Efficacy and tolerability of muscle relaxants for low back pain: Systematic review and meta-analysis

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Abstract

Muscle relaxants are commonly prescribed for low back pain (LBP); however, there is limited evidence of their clinical efficacy and tolerability. This review evaluated the efficacy and tolerability of muscle relaxants in people with LBP. We searched online databases including Medline, EMBASE, CENTRAL and PsycINFO (inception to end October 2015) and performed citation tracking for eligible randomized controlled trials (RCTs). Two authors independently extracted data and assessed risk of bias of randomized controlled trials of muscle relaxants. Pain outcomes were converted to a common 0–100 scale. Data were pooled using a random effects model with strength of evidence assessed using GRADE. Fifteen trials (3362 participants) were evaluated in this review. A total of five trials (496 participants) provide high quality evidence that muscle relaxants provide clinically significant pain relief in the short term for acute LBP; MD -21.3, [-29.0, -13.5]. There was no information on long-term outcomes. The median adverse event rate in clinical trials for muscle relaxants was similar to placebo 14.1% IQR (7.0–28.7%) and 16.0% (4.1–31.2%); p = 0.5, respectively. There is no evidence for the efficacy of benzodiazepines in LBP. For people with acute LBP, muscle relaxants provide clinically significant short-term pain relief. For chronic LBP, the efficacy of muscle relaxants is largely unknown. There was no eligible RCT evidence to support the efficacy of benzodiazepines in LBP. Prolonged use of these medicines in LBP cannot be guided by trial evidence.

What does this review add?: Muscle relaxants provide clinically significant pain relief for acute low back pain. Caution must be taken with the interpretation of the findings as the evidence comes from specific muscle relaxant medicines.

1. Introduction

Low back pain (LBP) is a common problem with an estimated point prevalence of 23% (Vos et al., 2012). It is the leading cause of disability worldwide (Lim et al., 2012; Vos et al., 2012).

Muscle relaxants (a class of chemically unrelated drugs grouped together because of their indication) and benzodiazepines are more commonly prescribed for LBP (Australian Institute of Health and Welfare, 2009; Mafi et al., 2013) than international LBP...
guidelines recommend (National Health and Medical Research Council, 2004; van Tulder et al., 2006). The skeletal muscle relaxants, carisoprodol and cyclobenzaprine, are among the most commonly prescribed drugs for LBP in the USA (Luo et al., 2004; Mafi et al., 2013), whilst in both the United States and Australia prescription of the benzodiazepine, diazepam, is also common (Luo et al., 2004; National Health and Medical Research Council, 2004; van Tulder et al., 2006; Australian Institute of Health and Welfare, 2009). Guidelines recommend muscle relaxants or benzodiazepines be considered if simple analgesics (e.g. paracetamol or NSAIDs) or combination opioid analgesics provide insufficient pain relief (Waddell et al., 1999; See and Ginzburg, 2008).

Despite the widespread use of muscle relaxants for LBP, there is uncertainty around their clinical benefits whilst concerns over adverse events and diversion have risen in line with the increased use of these medicines (van Tulder et al., 1997, 2003).

The last review on muscle relaxants for non-specific LBP (van Tulder et al., 2003) is over a decade old; warranting an update of the available evidence. The aim of this systematic review was to evaluate the efficacy and tolerability of muscle relaxants in the management of people with LBP.

2. Methods

2.1 Data sources and searches

MEDLINE, EMBASE, Cochrane Database of Systematic Reviews, CENTRAL and PsycINFO (inception to October 2015) were searched for randomized controlled trials (RCTs) evaluating muscle relaxant and benzodiazepine medicines for non-specific LBP (Supporting Information Table S1). Additionally, we screened studies and reference lists from systematic reviews evaluating these medicines for patients with LBP to identify eligible RCTs (Fig. 1).

We adopted the definition of non-specific LBP employed previously (van Tulder et al., 2003):

‘Pain localized between the scapulas and inferior gluteal folds that may or may not radiate down towards the knees, for which specific aetiologies such as infections, neoplasms, metastases, osteoporosis, fractures, rheumatological disorders, neurologic disorders and other relevant pathologic entities have been ruled out clinically.’

One reviewer (CAS) screened titles and abstracts of retrieved studies. Two reviewers drawn from a pool of three reviewers (CAS, AJM and CGM) independently inspected the full manuscript of potentially eligible RCTs to determine eligibility, with disagreements resolved by consensus.

