Serious adverse events following lumbar spine mobilization or manipulation and potential associated factors: a systematic review protocol

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ABSTRACT

Objectives: The objectives of this review are to describe the serious adverse events reported in the literature following lumbopelvic mobilization and manipulation, and identify patient, provider and/or treatment factors that may be associated with serious adverse events after these interventions.

Introduction: Spinal mobilization and manipulation are types of conservative care commonly used to treat people with low back pain and other musculoskeletal conditions of the lumbar spine and pelvis. Although most adverse events following these interventions are benign and transient, serious adverse events have been reported mostly following spinal manipulative therapy. Given the significant impact serious adverse events can have on patients’ lives, identifying factors that may be associated with serious adverse events following spinal mobilization and manipulation of the low back and pelvis would allow for a more specific pre-treatment screening, potentially reducing the occurrence of serious adverse events following these popular interventions and contributing to a safer treatment delivery.

Inclusion criteria: This review will consider interventional and observational studies that report serious adverse events following lumbopelvic spinal mobilization or manipulation experienced by people of any age. Examples of serious adverse events include disc herniation, cauda equina syndrome, and vertebral fracture.

Methods: MEDLINE, Embase, CINAHL, Pubmed, The Cochrane Database of Systematic Reviews/Central Register of Controlled Trials, and Index to Chiropractic Literature (ICL) databases will be searched as well as OpenGrey and ProQuest. Two independent reviewers will screen titles and abstracts of identified references as well as the full-text of identified studies, and extract data following a standardized data extraction form. Data will be summarized, categorized, and a comprehensive narrative summary will be presented.

Systematic review registration number: PROSPERO (CRD42019122339)

Keywords adverse event; lumbar spine; pelvis spinal mobilization; spinal manipulation

Spinal mobilization and manipulation are commonly used by chiropractors, physiotherapists, osteopaths, and other health professions to treat people with low back pain and other musculoskeletal conditions of the lumbar spine and pelvis.\(^1\) While spinal mobilization consists of the application of a cyclic low-velocity force, spinal manipulation consists of the application of a high-velocity, low-amplitude force to the spine.\(^2\) Recent clinical practice guidelines for low back pain management include spinal manipulation as one of the recommended interventions.\(^3\) With increasing evidence supporting spinal mobilization and manipulation to reduce pain and improve function in patients with low back pain,\(^4\) the use of these interventions has also increased.\(^5\)

Patient safety continues to be a leading global health care challenge.\(^6\) A report by the Institute of Medicine has emphasised the importance of creating a constructive patient safety environment in order to develop strategies to reduce preventable adverse events.\(^7\) Given the increased use of spinal mobilization and manipulation, it is fundamental to understand the potential risks of this treatment. While previous studies have reported adverse events following spinal mobilization and manipulation of the lumbar spine, the majority are benign and transient (lasting up to 24 hours), such as increased pain and stiffness.\(^8\) Serious adverse events, such as cauda equina syndrome, vertebral fracture, and epidural hematoma are rare; however, these events have been reported, mainly following spinal manipulation.\(^9\) In 2015, a previous systematic review described the serious adverse events reported following spinal manipulative therapy of the low back region.\(^10\) It found that from a total of 77 serious adverse event cases reported after spinal manipulative therapy of the low back region, 29 cases presented signs and symptoms consistent with cauda equina syndrome and 23 cases consistent with lumbar disk herniation. Fracture (seven cases), hematoma or hemorrhagic cyst (six cases) and other adverse events (such as neurologic or vascular compromise, soft tissue trauma, muscle abscess formation, disrupted fracture healing, and esophageal rupture; 12 cases) were also reported. Despite the valuable information provided by the previous systematic review, it focused on spinal manipulative therapy and did not include spinal mobilization, which is a manual therapy modality that is also often used to treat low back pain. Given that the terms manipulation and mobilization are frequently used interchangeably in practice, but are distinct terms in research, clinically valuable information could have been missed.\(^11\) Additionally, although patient and treatment characteristics were tabulated when available, the authors called for better reporting related to patient presentation prior to spinal manipulation as there was not enough information to identify potential factors that might contribute to making one more at risk of experiencing a serious adverse event following spinal manipulation.

