

Van Tulder MW, Furlan TT, et al. Muscle relaxants for non-specific low back pain (Review).
Cochrane Database of Systematic Reviews 2003, Issue 4, art # CD004252.

Design: Meta-analysis of clinical trials

PICOS:

- Patient population: Patients diagnosed with nonspecific low back pain (NSLBP)
 - o Defined as pain localized between scapulae and gluteal fold, which may or may not radiate towards the knee
 - o Excluded conditions were specific etiologies such as infection, neoplasm, metastases, osteoporosis, fractures, and other relevant pathological entities
 - o Sciatica was included as NSLBP
 - o Pain was divided into acute and chronic; acute pain was less than 12 weeks and chronic pain was more than 12 weeks
- Intervention: Muscle relaxants as monotherapy or in combination with other therapies
 - o Relaxants included benzodiazepines, non-benzodiazepine antispasmodics, and antispasticity agents
- Comparison: placebo, acetaminophen, NSAIDS, other muscle relaxants
 - o Combinations of relaxants plus analgesics/NSAIDS with placebo plus the same analgesics/NSAIDS were also allowed
- Outcomes: pain and function
 - o Pain intensity on VAS or other numerical scale
 - o Global improvement assessed by the patient
 - o Functional scale such as Oswestry or Roland-Morris
 - o Return to work
 - o Physiological outcomes (range of motion, muscle strength, muscle spasm)
 - o General health status (SF-36 etc)
- Study types: Randomized controlled trials, double blind controlled clinical trials

Study selection:

- Databases were mostly MEDLINE, EMBASE, and the Cochrane Library
- Two authors independently reviewed candidate articles for inclusion and study quality
- Quality was judged by Cochrane Risk of Bias scale, an 11 item scale emphasizing randomization, allocation concealment, baseline similarity, blinding, dropouts, co-interventions, compliance with treatment, and intention-to-treat analysis
 - o High quality was 6 points or more; less than 6 points was low quality
 - o The 2 reviewers agreed on scores 73% of the time and disagreed 27% of the time

- Disagreements were due to subtle differences in interpreting ambiguous articles, and were readily resolved by discussion
- Strength of evidence was defined as strong, moderate, limited, conflicting, or no evidence; strong evidence was consistent findings in multiple high-quality trials

Main relevant results:

- A total of 30 studies met inclusion criteria; 23 of the 30 studies had quality scores of 6 or more, meeting the definition of high quality
 - The quality criterion most commonly lacking was inadequate concealment of allocation (93% of the included studies)
- For benzodiazepines, one low quality study provided limited evidence that diazepam administered IM followed by oral administration for 5 days was more effective than placebo for acute LBP, but with significant CNS side effects
- For oral non-benzodiazepines, 3 high quality studies (one of cyclobenzaprine and two of tizanidine) provided strong evidence of superiority to placebo for acute LBP in relieving pain and muscle spasm, but with greater CNS side effects, mainly drowsiness and dizziness
- For antispasticity drugs, 2 high quality trials (one of dantrolene and one of baclofen) provided strong evidence that antispasticity agents were more effective than placebo for acute LBP on short-term pain relief and muscle spasm
- One high quality study comparing carisoprodol with diazepam provided moderate evidence that carisoprodol was more effective than diazepam in relieving muscle spasm and showing global efficacy, but carisoprodol did not differ from cyclobenzaprine in the same comparisons
- No trials were found which directly compared muscle relaxants with acetaminophen or NSAIDS
- The authors did one sensitivity analysis in which they lowered the cutoff score for a high quality study from 6 points to 5 points, and another in which they raised the cutoff score from 6 points to 7 points, with few effects on the strength of evidence for the relevant comparisons

Authors' conclusions:

- There was strong evidence for significant symptomatic relief and overall improvement with oral non-benzodiazepine muscle relaxants compared with placebo
- The studies of antispasticity drugs, although of high quality, were of questionable relevance, due to their limited applications outside neurologic conditions characterized by spasticity
- Muscle relaxants must be used with caution because of CNS side effects and the risk of long-term dependence, risks that are not present with NSAIDS

- Muscle relaxants are recommended by clinical guidelines for use in patients who do not respond to NSAIDs and other analgesics

Comments:

- Many of the studies were of drugs not available in the United States and those comparisons are not relevant for guideline revision
- The authors rightly concluded that there is much room for improvement in the conduct and reporting of clinical trials of muscle relaxants, especially in adequate reporting of methods of randomization and concealment of allocation
- The precautions related to CNS side effects of even the non-benzodiazepine muscle relaxants appear to be prudent and appropriate
- Cyclobenzaprine and tizanidine were clustered together as non-benzodiazepine drugs, which implies that they are similar in effect, an assumption which is probably reasonable

Assessment: Supports a statement that there is strong evidence that non-benzodiazepine muscle relaxants are superior to placebo in relieving acute LBP, but that they should be used with caution because of CNS side effects