Adverse events associated with the use of cervical spine manipulation or mobilization and patient characteristics: A systematic review

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Abstract
Cervical spinal manipulation (CSM) and cervical mobilization are frequently used in patients with neck pain and headache. Pre-manipulative cervical instability and arterial integrity tests appear to be unreliable in identifying patients at risk for adverse events. It would be valuable if patients at risk could be identified by specific characteristics during the preliminary screening.

Objective was to identify characteristics of 1) patients, 2) practitioners, 3) treatment process and 4) adverse events (AE) occurring after CSM or cervical mobilization.

A systematic search was performed in PubMed, Embase, CINAHL, Web-of-science, AMED, and ICL (Index Chiropractic Literature) up to December 2014.

Of the initial 1043 studies, 144 studies were included, containing 227 cases. 117 cases described male patients with a mean age of 45 (SD 12) and a mean age of 39 (SD 11) for females. Most patients were treated by chiropractors (66%). Manipulation was reported in 95% of the cases, and neck pain was the most frequent indication. Cervical arterial dissection (CAD) was reported in 57% (P = 0.21) of the cases and 45.8% had immediate onset symptoms. The overall distribution of gender for CAD is 55% (n = 71) for female and therefore opposite of the total AE.

Patient characteristics were described poorly. No clear patient profile, related to the risk of AE after CSM, could be extracted. However, women seem more at risk for CAD. There seems to be under-reporting of cases. Further research should focus on a more uniform and complete registration of AE using standardized terminology.

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1. Introduction
Cervical Spinal Manipulation (CSM) and cervical mobilization are frequently applied in patients with neck pain and headache (Carlesso and Rivett, 2011). CSM is defined by the International Federation of Orthopedic Manipulative Physical Therapists (IFOMPT) as: “A passive, high velocity, low amplitude thrust applied to a joint complex within its anatomical limit with the intent to restore optimal motion, function, and/or to reduce pain.” (Beeton et al., 2010) Mobilization is defined as: “Low-grade/velocity, small or large amplitude, passive movement techniques or neuromuscular techniques within the patient’s range of cervical motion and control”. (Gross et al., 2004) In literature, the terms ‘manipulation’ and ‘mobilization’ are frequently interchanged or used to describe the same technique (Mintken et al., 2008).

Both non-specific neck pain and cervicogenic headache are indications for manipulation or mobilization. Non-specific neck pain is a commonly experienced disorder with a lifetime prevalence of 70% (Haldeman et al., 2009). Every year, 30% of the general population experiences neck pain, and 14% experience ongoing complaints for more than 6 months (Vos, 2006). Cervicogenic headache is described by The International Headache Society (IHS) as to originate due to nociception in the cervical area. The incidence of cervicogenic headache is estimated to be 2.2% (Antonacci and Sjaastad, 2011).
Adverse events (AE) or side effects following CSM and mobilization have been, although rarely, described in literature since 1907 (Roberts, 1907; Cassidy et al., 2008; Carlesso et al., 2010). An AE can be defined as the sequelae following a CSM that are medium to long term in duration, with moderate to severe symptoms, and of a nature that was serious, distressing, and unacceptable to the patient and required further treatment (Carnes et al., 2010; Puenteudra and O’Grady, 2015). Until recently, AE associated with CSM have only been described in case reports, retrospective case series, surveys from neurologists, or reviews (Hurwitz et al., 1996; Di Fabio, 1999; Ernst, 2002). These reporting methods may lead to selection bias. Additionally, major AE seem to be reported more frequently than minor AE (also frequently described as: “side effects”). Side effects are defined as short term, mild in nature, non-serious, transient and reversible consequences of the treatment such as an increase in neck pain, headache, discomfort and fatigue (Ernst, 2002, 2007; Puenteudra et al., 2012).

Cervical Arterial Disorders (CAD) are described in multiple studies as major AE following CSM (Ernst, 2007; Carlesso et al., 2010). CAD can cause stroke and have a described incidence of 2.6–2.9 per 100,000 (Giroud et al., 1994; Lee et al., 2006). Mean age of patients is in the early 40’s with a small majority for males (53 vs 47%). One third of CAD appear to occur more in winters (Touzé et al., 2003; Arnold et al., 2006; Piacaroni et al., 2006). One of the identified risk factors is recent infection, and this could explain this seasonal variance (Thanvi et al., 2005). Other risk factors described are hypertension, migraine, connective tissue disorders and a recent history of cervical trauma (Debette et al., 2011).

