

Pain management for the dermatologist

PERSPECTIVES FROM A PAIN
SPECIALIST

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Assessment of Pain

Onset

Pain Intensity

Pain Location

Duration

Pain Description/Quality

Alleviating/Exacerbating Factors

Impairment/Function (physical, psychosocial)

Previous Treatments

Other Psychological/Behavioral Factors

- Personality
- Emotional Functioning/Co-morbid Affective Factors
- Pain Beliefs and Coping

Risk factors for acute post surgical pain

Screen to identify high risk patients

- Depression, anxiety, pain catastrophizing
- Younger age (<31)
- History of hyperalgesia, fibromyalgia, CRPS
- Chronic opioid and/or anxiolytic use
- Multiple same day procedures

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APS/ASRA/ASA Guideline for postoperative pain management

Utilize multimodal analgesia

- Use of 2 or more medications with different MOA for analgesia, also non-pharmacologic interventions

Use acetaminophen and/or NSAIDs as part of multimodal analgesia if no contraindications

Consider surgical site specific peripheral regional anesthetic techniques for procedures with evidence indicating efficacy

See reference for full guideline



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Non-opioid Medications for pain

Acetaminophen

Mixed Agents (not truly non-opioid)

NSAIDs

Steroids

Alpha-2 agonists

NMDA receptor antagonists

Amine Re-uptake Inhibitors

Membrane Stabilizers

Muscle Relaxants

Topical Agents

Non-opioid Medications for acute pain

Acetaminophen and NSAIDs

- NSAIDs block pain and inflammation by either non-selective or selective COX receptor inhibition in the spinal cord and periphery, disruption of prostaglandin synthesis
 - 25-30% opioid sparing effect
 - GI, bleeding, and CV side effects/risks
- Acetaminophen inhibits prostaglandin synthesis in the CNS but not peripheral tissues; analgesic and antipyretic properties
 - Analgesia from single preoperative doses 500mg-1g are not dose dependent
 - Hepatotoxicity; 2600-3200 mg daily dose may be safer for chronic use, and no dosing should exceed 4g/day
- Dose prior to procedures for pre-emptive analgesia and on a scheduled basis following procedures for superior analgesia and opioid sparing effects

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Wardhan R, Chelly J. Recent advances in acute pain management: understanding the mechanisms of acute pain, the prescription of opioids, and the role of multimodal pain therapy. *F1000Res.* 2017 Nov 29;6:2065. doi: 10.12688/f1000research.12286.1. eCollection 2017.

Non-opioid Medications for acute pain

Steroids

- Block cyclooxygenase and lipoxygenase enzymes
 - Small reduction in opioid use in first 24 hrs after surgery, less rescue analgesia for intolerable pain, longer time until first analgesic use
- No increase in infection or delayed wound healing with one-time perioperative dose of dexamethasone
- Anti-emetic effects
- Will increase serum glucose levels
- Route of administration (IV, IM) and risk of perineal burning (IV) may limit use of dexamethasone in office based procedures

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Non-opioid Medications for acute pain

Alpha-2 agonists (clonidine, dexmedetomidine, tizanidine)

- Clonidine and dexmedetomidine up to 24 hr reduction in opioid requirements, greater magnitude with dexmedetomidine
 - Bradycardia, hypotension, sedation possible side effects
 - IV route of administration for dexmedetomidine may limit use in office based procedures
- Less postoperative pain with tizanidine 4 mg, 1 hr before surgery and BID during first postoperative week after inguinal hernia repair
 - Bradycardia, orthostatic hypotension, sedation possible side effects

Kumar K, Kirksey MA, Duong S, Wu CL. A Review of Opioid-Sparing Modalities in Perioperative Pain Management: Methods to Decrease Opioid Use Postoperatively. *Anesth Analg.* 2017 Nov;125(5):1749-1760.

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Non-opioid Medications for acute pain

NMDA receptor antagonists (ketamine, IV magnesium, dextromethorphan)

- NMDA receptor blockade results in less nociceptive and inflammatory pain transmission
- Ketamine also with analgesia via mu- and delta- opioid receptor effects
 - Low dose postoperative ketamine infusions have up to 40% opioid sparing effect; impact on pain scores does not necessarily correlate
 - Intranasal ketamine 45-50% bioavailable; alternative to intranasal fentanyl
- Dextromethorphan available via PO and IM route

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Radvansky BM, Shah K, Parikh A, et al. Role of ketamine in acute postoperative pain management: a narrative review. *Biomed Res Int.* 2015; 2015: 749837.