2.2 Study selection

We included studies in any language evaluating single ingredient or combination medicines containing a muscle relaxant or benzodiazepine for non-specific LBP. Study selection was not restricted by pain duration, comorbid condition(s) or concurrent mediation use (e.g. to treat hypertension) provided participants were stabilized on these medications and the pattern of use was unchanged throughout the study. We included the Anatomical Therapeutic Chemical (ATC) (World Health Organisation, 2011) codes for drug classes relevant to this review in the search.

Placebo-controlled RCTs and RCTs comparing two drugs from the same class or different doses of the same drug were eligible for inclusion. Trials were included if they reported pain, disability or adverse events outcomes. We considered short-term pain intensity as the primary outcome. Trials involving patients with various pain conditions were included if results for participants with LBP were able to be separately extracted.

2.3 Data extraction and quality assessment

Risk of bias was assessed using the PEDro scale (Supporting Information Table S2) (Maher et al., 2003; de Morton, 2009; Macedo et al., 2010). The PEDro scale is an 11-item scale (Supporting Information Table S2) that has been established as a valid and reliable method of rating methodological quality of individual RCTs (Maher et al., 2003; de Morton, 2009; Macedo et al., 2010). Each item (excluding the item for external validity) is scored as either present (1) or absent (0) to give a total score out of 10. Rating of trials was carried out by two independent raters (CAS + AJM or CGM) with disagreements resolved by an independent third rater.

Trials scoring <7/10 on the PEDro scale were defined as high risk of bias; those scoring 7 or more were considered low risk of bias (de Morton, 2009).

Two reviewers (CAS, CGM) independently extracted outcomes data from published studies (Supporting Information Table S3). Missing data were obtained by contacting authors or estimated using the methods described in the Cochrane Handbook (Higgins and Green, 2009). Analysis of data from a cross-over trial was performed according to recommendations in the Cochrane Handbook (Higgins and Green, 2009).
An adapted version of the GRADE criteria (Atkins et al., 2004) endorsed by the Cochrane Back Review Group was used to evaluate the strength of recommendations and the overall quality of the evidence for an intervention. This method is described elsewhere (Pinto et al., 2012a,b), but briefly the quality of evidence was downgraded a level for each of four factors: poor study design [25% or more of trials, weighted by sample size, have a low PEDro score (<7/10)], inconsistency of results (25% or more of the trials, weighted by sample size, have results which are not in the same direction), imprecision (sample size <300) and publication bias (assessed using funnel plot analysis/Egger’s regression test). Where Egger’s regression two-tailed p-value was <0.10 (Egger et al., 1997), the overall quality of evidence was downgraded by one level (Pinto et al., 2012b). We did not assess for indirectness (when the trial context is not the same as the review question) as this review encompassed a specific population.

Overall quality of evidence was defined as (Atkins et al., 2004):
- High quality – all domains satisfied, no suspected reporting bias, future research unlikely to change our confidence in the estimated effect;
- Moderate quality – 1 domain not met, future research likely to have an important impact on our confidence in the estimated effect and might change the effect;
- Low quality – 2 domains not met, future research likely to have a significant impact on our confidence in the estimated effect and is likely to change the effect;
- Very low quality – 3 or more domains not met, uncertain about the estimated effect.
Single RCTs with sample sizes <300 provided ‘low to very low quality evidence’ as these were deemed both inconsistent and imprecise (Pinto et al., 2012b). Effects sizes from fewer than three studies were downgraded for small study bias (Pinto et al., 2012b).

2.4 Data synthesis and analysis

Pain and disability outcomes were converted to a common 0–100 scale (0: no pain or disability; 100: worst possible pain or disability) (Roland and Fairbank, 2000; Pinto et al., 2012a,b). The pain intensity measures used in the retrieved trials were visual analogue scale (VAS) scores (scale range, 0–100) and numerical rating scale (NRS) scores (range, 0–10). The NRS was converted to the same 0–100 scale as in the VAS as these two pain measures have been shown to be highly correlated and when transformed, can be used interchangeably (Roland and Fairbank, 2000; Hjermstad et al., 2011). The disability measures used to calculate pooled effects were Oswestry Disability Index scores (range, 0–100) and Roland–Morris Disability Questionnaire (RMDQ) scores (range, 0–24). The RMDQ scores were converted to the same 0–100 scale as in the Oswestry Disability Index as these two questionnaires are highly correlated and share similar psychometric properties (Roland and Fairbank, 2000).