An extra cranial dissection of the internal carotid artery is diagnosed most often, followed by the vertebral artery (Thanvi et al., 2005). Initial signs and symptoms of an internal carotid artery dissection are neck pain, headache, Horner’s syndrome followed by retinal or cerebral ischemia (Debette et al., 2011). Vertebral artery dissection frequently originates with cervical-occipital pain followed by vertigo, dysarthria, visual deficits, ataxia and diplopia. The dissimilarities in signs and symptoms of both dissections can be explained by the fact that the vertebral artery supplies the posterior part of the brain and the internal carotid artery the ventral part (Blum and Yaghi, 2015).

As part of good practice, chiropractors and manipulative therapists perform a risk-benefit analysis prior to CSM. To perform a proper risk-benefit analysis, risk factors for AE related to CSM must be assessed. In pre-treatment risk-benefit analysis, the patient’s medical history appears to be an important instrument to detect patients with a greater risk for AE (Moore et al., 2005; Rushton et al., 2014; Thomas, 2016). Especially since pre-manipulative cervical instability and pre-manipulative cervical arterial tests seem to be invalid in identifying patients with a higher risk for AE (Hutting et al., 2013a, 2013b). It has been suggested that many AE can be prevented if a more detailed anamnesis and clinical reasoning is performed (Rivett, 2004; Puenteudra et al., 2012; Thomas, 2016). Therefore, patients’ characteristics, in which risks for AE occur, could be of importance for the patient history as part of the preliminary screening (Taylor and Kerry, 2010). Previous reviews mostly had the objective to identify adverse events. Therefore, adverse events and outcome were described and marginally for patient and clinician details. To the authors’ knowledge, detailed patient and clinician characteristics have never been inventoried (Ernst, 2002, 2007; Carlesso et al., 2010).

This review will add information concerning (major) AE associated with CSM or mobilization, especially related to the type of AE, the emergent signs and symptoms, prevalence and specific patient characteristics. The objective of this review was to identify the detailed clinical characteristics of 1) patients, 2) the practitioner, 3) the treatment process and 4) the AE occurring after CSM or cervical mobilization, in order to identify patients at risk during the preliminary CSM screening.

2. Methods

A systematic literature search was performed in PubMed, Embase, CINAHL (Cumulative Index to Nursing and Allied Health), Web-of-science, AMED (Allied and Alternative Medicine Database) and ICL (Index Chiropractic Literature) up to December 2014. The concept search strategies as made by H.A. Kranenburg were reviewed and adjusted by a senior librarian. Full search strategies are provided in Appendix 2.

Keywords used in the search string were: adverse effect, adverse event, complication, Stroke, Accident, Blood Vessel, Basilar Artery, Carotid Artery, Vertebral artery, Risk Factor, Neck, Injury, Cervical, Manipulation, Chiropractic, Osteopathic, Adult, Retrospective Study, Case Report and Retrospective case survey. Additional studies were identified by hand searching in journals and reference lists and related articles (PubMed function). A grey literature search was not included.

Prior to the review process, inclusion and exclusion criteria by two of the authors were set. Only published case reports or surveys were included, when they met the following criteria: published before 2015, written in English, Dutch, German or Norwegian, describing adult patients with AE following treatment with CSM or mobilization. Articles were excluded if: (1) no AE was described; (2) described that the patient received during the same session other spinal manipulation besides CSM or mobilization, or during the same session; (3) patient characteristics were not described; (4) the article was a systematic or literature review; (5) patients were not adults; or (6) articles in any other language than English, Dutch, German or Norwegian.

Only case reports, case series or surveys were included, for in those reports the most details are described. RCT’s and reviews do not describe specific patient and clinician information (Pitrou et al., 2009; Tsang et al., 2009).

At the start, two authors (H.A. Kranenburg and M.A. Schmitt) executed the whole assessment process together on three articles. This was in order to minimize differences in interpretation. The summary of the review process is described in- and exclusion criteria. After this training session, the same two authors ran through the review process independently, and discussed the results of each step in consensus meetings, prior to the next step. In the first step, all titles in the primary search were screened on inclusion criteria and duplicates. During the second step of the review process, full-text articles were independently screened and analyzed on inclusion and exclusion criteria. Subsequently, authors filled in a data-extraction form. During the consensus meetings, after each step in the review process, disagreements were discussed and resolved. The summary of the review process is described in Fig. 1.

During the review process, PRISMA guidelines, an evidence-based minimum set of items for reporting in systematic reviews and meta-analyses, were followed, although methodological quality of the case reports was not appraised (Moher et al., 2015). No risk of bias criteria were available for case reports, case series or surveys. Therefore, this was not assessed.

