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Taking Advantage of the Peripheral Opioid Receptor

Opioids applied in a topical cream that directly target the peripheral opioid receptors (which grow in inflammatory pain sites to attract natural endorphin compounds for pain relief and immune enhancement) may have advantages relative to oral opioids.

By Forest Tennant, MD, DrPH (/author/2391/tennant)

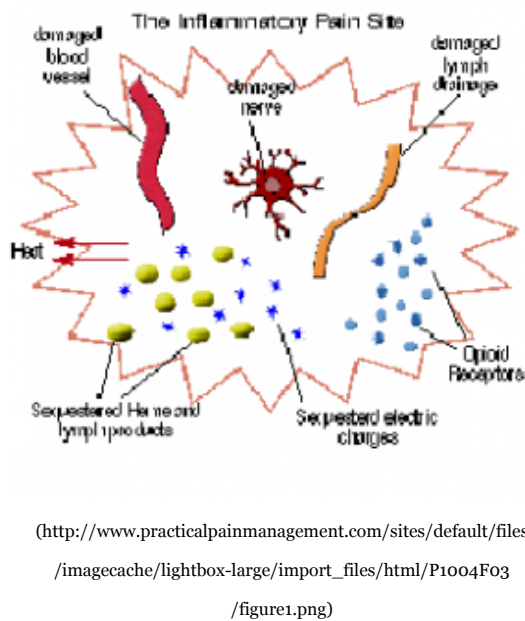
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History may arguably show the discovery of the peripheral opioid receptor to be the most important clinical discovery in pain treatment in the past 20 years.¹⁻⁶ This critical finding gives the practitioner and patient many therapeutic options other than oral opioids. About a year ago in these pages, I encouraged the use of topical morphine. Since that note, I have received much correspondence about the use of other topical opioids and I too have been experimenting with opioids other than morphine. In this effort, I have even encountered some patients who use topical morphine in enough quantity to produce a measurable blood level and some patients even report analgesic effects distant to the local, applied area. Of particular benefit has been the use of topical opioids for knee and spine pain.

The Inflammatory Pain Site

Shown here is an artist's rendition of the anatomical pain site (See Figure 1). It is fundamentally a wound in that it contains inflammatory compounds, sequestered electrical charges, and opioid receptors which are now known to propagate in inflamed tissue.⁷ The natural function of opioid receptors in inflammatory pain sites is to presumably attract the body's natural endorphin compounds for pain relief and immune enhancement. Re-tained or sequestered electrical charges in the pain site generate pain. The removal or displacement of sequestered electrical charges by various electromagnetic means including such simple measures as copper or magnets and various electromagnetic instruments—including electric currents, ultrasound, radiofrequency, infrared, and laser—are generally effective in reducing pain when electromagnetic measures are concomitantly used with topical opioids.



(http://www.practicalpainmanagement.com/sites/default/files/imagecache/lightbox-large/import_files/html/P1004Fo3/figure1.png)

Figure 1. Illustration of the inflammatory pain site.

Which Opioids?

Not all opioids provide topical pain relief. The opioids most commonly prescribed by the author are: (1) morphine; (2) hydromorphone; and (3) oxycodone. Although not officially classified as an opioid, carisoprodol, the notorious and abusable Soma®, produces considerable analgesia when topically applied. Some patients use methadone topically and find it effective. There are some opioids that are inert on the skin surface. Hydrocodone, codeine, and tramadol are pro-drugs which require liver metabolism to convert them to active compounds. Fentanyl is extremely soluble and dissolves quickly through the skin making it a very effective systemic, but poor topical opioid. Morphine, hydromorphone, and oxycodone are relatively insoluble and act directly on opioid receptors without requiring further metabolism.

Making The Topical Preparation

I teach patients to obtain a low cost cold cream and crush oral opioid tablets to mix in the cold cream. Inexpensive standard dosage oral tablets are recommended. Table 1 presents a summary of the opioid, tablet dosage, and strength of topical preparations.