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Non-opioid Medications for acute pain

Amine Re-uptake Inhibitors (TCA, SNRI)

- Acute perioperative duloxetine may have up to 48 hr opioid sparing effect but will not affect pain scores; may be due to fact that analgesic effects take up to 1 week to manifest with duloxetine use
- TCA's no clear benefit for opioid sparing effect with acute perioperative use

Membrane Stabilizers (Calcium channel modulators: gabapentin, pregabalin)

- Opioid sparing of perioperative gabapentin may have been overestimated, but likely still some effect
- Multiple studies have shown opioid reduction and improvement in pain with perioperative pregabalin use (even single dose may improve pain)
 - Sedation, hypotension possible side effects; renal dosing in patients with reduced GFR; caution in patients >65

Doleman B, Heinink TP, Read DJ, Faleiro RJ, Lund JN, Williams JP. A systematic review and meta-regression analysis of prophylactic gabapentin for postoperative pain. *Anaesthesia*. 2015;70:1186–1204.

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Eipe N, Penning J, Yazdi F, et al. Perioperative use of pregabalin for acute pain—a systematic review and meta-analysis. *Pain*. 2015;156:1284–1300.

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Non-opioid Medications for acute pain

Muscle Relaxants

- Indication for acute pain/spasm (1-3 weeks), limited data for chronic pain
 - Anti-histamine: orphenadrine, Sedative: carisoprodol, chlorzoxazone, metaxalone, methocarbamol, TCA similar: cyclobenzaprine, Central α -2 agonist: tizanidine, GABA agonist: baclofen, benzodiazepines
 - Significant side effect risks: CNS depression, respiratory depression (baclofen, benzodiazepines, carisoprodol), withdrawal (baclofen, carisoprodol, benzodiazepines, tizanidine), substance abuse risk (benzodiazepines, carisoprodol)

Topical Agents

- May reduce inflammation and/or PNS signaling to reduce pain
 - Pick agents that have peripheral mechanism of action since topical agents do not act systemically
 - Potential for reduced side effect and risk profile as compared to systemic agents
 - FDA approved: Lidocaine, Lidocaine/prilocaine, Diclofenac, Doxepin, Capsaicin

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C.E. Argoff: Topical Analgesics. **H.T. Benzon [et al.]** Practical Management of Pain: 5th ed. 2014. Mosby. Philadelphia. 575-581

Mixed Opioid/Non-opioid Medications for acute pain

Mixed Agents

- Tramadol
 - Binds to mu, and weakly to kappa and delta receptors; inhibits reuptake of serotonin and norepinephrine
 - Less respiratory depression than morphine at equianalgesic doses; contraindicated with MAOI's; seizure risk but incidence <1%, risk of serotonin syndrome
 - No evidence that tramadol is less addictive than other opioids

- Tapentadol
 - Weak mu agonist and norepinephrine reuptake inhibitor
 - Comparable analgesic efficacy to oxycodone, though 2-3 times less potent than morphine at mu receptors
 - May have less side effects, especially GI, compared to pure opioid agonists; though nausea still most common
 - May take longer to develop tolerance as compared to morphine
 - Avoid with severe renal or hepatic dysfunction
 - Risk of serotonin syndrome

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S.P. Stanos, M.D. Tyburski, S.S. Parikh: Minor and Short-Acting Analgesics, Including Opioid Combination Products. **H.T. Benzon [et al.]** Practical Management of Pain: 5th ed. 2014. Mosby. Philadelphia. 508-529

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Non-pharmacologic Treatment Options for Acute and Chronic Pain

Regional Anesthesia

Physical Therapy/occupational therapy/rehabilitation

Massage Therapy, Hot/Cold Manual Therapies

TENS

Pain Psychology

Psychiatry for co-morbid mood disorder/anxiety disorder

Integrative and Alternative Medicine

Multi-modal, Multi-disciplinary/Interdisciplinary Treatment of Pain

Psychiatry for co-morbid depression/ anxiety

Pain Psychology/ Cognitive-Behavioral Therapy

Pharmacologic Management

Complementary and Alternative Medicine

Other Social and Environmental Interventions

Interventional/ Injection Therapies

Lifestyle Modification/ Exercise/ Self-care

Physical Therapy and other Physical Modalities

Surgery

Patient Education



Opioids

Receptors within the CNS, DRG, and peripheral nerves

- Mu (Mu 1, Mu 2)- mechanical, chemical, and thermal stimuli
 - Analgesia (supraspinal, spinal), respiratory depression, slowing of GI transit, pruritus, nausea, vomiting, miosis, bradycardia, hypothermia, urinary retention, physical dependence, euphoria
- Kappa- thermal stimuli and chemical visceral pain
 - Analgesia (supraspinal, spinal), dysphoria, sedation, miosis, diuresis
- Delta- mechanical and inflammatory stimuli
 - Analgesia (supraspinal, spinal), mu receptor modulation, physical dependence