Following general epidemiological parameters were used in the inventory: gender, age, region, treating profession of the health care professional, profession of patient, sport, level of education, level of income, leisure time, anxiety, and depression. Also, specific parameters like: indication, time to onset of symptoms, technique used, type of AE, signs/symptoms, contra indications, precautions and risk factors were noted when present or absent in a patient. Parameters, used for the data-collection were based on the IFOMPT framework. This framework is a consensus document for best practice
examination of the cervical region prior to cervical manual interventions (Rushton et al., 2014). An explicit differentiation was made between types of AE (pathologies like vascular dissection or fracture) and signs and symptoms (i.e. neck pain or dizziness) since they are two substantially different elements as one is the result of the other (Rushton et al., 2014). The Mann-Whitney test was used to analyze differences in gender of patients with Cervical Arterial Disorders (CAD).

3. Results

The result of our search is presented in Fig. 1. A total of 1043 potentially relevant studies were identified. After comparing and discussing the results, 722 studies were excluded on title or duplicates. Of the remaining 386 studies, the same protocol as in round 1 was applied and 144 studies were excluded based on abstract and duplicates. The remaining 242 potentially relevant full text studies were analyzed individually (H.A. Kranenburg and M.A. Schmitt). Results were compared and discussed until consensus. Of those 242 a total of 98 articles were excluded due to: no full text available (n = 16), no CSM or mobilization described (n = 34), review (n = 15), language (n = 14), no AE described (n = 8), no patient characteristics described (n = 5), duplicate (n = 5) and entire spine manipulated (n = 1). A total of 227 cases reported in 144 articles left, were included and analyzed. Of the included cases 66.1% were published in case reports, 28.2% in retrospective case series and 5.7% in surveys.

Only a few parameters were well described in the reported cases (Fig. 2). For the parameters Precautions, Risk factors CAD Risk factors Upper Cervical Instability (UCI) and Contraindications the mean percentage of parameters described in the IFOMPT statement was calculated. (18) Detailed synopsis per case is described in Supplemental Table I.

Of the 227 cases, 117 (51.5%) were male. The mean (SD) age of all cases was 42 (12) years. However, the majority of male patients was approximately 5 years older with a mean age of 44.74 (SD 11.91, and a total range 17–87 years), while for female patients mean age was 39.22 (SD 11.12, Range 21–73).

3.1. Type of profession providing CSM

The majority of patients with reported major AE were treated by chiropractors (65.6%), 5.3% by non-clinicians, 4.8% by osteopaths, 3.1% by physical therapists, 2.6% by other medical professions (e.g. general practitioner), 2.2% (5 cases) by self-treatment, 0.4% by manual therapists. For 15.9% of the cases the profession was not described. In Fig. 3 a cross table combining health profession and region is provided.

3.2. Type of manipulation provided

Manipulation was the most frequently reported technique (95.2%). In 62.6% of the cases, patients received a non-specified manipulation
(i.e. impulse and/or direction was not specified), 26.9% a rotation manipulation, 2.6% a traction manipulation and 3.1% another type of manipulation. In 1.7%, patients were treated with mobilizations. For 3.1% of the patients the technique was not described.

3.3. Indications for manipulation

Indications for the use of CSM were only described in 87.6% of the patient cases. Neck pain or stiffness was the most commonly reported indication for 147 of the 227 (64.8%) patients (77 males). Headache was the next frequent indication in 40 of the 227 (17.6%) patients (27 females). Interestingly, dizziness was the reported indication for CSM in 2 female patients, and 31 patients (22 males) had other indications. For the final 28 patients (10 males) there was no treatment indication reported.

3.4. Type of AE

The most commonly reported type of AE was cervical arterial dissection (CAD) (57% of the cases), and this was a combination of all reported vascular dissections. The overall distribution of gender for dissections was 55% (n = 71) for female and 45% (n = 58) for male. As shown in Fig. 4, the most frequently reported specific type of AE was the Vertebral Artery dissection. Of all vertebral artery dissections in our sample (53 cases), 65.9% were female and 30 (36.15%) were counted.

3.5. Type of signs and symptoms associated with AE

The most frequently described symptom was a disturbance of control of voluntary movements (104), followed by altered sensation (97), pain (82), paresis (71), visual disturbance (54), nausea (48), headache (47), vomiting (44), and vertigo (43). The full enumeration is shown in Fig. 5.

3.6. Onset of signs and symptoms

Immediate onset of the signs and symptoms was reported in 45.8% of the cases, and of these, 53% were male and 47% were female. The majority of symptoms had an onset within 1 week with 84.5% (83.7% Male and 87.2% Female). Overall, in 2.6% symptoms started within 1–2 weeks and in 1.8% in took more than 2 weeks. In 23 cases (10.2%) time to onset was not described.