We present results as mean differences (MD) rather than standardized mean differences (SMD) as the benchmarks for clinically important difference in pain and disability are expressed in points on a 0–100 pain scale not proportions of a standard deviation (Dworkin et al., 2008; Ostelo et al., 2008). We considered a 10-point difference on this 0–100 scale as a ‘minimal’ difference and a 20-point difference on this 0–100 scale as clinically significant, consistent with the proposed thresholds for clinically important changes in chronic pain (Dworkin et al., 2008) and the LBP literature (Ostelo et al., 2008).

Outcomes were grouped into three time categories (with respect to follow-up): short term (≤3 months), intermediate (>3 months, ≤12 months) and long term (>12 months). Where multiple time points were available for a single category, the time closest to 6 weeks was chosen for short term, 6 months for the intermediate term and 12 months for the long term.

Meta-analysis was carried out using RevMan 5.1 and Comprehensive Meta-Analysis (2014). Pooled effects were calculated using a random effects model. Where possible, we explored possible causes of heterogeneity for $I^2$ values >40%.

3. Results

We identified 15 muscle relaxant trials [3362 participants], as eligible for inclusion in this review (Table 1). No eligible RCTs evaluating benzodiazepines in LBP were identified. PEDro ratings are summarized in Supporting Information Table S2.

Muscle relaxant trials evaluated eperisone (Cabitza and Randelli, 2008; Chandanwale et al., 2011; Rossi et al., 2012). carisoprodol (Hindle, 1972; Rollings, 1983; Ralph et al., 2008; Serfer et al., 2010), thiocolchicoside (Aksoy et al., 2002; Tuzun et al., 2003; Ketenci et al., 2005), tizanidine (Berry and Hutchinson, 1988a,b; Pareek et al., 2009; Rossi et al., 2012), flupirtine (Uberall et al., 2012), pridonol (Pipino et al., 1991), and cyclobenzaprine (Rollings, 1983). Eleven muscle relaxant trials evaluated participants with acute LBP and three trials evaluated people with chronic LBP (Pipino et al., 1991; Rossi et al., 2012; Uberall et al., 2012).

3.1 Pain

There is high quality evidence from five trials ($n = 496$ participants) that muscle relaxants provide clinically significant pain relief in the short-term MD $-21.3, [-29.0, -13.5]$; $p < 0.001$ for acute low back pain (Fig. 2). There was no information on longer term outcomes.

There is a paucity of evidence around the use of muscle relaxants in people with chronic LBP, with one placebo-controlled trial of flupirtine (Uberall et al., 2012) providing very low quality evidence that there is no clinically significant effect on pain in the short-term MD $-4.0 [-8.6, 0.6]$; $p = 0.09$.

Head-to-head comparisons of muscle relaxant trials are summarized in Fig. 3.

