DEM Journal Club

Article Appraisal

Article: Naproxen with Cyclobenzaprine, Oxycodone/Acetaminophen, or Placebo for Treating Acute Low Back Pain: A Randomized Clinical

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Background and Study Objective(s):

Randomized controlled trial (RCT) to determine whether a 10-day course of muscle relaxants or opioids combined with NSAIDs is more effective than NSAID monotherapy for the treatment of acute non-traumatic non-radicular low back pain.

Study Design:

Study was performed in an urban teaching hospital with more than 100 000 adult visits annually. Patients met inclusion criteria if: aged 21 to 64 years, LBP, defined as pain originating between the lower border of the scapulae and the upper gluteal folds, and received a diagnosis consistent with non-traumatic non-radicular, musculoskeletal LBP. Required to have functionally impairing back pain, which we defined as a score of greater than 5 on the Roland-Morris Disability Questionnaire (RMDQ).

Patients excluded if: radicular pain, (defined as pain radiating below the gluteal folds), direct trauma to the back within the previous month, pain duration for more than 2 weeks, or recent history of greater than 1 LBP episode per month; pregnant or lactating, unavailable for follow-up, with allergy or contraindication to the investigational medications, or had chronic opioid use currently or in the past, could only be enrolled once (no repeat enrollment over course of 2 yrs).

Patients were dispensed a 10-day supply of medication, (naproxen, twenty 500-mg tablets, taken as 1 every 12 hours + 60 tablets of one of the following investigational medications, to be taken as 1 or 2 tablets every 8 hours: (1) placebo; (2) cyclobenzaprine, 5 mg; or (3) oxycodone, 5 mg/acetaminophen, 325 mg).

Primary outcome was improvement on the RMDQ between ED discharge and the 7-day telephone follow-up. There were numerous exploratory out comes at one week and then at 3 month follow-up which included: worst LBP during the previous 24 hours; frequency of any analgesic or LBP medication use during the previous 24 hours; frequency of LBP during the previous 24 hours; satisfaction with treatment (at one week); day on which the participant was able to return to work and resume all usual activities; frequency of visits to any clinician. Exploratory outcome at 3 months included: worst LBP during the previous 72 hours; frequency of LBP during the previous 72 hours; frequency

of use of any LBP medication during the previous 72 hours; frequency of opiate use.

Results:

At 1 week follow-up, no significant difference in RMDQ between the three groups. Patients randomized to receive naproxen + placebo improved by a mean of 9.8 (98.3% CI, 7.9 to 11.7) on the RMDQ, those randomized to naproxen + cyclobenzaprine improved by 10.1 (98.3% CI, 7.9 to 12.3), and those randomized to naproxen + oxycodone/acetaminophen improved by 11.1 (98.3% CI, 9.0 to 13.2).

There was no statistical significant difference in any of the exploratory outcomes at 1 week or 3 month follow up. Any adverse effect was greatest with opiate use: Opiate NNH 5.3 > cyclobenzaprine NNH 7.8 > placebo; No difference in stomach irritation between groups. Patients in the opiate group were more likely to experience tiredness and dizziness.

Validity of Results:

Randomization:
Pharmacist performed a stratified randomization in blocks of 6 based on 2 sequences using a randomization plan generator. Patients were stratified based on results of the baseline RMDQ. In this case, this is to have similarly disabled people in the blocks of 6 thereby reducing bias and enrolling patient in a way that would provide the best estimate of effect. Resulted in very similar groups at the start of the trial (see Table 1).

Blinding:
The pharmacist masked the medication by placing cyclobenzaprine, oxycodone/acetaminophen, or placebo into identical unmarked capsules, which were then packed with small amounts of lactose and sealed. The pharmacist created research packets, each with 2 vials of medication, one containing naproxen and the other containing the masked investigational medication. Research packets were dispensed to study participants by research personnel. Researchers did not evaluate the adequacy of patient blinding. Thus, unknown whether patients' assumptions about the investigational medication they were receiving influenced their self-reports of pain and functional outcomes.
Groups treated equally:
Intervention identical: masked the medication by placing cyclobenzaprine, oxycodone/acetaminophen, or placebo into identical unmarked capsules, which were then packed with small amounts of lactose and sealed. The pharmacist created research packets, each with 2 vials of medication, one containing naproxen and the other containing the masked investigational medication
Other: Each participant was informed that carefully chosen exercises and stretches may help alleviate pain and prevent future occurrences and that hot or cold packs, physical therapy, massage therapy, and acupuncture help some patients.

Statistical Analysis:
Intention to Rx analysis
Primary outcome: 3 pairwise comparisons of the change in RMDQ between baseline at ED discharge and 1 week, with CI of 98.3%; and significance level set at 0.02. This unconventional alpha represents a "Bonferoni correction factor" to minimize risk of a type 1 error when performing multiple comparisons.

Generalizability of Results:

Population studied is from single academic hospital in marginalized area of NY (Bronx), and patients were provided with extra resources including in-depth non-pharmacological treatment strategies that may not be realistic in a busy ED.

The Bottom Line:

1) Adds to evidence demonstrating that opiates are of little to zero role in Rx of acute back pain
2) Back pain is a huge issue but this study was a subset (20%) of pts with low back pain and from one hospital with a relatively specific population.