4. Discussion

The results of this review identified some of the clinical characteristics of patients in which AE occurred after CSM or mobilization. This review showed that women seem to be more at risk for CAD however, no clear patient profile could be extracted from the reported parameters. Gender was the only characteristic reported in all cases, and age was reported in all but one of the 227 included cases. The results show that gender and age characteristics were consistent with other literature (Puentedura et al., 2012; Blum and Yaghi, 2015). Therefore, from the reported literature reviewed, one could conclude that a person (male or female almost equal) around their 40’s is most at risk (Blum and Yaghi, 2015; Kosloff et al., 2015). Other patient related details were marginally described, if stated at all, therefore, we were unable to draw any conclusions on this. This review also identified that the majority of AE patients were treated by chiropractors. Neck pain or stiffness was the primary indication,
and manipulation, rather than mobilization, was the technique most often used. The most frequently reported AE was vertebral artery dissection, and the loss of control of voluntary movements was the most often reported symptom with the majority of symptoms onset within a week after the intervention.

Despite the fact that clinical characteristics such as smoking, cervical trauma, recent infection, hypertension, migraine, low cholesterol and low body mass index are well described as possible risk factors for all AE dissections in the literature (Engelter et al., 2013; Debette, 2014), we found them scarcely described in the reported cases. It seems unlikely that the limited description of these items is due to difference in guidelines, procedures and standards, as the majority of items in those documents should be overlap and therefore, cannot be the explanation for the large absence of data. It could be that they were not described because they were not present in the patients in the published cases. Or it might be that the manipulating professionals did not see the need to report or were unaware of these items. Another explanation could be that although not specifically inventoried, both reviewers (H.A. Kranenburg and M.A. Schmitt) noted that a substantially number of publishing authors had a medical background (i.e. neurologist) and were more focused on the AE treatment strategy and recovery after hospitalization. As they have a different scope, aim and body of knowledge, they may have reasonably described other items. Similar calls to improve quality of case reports have been done in adjacent medical fields (Kaszkin-Bettag and Hildebrandt, 2012). In 2013 the CARE statement was published to guide transparency and accuracy of case reports as well as to improve the quality of case reports (Richason et al., 2009; Gagnier et al., 2014).

In the published case reports, we found most the frequently described the type of AE to be cervical arterial dissection (CAD) (57% of the cases). The overall distribution of gender for dissections have been done in adjacent medical fields (Kaszkin-Bettag and Hildebrandt, 2012). In 2013 the CARE statement was published to guide transparency and accuracy of case reports as well as to improve the quality of case reports (Richason et al., 2009; Gagnier et al., 2014).

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In the published case reports, we found most the frequently described the type of AE to be cervical arterial dissection (CAD) (57% of the cases). The overall distribution of gender for dissections was 55% (n = 71) for female and 45% (n = 58) for male. Although no statistically significant difference was found in our review, it is in contrast to other studies which were large cohort studies and included mostly ‘non-manipulative’ CAD patients. In those studies, male cases were more prevalent (Debette et al., 2009; Engelter et al., 2013). This difference seems hard to explain anatomically, and may simply be a factor of greater reporting of case studies involving male patients suffering AEs after CSM. Metso et al. described that a CAD was more common in males (57.6% vs 43.3%) (Metso et al., 2012). However, he also noted that in the CAD group, more female patients experienced clinical signs and symptoms than men after chiropractic manipulation.

In accordance with other literature including the non-manipulative population, the majority of patients in our review were slightly younger than 45 years (Kosloff et al., 2015). As in other studies, the vertebral artery dissection was the most frequently described type of AE after CSM (Ernst, 2007; Leon-Sanchez et al., 2007; Biller et al., 2014). Remarkably, in the general European population of patients with CAD, carotid dissections are more common than VAD with a ratio of 1.7 to 1 (Lee et al., 2006). A commonly described explanatory mechanism is the stretch in the vertebral artery in the manipulative position of the cervical spine. Approximately 50% of the cervical rotation occurs in the atlantoaxial joint. The other 5 most frequently described types of AE (Fig. 3) were in accordance with a comparable previous study (Puentedura et al., 2012).