3.2 Disability

A total of three trials (Aksoy et al., 2002; Ralph et al., 2008; Serfer et al., 2010) reported on disability. One muscle relaxant trial (Aksoy et al., 2002) provided low quality evidence of reduction in disability with thiocolchicoside in the short term MD $-18.8 p < 0.001$, although this effect is under the clinically important threshold. Pooled effects from two placebo-controlled trials of carisoprodol (Ralph et al., 2008; Serfer et al., 2010) provide moderate quality evidence that there is no clinically significant benefit on disability in the short-term MD $-6.5 [-10.9, -2.1]$; $p = 0.004$ – Fig. 4.
<table>
<thead>
<tr>
<th>Study</th>
<th>Patient population baseline</th>
<th>Setting</th>
<th>Intervention</th>
<th>Comparison</th>
<th>Length of treatment</th>
<th>Follow-up</th>
<th>Eligible outcome measure(s)</th>
</tr>
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<tbody>
<tr>
<td>Aksoy</td>
<td>329 patients with acute/subacute LBP 119♂ 210♀ mean age 40.0 years</td>
<td>93 Turkish centres</td>
<td>Standard treatment (NSAID) for 5–7 days n = 155</td>
<td>Standards treatment plus Thiocolchicoside 8 mg for 5–7 days n = 174</td>
<td>5–7 days</td>
<td>Day 7 and 31</td>
<td>VAS RMDQ</td>
</tr>
<tr>
<td>Berry</td>
<td>105 patients with acute LBP 58♂ 47♀ mean age 42.5 years</td>
<td>UK</td>
<td>Tizanidine 4 mg three times a day plus ibuprofen 400 mg three times a day n = 51</td>
<td>Placebo plus ibuprofen 400 mg three times a day n = 54</td>
<td>1 week</td>
<td>1 week</td>
<td>VAS [at rest]</td>
</tr>
<tr>
<td>Berry</td>
<td>112 patients with acute LBP 57♂ 55♀ mean age 40 years</td>
<td>UK</td>
<td>Tizanidine 4 mg three times a day n = 45</td>
<td>Placebo n = 45</td>
<td>1 week</td>
<td>1 week</td>
<td>VAS</td>
</tr>
<tr>
<td>Cabitza</td>
<td>160 patients with acute LBP 49♂ 111♀ mean age 48.0 years</td>
<td>Italy</td>
<td>Eperisone 100 mg three times daily n = 80</td>
<td>Thiocolchicoside 8 mg twice daily n = 80</td>
<td>12 days</td>
<td>Day 7</td>
<td>VAS ('spontaneous pain')</td>
</tr>
<tr>
<td>Chandanwale</td>
<td>225 patients with acute LBP 106♂ 119♀ mean age 41.4 years</td>
<td>5 tertiary care orthopaedic centres across India</td>
<td>Eperisone 50 mg three times daily for 14 days n = 112</td>
<td>Placebo n = 113</td>
<td>2 weeks</td>
<td>Day 7</td>
<td>VAS</td>
</tr>
<tr>
<td>Hindle</td>
<td>48 patients with acute LBP 27♂ 219♀ mean age 38.2 years</td>
<td>California</td>
<td>Carisoprodol 350 mg four times daily for 4 days n = 14</td>
<td>Placebo n = 14</td>
<td>4 days</td>
<td>Day 4</td>
<td>0–100 pain intensity scale (current pain)</td>
</tr>
<tr>
<td>Ketenci</td>
<td>97 patients with acute LBP 47♂ 50♀ mean age 38.0 years</td>
<td>Istanbul</td>
<td>Thiocolchicoside 8 mg twice a day n = 38</td>
<td>Tizanidine 6 mg at night + placebo n = 32</td>
<td>5–7 days</td>
<td>Day 7</td>
<td>VAS [at rest]</td>
</tr>
<tr>
<td>Pareek</td>
<td>197 patients with acute LBP 120♂ 77♀ mean age 43.4 years</td>
<td>Secondary care – inpatients and outpatients</td>
<td>Aceclofenac (100 mg) plus tizanidine (2 mg) twice daily for 7 days n=94</td>
<td>Aceclofenac (100 mg) alone twice daily for 7 days n=91</td>
<td>1 week</td>
<td>Day 7</td>
<td>VAS at rest</td>
</tr>
<tr>
<td>Pipino</td>
<td>120 patients with chronic LBP 51♂ 69♀ mean age 53.1 years</td>
<td>49 sites in the US</td>
<td>Pridanol mesilate 4 mg intramuscular injection twice a day for 3 days followed by orally administered pridinol 2 mg twice a day for 4 days n = 60</td>
<td>Thiocolchicoside 4 mg intramuscular injection twice a day for 3 days followed by orally administered thiocolchicoside 8 mg twice a day for 4 days n = 60</td>
<td>7 days</td>
<td>Baseline, day 4 and day 7</td>
<td>VAS ('spontaneous pain')</td>
</tr>
<tr>
<td>Ralph</td>
<td>547 patients with acute LBP 263♂ 284♀ mean age 40.4 years</td>
<td>49 sites in the US</td>
<td>Carisoprodol 250 mg once daily n = 269</td>
<td>Placebo n = 278</td>
<td>7 days</td>
<td>Day 7</td>
<td>RMDQ</td>
</tr>
<tr>
<td>Rollings</td>
<td>58 patients with acute LBP 31♂ 27♀ mean age 42.0 years</td>
<td>USA</td>
<td>Carisoprodol 350 mg four times daily for 7 days n = 28</td>
<td>Cyclobenzaprine 10 mg four times daily for 7 days n = 28</td>
<td>1 week</td>
<td>Day 7</td>
<td>VAS</td>
</tr>
</tbody>
</table>
3.3 Reasons for study drop-out/withdrawal

Muscle relaxant trials reported a low withdrawal rate overall (largest loss 25.6%) (Rollings, 1983) with common reasons being loss to follow-up and to a lesser extent lack of efficacy and adverse events (Supporting Information Table S4).