Establishing causal relationships between spinal mobilization and manipulation and serious adverse events is challenging due to methodological limitations of published studies in this area.\(^12\) However, the significant impact serious adverse events can have on patients’ lives highlights the importance of identifying potentially associated factors as well as developing prevention and mitigation strategies.\(^13\) Although randomized controlled trials are the preferred design for assessing therapeutic effectiveness, the rare occurrence of serious adverse events endorse observational clinical studies to provide important insights related to their potential associated factors, providing a starting point for future studies to further investigate their causal relationship and risk factors.\(^14\) Serious adverse events such as cauda equina syndrome and vertebral fracture are debilitating and negatively affect patients’ quality of life. While establishing causation and risk factors may not be possible at this time, identifying factors that may be associated with serious adverse events following spinal mobilization and manipulation of the lumbar spine and pelvis has the potential to improve our current knowledge related to the safety of these interventions and better inform clinical decision-making, promoting a safer treatment delivery and increased quality of care. Therefore, the aims of this study are to: 1) update the previous systematic review on the serious adverse events reported in the literature following lumbopelvic mobilization and manipulation; and 2) identify patient, provider, and/or treatment factors that may be associated with serious adverse events after these interventions.

**Review questions**

i. What are the reported serious adverse events following lumbopelvic spinal mobilization or manipulation?
ii. Are there any patient, provider, and/or treatment factors that may be associated with serious adverse events after lumbopelvic spinal mobilization or manipulation?

**Inclusion criteria**

**Participants**

This review will consider studies that include patients of any sex and age who sought conservative care for any musculoskeletal condition (back pain, lower extremity pain, etc).

**Exposure**

This review will consider studies that report the application of lumbopelvic mobilization or manipulation. Specifically, spinal mobilization will be defined as a manual therapy technique comprising a continuum of skilled passive movements that are applied at varying speeds and amplitudes to joints, muscles, or nerves. Spinal manipulation will be defined as a passive, high velocity, low amplitude thrust applied to a joint complex within its anatomical limit (the range of motion of the joint complex in which active and passive motion occurs and not beyond the joint’s anatomic limit). Studies including lumbopelvic mobilization or manipulation under anesthesia will be excluded as this review will focus on the treatments provided by primary care providers using conservative interventions, such as physiotherapists, chiropractors, and osteopaths.

**Outcomes**

This review will consider studies that report and describe serious adverse events after the intervention of interest (ie, lumbopelvic manipulation or mobilization). Serious adverse events will be defined as “any unfavorable sign, symptom, or disease temporally associated with the treatment, whether or not caused by the treatment that results in death or is life-threatening or results in inpatient hospitalization or prolongation of existing hospitalization for more than 24 hours with a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions.”

**Types of Studies**

This review will consider all primary study designs, including case reports, experimental, and observational studies. While case reports and observational studies will be considered due to their ability to report more detailed information of rare serious adverse events, experimental studies will be considered as they represent a higher level of evidence. Review articles (narrative, critical, systematic, scoping reviews, etc) will be excluded, although their reference lists will be searched to identify primary studies.

**Methods**

This study will follow the JBI methodology for systematic reviews for association (etiology and risk). The review will be reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. This protocol is registered in PROSPERO (CRD42019122339).

**Search Strategy**

The search strategy will aim to identify relevant published studies. This review will proceed with a three-stage search strategy: An initial search of PubMed will be conducted, followed by an analysis of the text words contained in the titles and abstracts, and of the index terms used to describe these articles. Based on the initial search, the search strategy will be developed including all identified keywords and index terms and will be peer-reviewed by other librarians from the same institution using the Peer Review of Electronic Search Strategies (PRESS) checklist. A second search using the developed search strategy will then be undertaken across all relevant databases. Third, the reference list of relevant reports and articles will be searched for additional studies. Studies published since database inception until present in English, Portuguese, Dutch or German will be considered for inclusion in this review.

**Information sources**

The following databases will be searched from their inception until present for potentially eligible studies: MEDLINE (Ovid), PubMed, Embase (Ovid), CINAHL (EBSCO), The Cochrane Database of Systematic Reviews/Central Register of Controlled Trials (Wiley), and Index to Chiropractic Literature (ICL). Gray literature will be search on OpenGrey and theses and dissertations on ProQuest Dissertations and Theses. An initial draft search strategy for PubMed
is included in Appendix I. This search strategy will be further refined and customized for each database.

**Study Selection**

Following the search, all identified citations will be imported into a bibliographic software or citation management system and duplicates removed. Citations will then be imported into Rayyan QCRI (Qatar Computing Research Institute [Data Analytics], Doha, Qatar) for screening. Titles and abstracts will be screened by two independent review authors for assessment against the inclusion criteria for the review. Studies that meet the inclusion criteria will be retrieved in full. Two independent review authors will then assess the full text of selected studies against the inclusion criteria. Full text studies that do not meet the inclusion criteria will be excluded and the reasons for exclusion provided in the systematic review. At each stage of the study selection process, any discrepancies between the review authors will be reconciled through discussion. If a consensus cannot be reached, a third review author will be consulted. Results of the search will be reported in the final report and presented in a PRISMA flow diagram.