Variations in absorption, clearance, and receptor individuality affect clinical analgesia

D. Besse, M.C. Lombard, J.M. Zajac, et al.: Pre- and post-synaptic distribution of mu, delta and kappa opioid receptors in the superficial layers of the cervical dorsal horn of the rat spinal cord. *Brain Res.* 521:15-22 1990

M. Martin, A. Matifas, R. Maldonado, et al.: Acute antinociceptive responses in single and combinatorial opioid receptor knockout mice: distinct mu, delta and kappa tones. *Eur J Neurosci.* 24:198-205 2003

P.K. Janicki, W.C. Parris: Clinical pharmacology of opioids. **H.S. Smith** *Drugs for Pain.* 2003 Hanley & Belfus Philadelphia 97-118

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D. Koyyalagunta, S.D. Waldman: Opioid Analgesics. **S.D. Waldman, et al.** *Pain Management.* 2011. Churchill Livingstone. Philadelphia. 890-912

Opioids

Adverse effects:

- Constipation
- Nausea/vomiting
- Pruritus
- Sedation
- Respiratory Depression
- Immunologic Effects
- Hormonal Changes
- Sleep Disturbance
- Cognitive and motor effects
- Tolerance/physical dependence
- Hyperalgesia
- Addiction

Opioids for acute vs chronic Pain

Based on systematic review of RCT, opioids show efficacy over the usual 12- week duration of trials with pain intensity reduced approximately 30% more than placebo, with variable effects on function.

- If function was evaluated, it was usually evaluation of one body part rather than the whole person
- Pain relief did not always produce expected improvement in function
- Patients with mental health and substance abuse disorders were generally excluded
- Enriched designs (like excluding patients with response to placebo) were used to try to increase the chance of showing opioid effectiveness
- Some trials allowed open label follow-up at up to 24 months (though difficult to draw conclusion from self-selecting population)
- Most patients stopped opioids due to lack of efficacy or side effects, though minority of patients who continued did report significant relief

Many prospective population studies have demonstrated that long-term analgesic and health effects of chronic opioid therapy are poor

Sullivan MD, Howe CQ. Opioid therapy for chronic pain in the United States: promises and perils. *Pain*. 2013;154 (suppl 1):S94–S100.

Ballantyne J. Opioids for the Treatment of Chronic Pain: Mistakes Made, Lessons Learned, and Future Directions. *Anesthesia and Analgesia*. 2017 125:1769-1778.

Opioid Dose Comparison/Conversion

Never use MME to convert 100% from one opioid to another; the dose for the new opioid will have to be lower to avoid unintentional overdose because of incomplete cross-tolerance or differences in opioid pharmacokinetics

Visit [cdc.gov](https://www.cdc.gov) for more information on opioid conversion and morphine equivalent dose table

www.cdc.gov/drugoverdose/prescribing/guideline.html

https://www.cdc.gov/drugoverdose/pdf/calculating_total_daily_dose-a.pdf

CDC Guideline for Prescribing Opioids for Chronic Pain

Recommendations made based on:

- “No evidence shows a long-term benefit of opioids in pain and function versus no opioids for chronic pain with outcomes examined at least 1 year later (with most placebo-controlled randomized trials ≤ 6 weeks in duration)”.
- “Extensive evidence shows the possible harms of opioids (including opioid use disorder, overdose, and motor vehicle injury)”.
- “Extensive evidence suggests some benefits of nonpharmacologic and nonopioid pharmacologic treatments compared with long-term opioid therapy, with less harm”.

See reference for full
guideline



CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016
Recommendations and Reports / March 18, 2016 / 65(1);1–49

CDC Guideline for Prescribing Opioids for Chronic Pain

Guideline has 12 different recommendations that focus on:

- Determining When to Initiate or Continue Opioids for Chronic Pain
- Opioid Selection, Dosage, Duration, Follow-Up, and Discontinuation
- Assessing Risk and Addressing Harms of Opioid Use

CDC: Determining when to initiate or continue opioids for chronic pain

Non-pharmacologic and non-opioid therapy preferred for chronic pain; Only consider opioids if expected benefits outweigh the risks.