3.4 Adverse events

A detailed analysis of adverse events is presented in Supporting Information Table S5. There were six muscle relaxant versus placebo trials (Berry and Hutchinson, 1988a,b; Tuzun et al., 2003; Ralph et al., 2008; Serfer et al., 2010; Chandanwale et al., 2011; Uberall et al., 2012) for which adverse events outcomes were available, four of which (Berry and Hutchinson, 1988a,b; Tuzun et al., 2003; Chandanwale et al., 2011; Uberall et al., 2012) reported the proportion of participants experiencing at least one adverse event (Supporting Information Table S6). The median adverse event rate for muscle relaxants was similar to placebo 14.1% IQR (7.0–28.7%) and 16.0% (4.1–31.2%); $p = 0.5$. Common adverse events included nausea, dizziness and headache (Supporting Information Table S5).

See Supporting Information Table S7 for grading of evidence.

4. Discussion

There is evidence that muscle relaxant drugs provide clinically significant pain relief in the short term for acute (but not chronic) LBP. There is no evidence to support the use of benzodiazepines in LBP. There is a paucity of evidence on long-term use, and effects on disability for these classes of medicines.

Strengths of this review include a comprehensive search strategy and coverage of medicines which are widely used to manage LBP. The PEDro scale was used to assess risk of bias because it has acceptably high clinimetric properties (Maher et al., 2003; de Morton, 2009; Macedo et al., 2010), whereas limitations have been reported for the Cochrane risk of bias scale (Hartling et al., 2009; Armijo-Olivo et al., 2012). Limitations of this study include possible publication bias, as only studies published in peer-reviewed journals were included.

This review evaluates muscle relaxants for LBP with treatment effect expressed as a mean between group difference, with 95% CI, for pain outcomes on

<table>
<thead>
<tr>
<th>Study</th>
<th>Patient population baseline</th>
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<th>Follow-up</th>
<th>Eligible outcome measure(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rossi</td>
<td>60 patients with chronic LBP 18+</td>
<td>42 years mean age 62.8 years</td>
<td>Tramadol MR 100 mg/day plus eperisone 100 mg three times daily for 10 days then eperisone 100 mg daily for a further 20 days n = 30</td>
<td>Tramadol MR 100 mg/day plus tizanidine 2 mg three times daily then tizanidine 2 mg daily for a further 20 days n = 30</td>
<td>30 days</td>
<td>Days 2, 15 and 30</td>
<td>VAS (at rest)</td>
</tr>
<tr>
<td>Serfer</td>
<td>806 patients with acute LBP/spasm</td>
<td>35 years mean age 47 years</td>
<td>Carisoprodol 250 mg n = 264 three times daily and at bedtime or Carisoprodol 350 mg n = 273 three times daily and at bedtime</td>
<td>Placebo three times daily and at bedtime n = 269</td>
<td>1 week</td>
<td>Day 3</td>
<td>RMDQ</td>
</tr>
<tr>
<td>Tuzun</td>
<td>143 patients with acute LBP 66+</td>
<td>77 years mean age 40.9 years</td>
<td>Thiocolchicoside (intramuscular injection) 4 mg twice daily for 5 days n = 73</td>
<td>Placebo n = 68</td>
<td>5 days</td>
<td>Day 5</td>
<td>VAS (&quot;spontaneous pain at rest&quot;)</td>
</tr>
<tr>
<td>Uberall</td>
<td>355 patients with chronic LBP 135+</td>
<td>220 years mean age 58.5 years</td>
<td>Flupirtine MR 400 mg daily n = 109</td>
<td>Placebo n = 110</td>
<td>6 weeks</td>
<td>4 weeks</td>
<td>NRS (average NRS within preceding 24 h)</td>
</tr>
</tbody>
</table>

VAS, visual analogue scale; NRS, numeric rating scale; RMDQ, Roland Morris disability questionnaire.
a 0–100 scale. This practice is in line with previous research exploring the efficacy of opioid analgesics medications for LBP (Abdel Shaheed et al., 2016). Previous reviews in the area have typically focussed on \( p \) values; a practice which does not assist readers to judge if the treatment effect is clinically worthwhile, or appreciate the precision of the estimate of the treatment effect. The present review also provides an update of the evidence, including RCTs which were published after the latest review of muscle relaxants for low back pain. The findings are particularly significant given the paucity of evidence around the efficacy of opioid analgesics for acute low back pain (Abdel Shaheed et al., 2016). It also adds to existing knowledge around effects of treatments commonly used for non-specific back pain and can therefore inform the clinical decision making of prescribers.