Considering the fact that CAD is the most frequently occurring AE, it may be disconcerting that neck pain or stiffness was found to be the most frequent indication. This is because neck pain is also one of the main symptoms of CAD. Church et al. therefore described neck pain as the potential confounder and it is possible that patients attend for treatment with a pre-existing arterial dissection (neck pain and headache being the pre-ischaemic symptoms) and that CSM had not caused the neurovascular symptoms that would have naturally developed regardless of their intervention (Church et al., 2016). Furthermore, in the most described cases, no (suggestion for) causality was described. Although evidence is thin, no causal relationship seems to exist between CSM and CAD. (Church et al., 2016). Therefore, an inventory with indications of possible causations would be unreliable, as it would be based on assumptions by judgement, and not founded with criteria of causation. Therefore, this review does not contain any description or suggestions of causation related to the artery dissections.
Taken together, clinicians are strongly advised to incorporate vascular examination (i.e. blood pressure) in their risk assessment and vascular pathologies in their clinical reasoning process, prior to considering CSM for their patient.

Perhaps the most serious AE following CSM, and often mentioned in debates, guidelines or procedures, is death. It was described in only 11 of the 227 cases (4.8%) with major AE. As most of the AE were due to arterial dissections, these numbers are in concordance with the survival rates in other literature (Biller et al., 2014; Rushton et al., 2014). Recovery report or health status was not inventoried during this review.

Most of the included cases involved chiropractors or chiropractic manipulations (65.6%), and other authors found similar percentages as mentioned in Fig. 5 (Ernst, 2007; Puentedura et al., 2012). Explanations might be, that CSM are more frequently used by chiropractors, that there may be a greater readiness on the part of authors to publish case reports of AE involving chiropractors, more people at risk seek help from chiropractors or that they have a more hazardous way of performing their manipulations (Di Fabio, 1999).

Underreporting of AE after CSM may be the case, when comparing the reported cases to calculated incidence rates. VAD has a reported annual incidence rate of 1–1.5 per 100.000 while Internal Carotid Artery Dissection (ICAD) has a reported annual incidence rate of 2.6–3 per 100.000 (Schievink et al., 1994; Micheli et al., 2010). In 2008, Cassidy reported that 7.8% of his population had visited a chiropractor within 7 days, whereas Engelter found a 6.9% rate (Cassidy et al., 2008; Engelter et al., 2013). As of July 1st, 2014, there were approximately 318.857.056 US citizens, and using the above incidence rates, it would mean approximately 220,011 VAD patients annually with recent manipulation (U.S. Department of Commerce, 2014). Taken into account that the first case in this review was reported in 1907, the 227 included cases (worldwide) in such a long period suggests that it must be the proverbial tip of the iceberg.

This review has some limitations. Interpretation and classification of described signs and symptoms caused considerable debate between the reviewers (H.A. Kranenburg and M.A. Schmitt). Even though we used the ICF and ICD criteria, there was an overlap in definitions for pain, radiating pain, increased pain during movement and headache. The broad possibility of interpretation of definitions could be an issue in the differences in interpretation of the data, for example: Control of voluntary movements (ICF-B760). Loss of muscle strength or weakness was included is this parameter, whereas other studies did not (Puentedura et al., 2012).

Another note of caution is due here since appraising the quality of case reports is difficult, as no validated tool is available. The authors decided not to create a tool to appraise methodological quality, for instance based on the CARE statement, for case reports. A case report either contains or does not contain information, so methodological quality is less relevant.

Furthermore, in the literature manipulation terminology is known to be interchanged. Because we included both, manipulation and mobilization, this issue should not affect the initial search results of this study (Mintken et al., 2008). It could however have influenced the results of techniques used, as 62.6% of the included patients received a non-specified manipulation. Although in many of those cases, patients mentioned that there was a sudden fast impulse, followed by a crack, one could question these outcomes. However, as far as we know this is the largest cohort describing AE associated with CSM or mobilization, especially related to the sort, prevalence and patient characteristics.

5. Summary and recommendations

To gain more insight in incidence rates and patient characteristics in order to identify patients at risk, the authors recommend that manipulating professionals report their AE cases themselves. Alternatively, they should report as thoroughly as possible, all of the patient characteristics, in co-operation with the involved physician. For those future reports, we recommend incorporation of the advice of Mintken et al. complemented with Puentedura’s advice in the CARE template (Mintken et al., 2008; Gagnier et al., 2014; Puentedura and O’Grady, 2015). We also suggest the use of concrete medical terminology, preferably based on the International Classification of Diseases (ICD) or International Classification of Functioning (ICF) as published by the World Health Organization (WHO). Furthermore, we urgently appeal the professional organizations to communicate clearly to their members where and what to report and facilitate clear protocol based on the above mentioned.

Fig. 5. Signs and Symptoms – Frequency table.
Disclosures

None.

Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.mscs.2017.01.008.

References