Table 1. Summary of the Opioid, Tablet Dosage, and Strength of Topical Preparations

Opioid	Dosage of Tablets(mg)	Tablets Mixed in Cold Cream
Morphine	30	1 or 2 per ounce
Hydromorphone	4 or 8	Same
Oxycodone	30	Same
Carisoprodal	350	Same

Some patients get creative. They find creams, oils, lotions, and gel preparations they feel get them better relief than ordinary cold cream. Some compounding pharmacists utilize very soluble, effective carrier creams. Cost and insurance coverage is usually the barrier to this approach. With a little instruction to patients, however, inexpensive cold cream will get the job done.

Use of Electromagnetic Devices

Essentially all of the electromagnetic devices on the market will drive topical opioids through the skin and deep into the tissue. These include electric currents, ultrasound, radiofrequency, infrared, and laser. Plain heat, massage, and vibration also enhance the penetration of topical opioids. Table 2 presents a summary of electromagnetic measures for use with topical opioids. These devices and techniques have the added advantage of removing or displacing sequestered electric charges in the pain site. Electromagnetic treatments may also

promote blood flow and activate tissue to heal. When topical opioids that attach to peri-pheral receptors are combined with electromagnetic measures, a powerful healing and therapeutic approach is initiated. Ultrasound, infrared, electric current, and vibrator/massage devices are now quite available, inexpensive, and can be used at-home by patients (See Figures 2-4). Rather than take additional opioids for pain flares or breakthrough pain, some patients will use a topical opioid and an electromagnetic device for enhanced relief.

Table 2. Electromagnetic Measures for Use with Topical Opioids

Ultrasound
Vibrator/massage
Radiofrequency
Infrared
Electric currents



(http://www.practicalpainmanagement.com/sites/default/files/imagecache/lightbox-large/import_files/html/P1004F03/figure2.png)

Figure 2. Topical morphine is applied to the back under an inexpensive at-home ultrasound device.



(http://www.practicalpainmanagement.com/sites/default/files/imagecache/lightbox-large/import_files/html/P1004F03/figure3.png)

Figure 3. Topical morphine is applied to the knee under an inexpensive at-home, infrared device.



(http://www.practicalpainmanagement.com/sites/default/files/imagecache/lightbox-large/import_files/html/P1004F03/figure4.png)

Figure 4. *Topical morphine is applied to the anterior chest wall beneath an inexpensive, at-home, battery-powered vibrator.*

Systemic Effects

In my early studies, I found no morphine in blood or urine following topical use.⁸ I've now observed a few patients who show low levels of morphine in blood and/or urine. Patients who use topical morphine regularly may show morphine in body fluids following topical application. In fact, they usually report that topical morphine is their mainstay for pain control or their major measure to control pain flares. Reported here are two such cases.

Case 1

A 54 year old male has severe, intractable pain in his right hand, arm, shoulder and chest wall. This neuropathic state was caused by a motor vehicle accident. Each day he applies an average of about 240mg of topical morphine. He covers his entire right arm, shoulder and chest wall with it. His blood concentration of morphine is 58.7ng/ml, and, at the time this blood specimen was taken, he submitted a urine sample which showed over 10,000ng/ml. He has reduced his intake of oral opioids by using topical morphine and he now considers topical morphine to be his primary pain treatment. Without topical morphine his right arm and hand are non-functional.

Case 2

A 62-year-old female has severe spine degeneration with multiple disc replacements. She also has severe bilateral knee degeneration. Genetic testing revealed Cytochrome P450-2C9 deficiency. Consequently, she poorly metabolizes oral opioids and requires a very high oral dosage to obtain even modest pain relief. Topical morphine applied to the skin over her spine and knees provide great relief. In her words, "I can hardly walk without putting morphine on my knees." She applies about 60mg a day. Her blood concentration of morphine shows a trace at less than 5ng/ml and she shows 60ng/ml in her urine. She claims that without topical morphine she is house-bound.

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Phantom Limb Syndrome

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