Current guidelines report that there is conflicting evidence as to whether muscle relaxants are more...
effective than placebo for acute LBP (National Health and Medical Research Council, 2004). This review has shown that muscle relaxants do provide clinically significant pain relief compared with placebo for acute LBP. The majority of guidelines recommend that muscle relaxants either be avoided in acute LBP or considered only when an adequate trial of simple analgesics and/or combination opioid analgesics has been unsuccessful (National Health and Medical Research Council, 2004). The present review would suggest it is appropriate to consider brief treatment with a muscle relaxant ahead of combination or single ingredient opioid analgesics, especially as there is a paucity of evidence around opioid analgesic for acute LBP from placebo-controlled trials. The benefit on pain with muscle relaxants identified in this review therefore challenges the notion that there should be strict prerequisites to their use in people with acute LBP. Nevertheless, the review supports existing recommendations that treatment should be very brief (<1–2 weeks) for an acute episode of LBP (Waddell et al., 1999) given the paucity of evidence on long-term outcomes. Very few muscle relaxant trials reported on global recovery outcomes, and the effects on disability, where reported in this review were small. It is possible that the combination with non-pharmacological management strategies such as light physical activity may have a synergistic effect and future research should focus on evaluating the benefits of such an approach.

The findings from this review must be balanced against the individual risks of the muscle relaxants evaluated, as the adverse events outcomes reported were very limited. For example thiocolchicoside, the muscle relaxant found to have greatest benefit on pain, now has restrictions around its use (European Medical Agency, 2013) following claims that aneuploidy – a rare complication affecting chromosomes in the body – is linked with the drug.

Previous systematic reviews (van Tulder et al., 1997, 2003) of muscle relaxants showed a significant effect of tizanidine, cyclobenzaprine, dantrolene, carisoprodol, baclofen and orphenadrine compared with placebo; however, not all of these trials met the eligibility criteria for inclusion in the present review. A number of studies on cyclobenzaprine and tizanidine for instance, reported pain relief (Bianchi, 1978; Nibbelink et al., 1978; Baratta, 1982; Baptista et al., 1988; Corts Giner, 1989) and whilst these have shown statistically significant benefit compared with placebo, this may not necessarily translate to clinically important effects. In the present review, the pooled estimates from the three trials which evaluated tizanidine were not clinically significant. Additionally, given the abuse potential and sedative effects of some muscle relaxant drugs, such as carisoprodol (van Tulder et al., 2003), care must be taken in providing recommendations for use based on statistical significance. Importantly, this review shows there are insufficient outcomes data beyond the short term for any muscle relaxant drug to support the long term, unmonitored use of these medicines.

There was no eligible RCT evidence supporting the efficacy of benzodiazepines in people with LBP yet...
paradoxically, diazepam – a benzodiazepine with sedative properties (Chouinard, 2004) – is ranked among the most commonly prescribed medications for back pain in Australia and the United States (National Health and Medical Research Council, 2004; Australian Institute of Health and Welfare (AIHW), 2009).

Future research should focus on evaluating the efficacy and safety of muscle relaxant drugs in combination with physical activity and other non-pharmacological measures such as heat wrap therapy, to see whether there could be synergistic effects on pain and disability outcomes.

5. Conclusion

Muscle relaxant drugs do not provide clinically significant pain relief in the short term for people with acute LBP. There was a paucity of evidence around the use of benzodiazepines for LBP and effects of the three classes of medicines on disability. The present evidence does not support the recommendation for prolonged use of any of these drugs in the management of people with LBP.

Author contributions

CAS: Literature search, figures and tables, study design, data collection, data analysis, data interpretation, writing. AJM and CGM: Study design, data collection and analysis, data interpretation and writing. KAW: Data interpretation and writing.

References


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Supporting Information

Additional Supporting Information may be found online in the supporting information tab for this article:

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| Table S2. | Pedro ratings for eligible trials. |
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| Table S4. | Drop-out rates for muscle relaxant trials. |
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