthritic pain and was generally well tolerated."[3]

Topical NSAIDs rather than systemic therapy is suggested for patients with mild OA localized to the knee or with concomitant hand involvement. The drugs studied with the most frequency are diclofenac gel or solution and ketoprofen, applied over the affected knee two to four times daily, for the duration necessary to control symptoms.[5,6]

Products & Formulations:[4]

Diclofenac epolamine

- Rx topical patch: Flector® 1.3%

Diclofenac sodium

- Rx gel: Voltaren® 1%, Solaraze® 3%
- Rx cream: EnovaRx 2.5% external cream *compounding kit*
- Rx solution: Diclofenac sodium 1.5%, Pennsaid 2%

Ketoprofen

- Rx cream: Active-Ketoprofen 5% kit for *compounding*

Indications:

Diclofenac

- Osteoarthritis-related pain
- Acute mild pain or moderate pain due to minor strains, sprains, and contusions
- Actinic keratosis

Ketoprofen

- Osteoarthritis-related pain

COMMERCIAL TRICYCLIC ANTI-DEPRESSANTS (TCAS)

Doxepin

Topical doxepin had only minimal effect on pain reduction in one small trial.[3,5]

Products & Formulations:[4]

- Rx cream: 5% (Prudoxin®, Zonalon®)

Indication:

- Eczematous dermatitis (atopical dermatitis, eczema, or lichen simplex chronicus)

COMPOUNDS – SINGLE AGENT PRODUCTS

Topical single-agent compounds are widely utilized as monotherapy and adjunctive therapy for localized pain in the hospice patient population. Topical application of these agents is generally regarded as safe however supporting data is sparse. In the setting of refractory pain, a trial may be reasonable if cost is not prohibitive.[7]

Ketamine

Limited evidence suggests that ketamine is effective and well tolerated when compounded into a gel and applied topically for well localized peripheral neuropathy. The amount of the application does not have to cover the entire area of pain, only to the most painful area of intact skin. Usually an effective dose is 0.4mg/kg/dose of ketamine applied three times a day.[8-12]

Morphine

Morphine pluronic acid and lecithin organogel (PLO) gel and Morphine Intrasite gel are both compounded topical medications indicated for the topical treatment of local pain from wounds, pressure ulcers and sores. It is important to note that these products should be used for local pain management only as they have not demonstrated systemic analgesic effects when used topically.

- Morphine PLO gel is morphine suspended in a gel consisting of water and two plant derivatives, pluronic acid and lecithin organogel (PLO). These components work together to temporarily disorganize the outermost layer of the skin to enhance the absorption of morphine.[1] Morphine PLO gel works best when applied to the periphery and not directly in the wound bed.

- Morphine Intrasite gel is a product composed of injectable morphine suspended in Intrasite gel.[2] "Intrasite gel" is a hydrogel containing water, propylene glycol and carboxymethylcellulose. When placed in contact with a wound, Intrasite gel absorbs excess exudates and produces a moist environment at the wound surface. It is also promotes debridement of necrotic tissue and works well for wounds that are granulating and epithelializing.[3] Due to its utility and for best results, morphine Intrasite gel should be applied directly to the wound bed or pressure ulcer. It is recommended to utilize a new sterile tongue depressor to remove the gel from the container for each administration to prevent contamination.[13-15]

OTHERS SINGLE-AGENT COMPOUNDS WITH SOME CASE-BASED/EXPERT OPINION SUPPORT

- Amitriptyline
- Baclofen
- Clonidine
- Gabapentin
- Phenytoin

COMPOUNDS – COMBINATION PRODUCTS

Some prescribers use customized compounded topical formulations for the treatment of pain. These products can include various combinations of NSAIDs, muscle relaxants, anesthetics, vasodilators (e.g., nifedipine), neuralgia agents (e.g., amitriptyline, gabapentin), and/or other ingredients in a variety of vehicles. There are very little data available for the efficacy and/or safety of these preparations.[1,16]

Researchers at a military treatment facility evaluated 399 patients with local pain in a randomized, double-blind, placebo-vehicle controlled, intention-to-treat, 3 parallel armed study. Subjects were prescribed one of 3 multi-drug compounded creams or a placebo/vehicle cream and applied to the painful region three times a day. For neuropathic pain, the combination cream contained ketamine, gabapentin, clonidine and lidocaine and for nociceptive pain, a combination of ketoprofen, baclofen, cyclobenzaprine and lidocaine. Subjects with mixed pain received a cream with ketamine, gabapentin, diclofenac, baclofen, cyclobenzaprine and lidocaine. The compounded creams offered no benefit over placebo in pain relief.[17,18]

PATIENT-SPECIFIC GUIDANCE[16]

- Typically applied to unbroken skin
- External heat sources (e.g., heating pads) should not be applied over topical analgesics due to risk of increased absorption.
- Avoid covering the application site with occlusive dressings as this will also increase absorption
- Over-the-counter (OTC) patches may contain additional ingredients – check labels and ensure patient tolerability

SUMMARY

There is indeed reliable evidence about a number of topical analgesics in acute and chronic pain. It's important for clinicians to recognize this and that drug and formulation matter. At the same time, evidence won't account for benefits seen in a small number of patients. An experienced clinician may still choose to use agents with less supporting evidence based on their professional experience.[2]

For additional information on this topic, please review these references:

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