



ATYPICAL ANALGESICS

Michael Davies MBBS, MPH, Mmed(Pain mgt, FRACS, FFPMANZCA

AOA/ACLM MEETING 13 SEPTEMBER 2024

DISCLOSURES

- No disclosures

PALMITOYLETHANOLAMIDE (PEA)

- Fatty acid that belongs to family of N-acylethanolamines
- Released from cells in response to noxious stimuli
- Also found in some vegetables (peas, beans, potatoes, tomatoes) and human, bovine and moose milk
- Anti-inflammatory and immune-modulating properties

PALMITOYLETHANOLAMIDE

- Reduces activation of mast cells at sites of nerve injury
- Inhibits microglia activation of inflammatory cascade
- Efficacy in chronic neuropathic pain in several animal pain models
 - Painful diabetic neuropathy
 - Chemotherapy induced neuropathic pain
 - CRPS
 - fibromyalgia

PALMITOYLETHANOLAMIDE

- No known serious side effects
- No interactions with other medications
- Insufficient data to comment on uncommon or rare adverse events
- Lack of data about long-term use of PEA (>60days)
- Personal experience
 - Nausea
 - Diarrhoea
 - Facial rash
 - hyperstimulation

PALMITOYLETHANOLAMIDE

- Not available on PBS/RPBS, no private health rebate
- Some OTC preparations, but tend to be expensive
- Can be compounded for about \$45-50 per month
- 900 -1200mg per day in 2-3 divided doses
- Takes time to have effect
- If no better after 2 months, cease

LOW DOSE NALTREXONE (LDN)

- Best known for treating opioid addiction, using 50-100mg daily
- Low dose naltrexone can help reduce pain
- ?reduces inflammation in immune system
- ?reduces activation of glia cells, which are activated by trauma, infection, injury, opioids
- Activated glia produce inflammatory and excitatory factors
- May become cytotoxic when chronically activated

LOW DOSE NALTREXONE

- Used in CRPS, painful diabetic peripheral neuropathy, neuropathic pain, fibromyalgia, chronic fatigue/myalgic encephalitis
- Best evidence for effect is in Crohn's disease
 - Reduced pain and reduced inflammatory markers

LOW DOSE NALTREXONE

- Does not work immediately; can take weeks to months
- Dose ranges from 1.5 – 4.5mg per day as single dose
- Literature recommends taking at night
- Commonest SE is vivid dreams – take in morning if that happens
- Can't be used if patient on opioids

LOW DOSE NALTREXONE

- Little in the way of interactions
- Side effects not common
 - Insomnia
 - Vivid dreams
 - Anxiety, tachycardia, fatigue, mood swings, decreased appetite, nausea, constipation, diarrhoea
 - No information regarding safety in long-term use

LOW DOSE NALTREXONE

- Currently not available on PBS/RPBS
- No rebate from private health funds
- Needs to be compounded
- Costs about \$80-100 for 100 capsules

MEDICINAL CANNABIS

- Controversial
- Driven by public pressure against advice from medical community
- FPM and IASP both recommend against use except in clinical trials
- Lack of high quality scientific evidence
- Evidence in pain limited and mostly low quality
- No guidelines regarding dosage

MEDICINAL CANNABIS

- Cannabidiol and tetrahydrocannabinol are main forms used
- Mechanism of action unclear
- CBD can help as add-on in drug-resistant epilepsy (children and young adults)
- 1:1 mixture CBD:THC can help muscle spasticity in multiple sclerosis
- Some evidence for pain in MS
- Some evidence for neuropathic pain, usually only modest reduction

MEDICINAL CANNABIS

- Some studies show reduction in opioid use with cannabis
- May help in chemotherapy induced nausea and vomiting, particularly THC
- Side effects: fatigue, sedation, nausea/vomiting, vertigo, altered appetite, diarrhoea, convulsions, depression, confusion, hallucinations, psychosis, paranoid delusions
- CBD alone can help sleep and anxiety
- CBD:THC mix helps pain in some patients; CBD thought to reduce psychoactive effects of THC

STIMULANTS

- No experience using stimulants
- Literature search shows multiple articles published since 1944
- 2 recent papers about use in pelvic pain
- Proposed mechanism is replacing inadequate endogenous levels of catecholamines due to inflamed microglia
- Claims they can help reduce opioid use

STIMULANTS

- Brompton Cocktail developed 1896
- Dextroamphetamine and morphine used for pain relief in World War 2
- Animal and human studies 2nd half of 20th century show enhanced pain relief when used together
- Improved mental & physical performance, less sedation and less respiratory depression compared with opioids alone
- 2 recent papers regarding use in pelvic pain

STIMULANTS

- Many of the drugs we use for pain cause increased endogenous stimulants (serotonin, noradrenaline)
 - Tramadol, tapentadol, SSRIs, SNRIs
- Stimulants have a risk of abuse, addiction and diversion.
- Doses for pain not specified – “considerably lower” than level needed for abuse