

FAST FACTS AND CONCEPTS #327 TOPICAL TREATMENTS FOR ACUTE AND CHRONIC WOUND PAIN

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Acute and chronic wounds can be a significant source of pain in advanced illness. Systemic opioids have been predominantly utilized for wound-related pain, however, for many patients, dose-limiting side effects can hinder their effectiveness. This *Fast Fact* will discuss topical options for acute and chronic wound pain. See *Fast Facts* #46 & #218 for guidance on malignant wounds and wound odor.

Pain Classification Painful wounds can arise from many sources. Often wound pain is a combination of nociceptive or neuropathic pain (1).

- **Nociceptive pain:** Typically caused by damage to body tissue. Common wound-related etiologies include decubitus ulcers, mucositis, and procedures such as debridement, dressing changes or radiation treatments (2,3). This pain is often described as sharp, aching, or throbbing.
- **Neuropathic pain:** Typically, chronic in nature due to long-term inflammation or injury to nerve fibers (1). This may be seen in certain malignant wounds or refractory mucositis (2,4). This pain is usually described as burning, stabbing, or sharp (4).

Topical Drug Treatment Options

Local anesthetics: A Cochrane review found adequate evidence supporting the use of Eutetic Mixture of Local Anesthetics (EMLA) cream (which is a combination of lidocaine and prilocaine) for pain associated with dressing changes or debridement of a wound (5,6). It is recommended that the cream be applied 20 minutes before the dressing change or debridement procedure to minimize discomfort; open wounds should be avoided (5). As long as no more than 10 grams of 5% EMLA cream are applied, there is little concern for CNS toxicity. Only minor side effects like a burning sensation, local erythema, or pallor have been documented (7). There is some controversy whether local anesthetics negatively impact the first two stages of wound healing at a clinically significant degree (8). A 30 g container of EMLA cream costs approximately \$53.

Ketamine: While there are no high quality controlled trials on the use of topical ketamine for wound pain, anecdotal accounts of the effective use of topical ketamine as a gel, cream, ointment, or spray has been documented with few side effects at concentrations up to 20% (9). Often, ketamine is compounded with other analgesics such as baclofen, amitriptyline, or pregabalin. Coverage by insurance is variable. A 30 gram jar of a 15% ketamine/15% lidocaine cream or a 30 mL bottle of 5-10% ketamine spray mixed with 1% lidocaine and 5% morphine costs about \$70 to \$100 without insurance (10). The spray is typically applied to an entire wound bed prior to dressing changes 4 times per day as needed. Use of the spray has also been described for post-operative pain relief in children (9,10).

Anti-inflammatory foam dressings (Available in Canada but not in the US): These treatments commonly utilize diclofenac or ibuprofen as their active ingredient to inhibit synthesis of prostaglandins in body tissues and decrease proinflammatory cytokine activity. In some studies, anti-inflammatory foam dressings have been found to be more effective in treating nociceptive wound pain, such as chronic leg ulcers, than the local best practice (moist healing and antimicrobial dressings) (9).

Tricyclic Antidepressants: Amitriptyline has shown effectiveness for acute nociceptive and chronic neuropathic wound pain (11,12). Similar to ketamine, its topical use requires the assistance of an experienced compounding pharmacist. The cost of a 30 gram jar of 2.5% amitriptyline cream compounded with 2-4% baclofen and 2-5% gabapentin is estimated to be about \$70 to \$90 per month when used 2-4 times per day as needed.

Topical Opioids: See *Fast Facts* #185 and #325. Applying opioids topically to painful wounds like skin ulcers or calciphylaxis-related wounds has the theoretical advantage of offering a more localized effect with less systemic absorption and side effects. While morphine infused into a gel form is most frequently used in this manner, the use of topical methadone and buprenorphine has also been described (13,14). In several case studies and many, but not all, controlled trials, most patients were able to reduce their

systemic analgesic doses when 10 mg diamorphine per 10 mL gel was applied to the entire surface of a wound and covered with gauze twice daily (9). Morphine has also been utilized as a mouthwash to reduce mucositis pain associated with cancer or cancer treatment (15)

Other: Topical aspirin, capsaicin (0.025 to 0.075%), clonidine 0.1% gel, and menthol have all been described to reduce wound pain, but evidence regarding safety and efficacy are lacking. Although the analgesic effect of topical capsaicin is dose dependent, burning associated with the application at higher concentrations (e.g. 2.5 to 7.5%) often limits patient adherence (13).

Summary Complete healing of wounds is often an unrealistic goal in palliative settings. Dose-limiting side effects of systemic opioids can limit their efficacy. Hence, clinicians may turn to empiric options, including topical analgesics. Clinicians should be aware that most of these formulations are not standardized and are poorly researched.

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