Randomized crossover trial of transdermal fentanyl and sustained release oral morphine for treating chronic non-cancer pain

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Study Type: POE (not sure it matters)

Purpose: In patients with chronic non-cancer pain, which treatment would be preferred by the patient; transderm fentanyl or sustain-release morphine?

Study Duration: 1 month

Trial Design: randomized, open-label, crossover, multicenter (53 pain centers in Europe and Canada),

Medications: transdermal fentanyl 25, 50, 75, 100 mcg/hr vs morphine SR 10, 30, 60, 100, 200 mg

Rescue medication = regular release morphine 5 mg, titrated to response, maintenance meds were adjusted based on the amount of rescue dose utilized.

Patients: 212 patients, mean age 51 years, ~76 kg, 99% white, 9 year mean duration of pain, 25% have neuropathic pain, 50% with nociceptive pain, 25% with both, 40% with low back pain, 45% with continuous fluctuating severity, 35% results from degeneration, 30% from trauma, operation or burns, 75% were on morphine, 10 to 15% evaluate pain as “bad” or “very bad”.

Inclusion: 18 yrs and older, chronic non-cancer pain, on opioids at least 6 weeks before the trial, must have moderate relief from treatment a week before the trial

Exclusion: those likely to die from another illness, poor opioid response, a history of opioid allergy, reduced level of consciousness, social isolation, psychiatric disorder, history of substance abuse, relevant cardiac, neurological, respiratory disease

Outcome Events: Primary endpoints: patient preference and why, global efficacy assessment, rescue drug use, quality of life assessment (SF-36), Patient intensity (0 being low, 100 high), safety

1. Are the results valid?
   * randomized? yes
   * double-blinded? no
   * were groups similar? yes
   * all patients accounted for? yes

2. What were the results?

   Primary endpoint: Fentanyl preferred 65%, Morphine SR 28%, ABI 37%, P value .001, NNT ~3
   Lower pain intensity scores (0 being low, 100 high) 58 vs 63, P value .001
   Investigator global assessment 58% vs 33%, P value .001, NNT 4
   Mean rescue use 29 mg vs 24 mg, P value .05
   Crossover results
   Good pain relief 40% then 28%, P value .001, NNT 8

Other results:
   * QOL scores favored morphine SR for bodily pain, vitality, social functioning, mental health
   * ~25% got poor results no matter the drug choice

Adverse Events

   Constipation 29% vs 48%, ARI 19%, P value .001, NNH 5
   Nausea 26% vs 18%, ARI 8%, P value .001, NNH 13
   * 37 patients withdrew due to side effects
   * ~ twice as many patients withdrew from the trial that were using fentanyl

3. Will the results help me?

   Mean fentanyl dose was 57 mcg/hr; 133 mg SR morphine
   * Reasons for fentanyl preference - better pain relief, then convenience, then fewer adverse events
   * Limitations: selection bias - convenience factor with the patch

Conclusion: For every three patients treated with both medications, one would prefer transdermal fentanyl over morphine SR. For every 4 patients treated with either drug, the physician would think that one patient was significantly improved with transdermal fentanyl. For 100 patients placed on the patch, 20 would get constipated as compared to oral SR morphine. If the same 100 patients were switched over to SR morphine, 8 more would get nauseated. 25 of the 100 patients would not get adequate pain relief with either treatment.

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