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Provider Perspectives on the Use of Topical Pain Products

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Disclosures

- Speaker's Bureaus
  - Genentech
  - Insys

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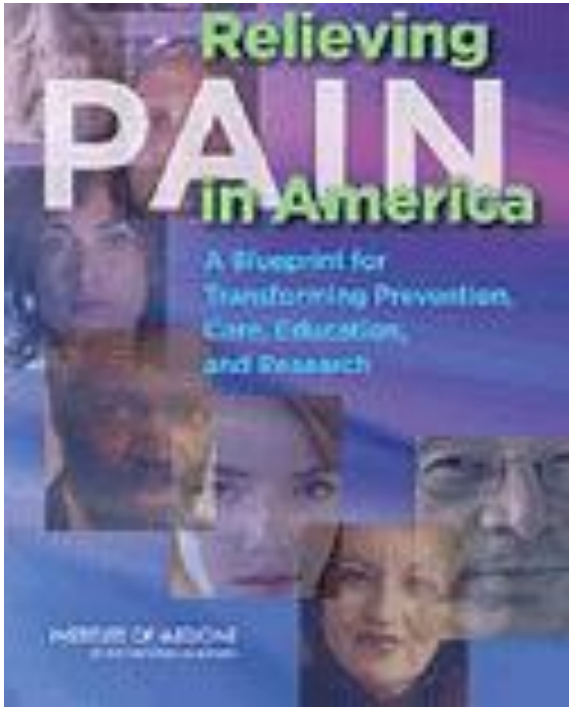
Overview

- Scope of the Problem
- Evidence on Compounded Topical Analgesics
- Risk/Benefit Perspectives
- Safe Dosing and Application
- Adherence
- Patient Education and Engagement

Scope of the Problem

- Chronic pain conditions affect approximately 1 million U.S. adults
- Cost $560 - $635 billion annually or about $2,000 for every person living in the U.S.
  - Direct treatment costs $261-300 billion
  - Loss of productivity $297-336 billion
  - Medicare bears ¼ of the costs for pain or 14% of all Medicare costs



Institute of Medicine, 2011

An Update

- 20.4% (11%-40%) of Americans have chronic pain
- 8% are greatly impacted
- Reliable treatment for chronic pain lacking
  - Disability rates persist despite treatment
  - Contribution to the opioid epidemic?

Dahlhamer et al. (2018), *Morbidity and Mortality Weekly Report*, CDC

Compounded Analgesic Creams

- 2001 Survey
  - 27% of physicians reported prescribing compounded analgesic creams
- Use is on the rise
  - Tricare paid $259 million for compounded medications in 2013
  - Rose to $746 million in 2014
  - Medicare reported costs > ½ billion $ in 2015

Ness et al., *Reg Anesth Pain Med*, 2002; U.S. Accountability Office, 2018; Appleby, *Washington Post*, 2018

Where's the Evidence?

- Single topical creams*
  - NSAIDS, salicylates, capsaicin, lidocaine
  - Cochrane review of 206 studies, 30,700 participants (50% relief)
    - Relief of osteoarthritis (NSAIDS) 1 in 5-10
    - Post-herpetic neuralgia (capsaicin) 1 in 12

- Compounded creams
  - Less evidence exists
  - Small effect sizes, NTT large
- Compounds
  - NMDA Antagonist - Ketamine
  - Anticonvulsant - Gabapentin
  - Alpha-2 - Clonidine
  - NSAIDS – Ketoprofen, Flurbiprofen
  - Antispasmodic - Baclofen
  - Muscle Relaxants - Cyclobenzaprine
  - Local anesthetics – Lidocaine, Bupivacaine
  - Topical nitrates
  - Opioids - Tramadol

* FDA Approved

Derry et al., *Cochrane Database of Systematic Reviews*, 2017

Assorted Studies

Study	Compounds/Arms	Results
RCT (n=399) Brutcher et al., *Ann Int Med*, 2019	1. K, G, C, L 2. KP, B, CB, L 3. K, G, D, B, CB, L	Pain improvement No sig differences
RCT, Voltaren control (n=2177) Somberg & Molnar, *Am J Ther*, 2015	1. F, T, C, CB, BP 2. F, B, C, G, L	Both creams had sign improvement compared to Voltaren $p<0.0001$
RCT, 3 controls (n=360, PHN) Lockhart, *J Pain,* 2004	1. K, G, A 2. Oral G, placebo cream or capsules	Sig improvement with cream compared to placebos (p=0.044); no sig difference with oral G
RCT (n=208, CIPN) Barton et al., *Support Care CA*, 2011	1. K, A, B	Trend for relief of pain (P=0.053) and motor fx (P=0.021)
RCT (n=462, CIPN) Gewadnter et al., *Support Care CA*, 2014	1. K, A	No sig difference

A – Amitriptylline, B – Baclofen, BP – Bupivacaine, C – Clonodine, CB – Cyclobenzaprine, D – Diclofenac, F – Flurbiprofen, K – Ketamine, KP – Ketoprofen, G – Gabapentin, L – Lidocaine, T – Tramadol; PHN – post-herpetic neuralgia; CIPN – chemotherapy-induced peripheral neuropathy

Challenges in the Literature

- Mixed results
- Lack of long-term follow-up (4-6 weeks)
- Compounding variability
  - Concentration of each agent
  - Which one is working, and which is not?
- Adherence in trials not well monitored
- Amounts and doses of application variable

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Cannabinoids?

- Topical cannabinoid enhances topical morphine antinociception
  - » Yesilyurt et al., *Pain*, 2003
- Transdermal cannabidiol reduces inflammation and pain-related behaviors in a rat model of arthritis
  - » Hammell et al., *E J Pain*, 2015

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Cannabinoids

- Increased requests for cannabinoid creams
- Uses: arthritis, muscle spasm, inflammation, peripheral neuropathy, radiation-related burns
- Topical creams
  - CBD salve 30 mg/1 ounce – nerve-related, rheumatoid
  - THC salve 1-1/2 mg THC/Gm of cream– muscular or arthritic-related
  - CBD/THC
  - Cannabis Oils – thin with cream
- Apply twice daily – a little goes a long way
  - Apply as much as desired

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CBD/THC Products

Risk/Benefit Perspectives

- Benefits
  - Minimal systemic absorption
  - Lack/minimal systemic side effects
  - Alternative option/ adjunct to opioids
  - Lack of drug-drug interactions
  - Placebo benefit
- Risks/Challenges
  - Local irritation can be a problem, especially those with capsaicin (4 in 10)
  - Lack of FDA approval
  - Cost
  - Dosing
  - Adherence

Safe Dosing and Application

- Apply to the area of soreness, pain
- Make sure area is clean, without other creams or lotions
- A little bit goes a long way
- One spatula, rub around the area
- Apply 2-3 times a day depending on pharmacokinetic properties
- Challenges
  - High degree of variability
  - Lack of standardization

Adherence

- Initial *buy in*
- Difficult to apply under clothing while in public places
- Inconvenient
- Forgetfulness
- Odors
- Depression
- Substance use disorder
- Socioeconomic status
- Lack of caregiver support
- One try – *It doesn't work*
- Lack of consistent application 2-3x/day
- Side effects

Jorge, Feres, Teles, *J Pain Res*, 2011

Patient Engagement

- Clear instructions
  - Teach back
  - Return demonstration
- Telephone follow-up
- Reinforcement at each visit
- Rewards for adherence
- Caregiver support
- Technology – reminder apps
- Patient-reported outcomes

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Discussion