If using opioids, combine with other appropriate non-pharmacologic and non-opioid pharmacologic therapies.

Discuss treatment goals (pain, function) with patients prior to opioid initiation. Only continue if meaningful improvement.

Consider how opioid therapy will be discontinued.

Before starting and periodically during opioid therapy, known risks and realistic benefits discussion as well as patient/clinician responsibilities.

See reference for full
guideline



CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016
Recommendations and Reports / March 18, 2016 / 65(1);1–49

CDC: Opioid selection, duration, follow-up, and discontinuation

When starting opioid therapy, immediate release opioids should be used rather than extended release; Lowest effective dose should be used.

Carefully assess individual risks and benefits when increasing to **≥50 morphine milligram equivalents (MME)/day**, avoid increasing dosage to **≥90 MME/day** or carefully justify a decision to titrate dosage to **≥90**

When opioids are used for acute pain, prescribe the lowest effective dose of immediate-release opioids and should prescribe no greater quantity than needed for the expected duration of pain severe enough to require opioids. Three days or less will often be sufficient; more than seven days will rarely be needed

See reference for full
guideline

CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016
Recommendations and Reports / March 18, 2016 / 65(1);1–49

CDC: Opioid selection, duration, follow-up, and discontinuation

Evaluate benefits/harms with patients within 1 to 4 weeks of starting opioid therapy for chronic pain or of dose escalation.

Evaluate benefits/harms of continued therapy with patients every 3 months or more frequently.

If benefits do not outweigh harms of continued opioid therapy, optimize other therapies and work with patients to taper opioids to lower dosages or to taper and discontinue opioids

See reference for full
guideline



CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016
Recommendations and Reports / March 18, 2016 / 65(1);1–49

CDC: Assessing risk and addressing harms of opioid use

Before starting and periodically during continuation of opioid therapy, evaluate risk factors for opioid-related harms.

Incorporate strategies to mitigate risk, including considering offering naloxone when factors that increase risk for opioid overdose are present (history of overdose, history of substance use disorder, higher opioid dosages (≥ 50 MME/day), concurrent benzodiazepine use).

Review the PDMP

Use urine drug testing before starting opioids and at least annually

See reference for full
guideline



CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016
Recommendations and Reports / March 18, 2016 / 65(1);1–49

CDC: Assessing risk and addressing harms of opioid use

Avoid prescribing opioid pain medication and benzodiazepines concurrently whenever possible

Offer or arrange evidence-based treatment (usually medication-assisted treatment with buprenorphine or methadone in combination with behavioral therapies) for patients with opioid use disorder

See reference for full
guideline



CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016
Recommendations and Reports / March 18, 2016 / 65(1);1–49

Opioid Use Disorder

- (DSM-V): problematic pattern of opioid use leading to significant impairment or distress manifested by at least 2 (within 12m period):
 - Opioid taken in larger amounts or over longer period than intended
 - Persistent desire or unsuccessful efforts to cut down or control use
 - Large amount of time spent on obtaining, using, or recovering from the effects of the opioid
 - Recurrent use results in inability to fulfill major role obligations (work, school, home)
 - Use continued despite persistent or recurrent social or interpersonal problems caused or exacerbated by the substance
 - Important social, occupational, or recreational activities reduced because of use
 - Recurrent use occurs in situations in which physically hazardous
 - Use continued despite knowledge of persistent physical or psychological problem likely caused by or exacerbated by the substance
 - Tolerance present (not applied to those taking under medical supervision)
 - Withdrawal occurs (not applied to those taking under medical supervision)
 - Craving or strong desire for use

Risk Factors for Opioid Misuse or Addiction

Personal or family history of substance addiction

History of comorbid psychiatric conditions, depression/anxiety

History of legal problems such as DUI/DWI, previous MVC related to substance use, previous drug conviction

Younger Age

Novelty/thrill-seeking personality

Smoker

History of physical, emotional, or sexual abuse

History of “process addiction”: sex, gambling, food, shopping

If previous history of alcohol dependence, not being a member of a 12-step program and poor social support

Social or family environments that encourage misuse

Kahan M, Srivastava A, Wilson L, et al.: Misuse of and dependence on opioids: study of chronic pain patients. *Can Fam Physician.* 52:1081-1087 2006

Savage S: Assessment for addiction in pain-treatment settings. *Clin J Pain.* 18:S28-S38 2002

Turk D, Swanson K, Gatchel R: Predicting opioid misuse by chronic pain patients: a systematic review and literature synthesis. *Clin J Pain.* 24:497-508 2008

Michna E, Ross E, Hynes W, et al.: Predicting aberrant drug behavior in patients treated for chronic pain: importance of abuse history. *J Pain Symptom Manage.* 28:250-258 2004

Dunbar MB, Katz NP: Chronic opioid therapy for nonmalignant pain in patients with a history of substance abuse: report of 20 cases. *J Pain Symptom Manage.* 11:163-171 1996

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Covington EC, Bailey JA: Pain and Addictive Disorders: Challenge and Opportunity. **Benzon HT [et al.]** Practical Management of Pain: 5th ed. 2014. Mosby. Philadelphia. 669-682

Webster L.: Risk Factors for Opioid Use Disorder and Overdose. *Anesthesia and Analgesia.* 125: 1741-1748. 2017

Addiction Behavior

Patterns of behavior that may suggest addiction:

- **Consequences**

- Intoxicated, somnolent, sedated
- Declining activity
- Irritable, anxious, labile mood
- Increasing sleep disturbance
- Increasing pain complaints
- Increasing relationship dysfunction

- **Impaired Control or Compulsive Use**

- Report of lost or stolen prescriptions
- Frequent early renewal requests
- Urgent calls or unscheduled visits

- Abusing other drugs or alcohol
- Cannot produce medications on request
- Withdrawal noted at clinic visit
- Observers report overuse or sporadic use

- **Craving**

- Frequently missed appointments unless opioid renewal anticipated
- Does not try non-opioid treatments
- Cannot tolerate most medications
- Requests medication with high reward
- No relief with anything else except opioids

Substance Abuse/Addiction Resources

Substance Abuse and Mental Health Services Administration (SAMHSA)

- www.samhsa.gov : opioid treatment program directory; behavioral health treatment services
 - Searchable by state for local resources
- National Helpline 1-800-662-HELP (4357)
 - referrals to local treatment facilities, support groups, and community-based organizations for individuals and family members facing mental and/or substance use disorders.
 - Free publications

Universal Precautions/Risk Mitigation Treating Patients with pain +/- Opioids

Standardize care as much as possible

Use diagnosis and risk stratification to help guide options and schedule appropriate follow-up

Utilize multi-modal analgesia, maximizing non-opioids before resorting to opioid medications

- Psychological assessment, substance abuse assessment, opioid risk assessment (SOAPP-R, ORT)

Follow CDC guidelines, FSMB guidelines, Federal and State Prescribing rules

Informed Consent, Treatment Agreement

Becker WC, Tobin DG & Fiellin DA. Nonmedical use of opioid analgesics obtained directly from physicians: Prevalence and correlates. *Archives of Internal Medicine* . 2011;171(11):1034-1036.

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Universal Precautions/Risk Mitigation Treating Patients with pain +/- Opioids

Pre- and post-intervention assessment of pain and function (subjective and objective)

- 4 A's: Activity, Analgesia, Adverse Effects, Aberrant Behavior, (5th?- Affect)

Assess for compliance (PDMP, UDS, pill counts; COMM)

Strategy to discontinue analgesics, opioid or non-opioid, if not helpful or if aberrancy

Periodically review pain diagnosis and co-morbid conditions including addiction; review need for continued opioids if utilized

Use lowest effective dose for the shortest duration

Minimize adverse effects from poly-pharmacy

Documentation, clinic policy

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When to Refer to a Pain Specialist

When pain persists beyond expected recovery period

Consider for patients with known addiction or other medical or psychological risk factors that make them high risk for non-opioid analgesic or opioid use

Consider when opioid dose/use, even if temporary, qualifies for higher risk categories

Patients who are high risk for severe post-surgical/post-procedural pain, opioid tolerant

If office/practice is not equipped for thorough pain and pain medication assessment, screening tests for compliance, assessment for aberrant drug-related behavior, and/or mitigation of opioid related adverse effects, misuse, and addiction

Consider when opioid prescribing is considered beyond 1-2 weeks

Access to adjunct and/or alternative therapies

Consider when prescribing long acting or continuous opioids