**Assessment of methodological quality**

Selected studies will be critically appraised by two independent review authors at the study level for methodological quality using the appropriate standardized critical appraisal instruments from JBI for each study design. Any disagreements between the review authors will be resolved through discussion, or in consultation with a third review author. The results of critical appraisal will be reported in narrative form and in a table. All studies will undergo data extraction and synthesis and studies will not be excluded based on methodological quality. The results of the critical appraisal will be reported, utilized to discuss the results of the synthesis, and be considered when determining conclusions.

**Data extraction**

Two review authors will independently extract data from included articles in the review following a standardized data extraction form that was developed based on JBI SUMARI. The provisional data extraction form is detailed in Appendix II. The data extracted will include specific details about the interventions, populations, study methods, and outcomes of significance to the review question and specific objectives (ie, serious adverse events following lumbopelvic mobilization or manipulation). Any disagreements between the reviewers will be resolved through discussion or with a third reviewer. Authors of included studies will be contacted for clarification or missing data.

**Data Synthesis**

Data from observational (case series, case reports, etc) and experimental (randomized controlled trials, etc) will be synthesized separately. Quantitative data will be pooled in statistical meta-analysis using Review Manager (RevMan) Version 5.3.5 (Copenhagen: The Nordic Cochrane Centre, Cochrane), if possible. Effect sizes will be expressed as either odds ratios (for categorical data) and weighted or standardized mean differences (for continuous data) and their 95% confidence intervals will be calculated for analysis. Heterogeneity will be assessed statistically using the standard $\chi^2$ and $I^2$ tests. Subgroup analyses will be explored where there is sufficient data for investigation. Subgrouping will include, but not be limited to, the following: intervention (lumbopelvic manipulation or mobilization, and specific technique), type of serious adverse event, and patient characteristics (eg, age and sex). Sensitivity analysis will be conducted to test the impact of studies with poorer methodological quality. Where statistical pooling is not possible, the findings will be presented and described in narrative form, including tables, figures, and qualitative synthesis to aid in data presentation where appropriate.

**Assessing certainty in the findings**

The Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach for grading the certainty of evidence will be followed and a Summary of Findings will be created using GRADEpro GDT software (McMaster University, ON, Canada). The Summary of Findings will present the following information where appropriate: absolute risks for the interventions, estimates of relative risk, and a ranking of the quality of the evidence based on the risk of bias, directness, heterogeneity, precision, and risk of publication bias of the review results. The outcomes reported in the Summary of Findings will include the intervention (spinal mobilization or manipulation) and type of serious adverse events.
Acknowledgements

Mr. Kent Murnaghan for his assistance with the search strategy described in this protocol.

References

22. Cagnie B, Vinck E, Beernaert A, Cambier D. How common are side effects of spinal manipulation and can these side effects be predicted? Man Ther 2004;9(3):151–6.
Appendix I: Search strategy

Initial draft search strategy for PubMed

Date searched: August 15, 2020

<table>
<thead>
<tr>
<th>Search</th>
<th>Results retrieved</th>
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<td>10,364</td>
</tr>
<tr>
<td>2. Search terms related to serious adverse events:</td>
<td>5,093,165</td>
</tr>
<tr>
<td>3. 1 AND 2</td>
<td>2202</td>
</tr>
<tr>
<td>4. 1 AND 2 NOT:</td>
<td>2158</td>
</tr>
<tr>
<td>(“addresses”[Publication Type] OR “biography”[Publication Type] OR “directory”[Publication Type] OR “festschrift”[Publication Type] OR “interview”[Publication Type] OR “lectures”[Publication Type] OR “legal cases”[Publication Type] OR “legislation”[Publication Type] OR “news”[Publication Type] OR “patient education handout”[Publication Type] OR “popular works”[Publication Type] OR “congresses”[Publication Type] OR “consensus development conference”[Publication Type] OR “consensus development conference, nih”[Publication Type]) NOT (animals[mh] NOT humans[mh])</td>
<td></td>
</tr>
</tbody>
</table>
Appendix II: Data extraction form

Study details
Author
Year of publication
Country of publication
Journal

Study method/characteristics
Study design
Setting

Participant characteristics (eg, age, sex, height, weight, BMI, condition)
Patient presentation (presenting symptom, complaint)

Patient potential associated factors (comorbidities, concurrent treatments [eg, medications, natural health products], number of spinal manipulative therapy previously received, history of other AEs related or not to spinal manipulative therapies)

Spinal mobilization or manipulation provided (quantity, technique, specific spinal level, etc.)
Provider (profession, years of practice/experience, other qualifications)

Results
Reported serious adverse event
Profession who reported the serious adverse event
Timing from spinal mobilization or manipulation to serious adverse event presentation
Duration of serious adverse event
Outcome of serious adverse event (ongoing, resolved)
Was causality formally assessed?

Reviewer comments