How are topical Opioids used to manage painful cutaneous lesions in palliative care? A critical review

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**Introduction:**  
Overview of pain experience of wounds:

![Fig. 1. Integrated wound-related pain model.](image)


Goal of palliative wound care is the following: control pain, to manage infection, odor, bleeding, exudate and maintain good quality of life. Malignant wounds may begin with a lesion that does not heal. Eventually the tumor develops own blood supply, which may outgrow and cause a central area of necrosis. The skin breaks down and turns from pink to red, violet, brown or flesh colored. Advanced malignant wounds can bleed, ulcerate, become infected and cause sinus tracts or fistulas. Therefore, it’s not surprising how painful cutaneous lesions are; they are, difficult to manage and usually unresponsive to systemic analgesics. There is an increasing consensus that the utility of topical opioids for inflammatory pain is promising with minimal systemic side effects. Currently, there is a lack of consensus and guidelines on how to utilize topical opioids in clinical practices for cutaneous lesions and inflammatory pain control. Important aspects to consider prior to prescribing is the following: wound aetiology, size, titration of dose and formulation, present of infection or inflammation, patient monitoring and their experience with treatment.

**Results:**  
Total of 77 articles found but 50 were excluded since they did not meet inclusion criteria. The excluded studies focused on burns, wound healing, animals, topical analgesics other than opioids, non cutaneous lesions, cutaneous leishmaniasis, acute injuries, lacerations and surgical
issues. 27 articles were included in this review with a total of 170 patients. 17 cases indicated topical opioids were clinically useful for reducing pain but no statistical analysis was conducted of their results. Topical opioids seemed to decrease pain up to 2 hrs post application but not after 6, 12 or 24 hrs suggesting a need for increased dose and frequency. 3 controlled studies found topical opioids not useful. Topical opioids are less effective for arterial and venous ulcers. 2 studies reported that wound size appears to affect the pharmokinetics-absorption of a topical opioid. 7 articles titrated doses to achieve adequate pain level- but the method of titrating varied between studies with minimal explanation.

Overall, the results of the review indicate that topical opioids are clinically useful and safe in controlling inflammatory pain in wounds. The systemic absorption of the topical opioids are within safe levels.

**Strengths**
Wide range of sources for literature searches. Inclusion criteria described (patients with painful cutaneous skin lesions, interventions with topical opioids, studies which found topical opioids to be effective and noneffective in English/German/French/Italian). Included all types of study designs except reviews.
The following was extracted from each article: wound aetiology, size, topical opioid used, details of titration, frequency of application, local and systemic side effects, systemic medication, outcomes and authors comments. A narrative analysis was conducted.

**Weaknesses:**
Small sample size n=170 patients. Heterogeneous population. Aetiology varied as well consisting of pressure ulcers, diabetic foot ulcers, carcinoma of breast and other malignancies, melanoma, hidradenitis suppurative lesions, sickle cell anemia, pyoderma gangrenosum of breast tissue, arterial/venous ulcers, mucositis. Wound sizes varied and some wounds were necrotic with discharge and weeping.
The types of topical morphine varied significantly. Adjuvant therapy such as systemic opioids, acetaminophen, diclofenac, fentanyl patches, xylocaine gel were also used in some studies. No standard pain scale- subjective findings with regards to pain relief. Overall patient views were under represented. Needs to differentiate between the pain from inflammation or pain from wound infection.

How to relate to palliative Care: With a large population which may have various wound ulcers, infections in addition to malignant wounds, identifying topical pain relief would be beneficial. However, a systematic approach to establishing effectiveness and dose response relationship of topical opioids in order to standardize therapies is still needed.

References: