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Adverse events following cervical manual physical therapy techniques

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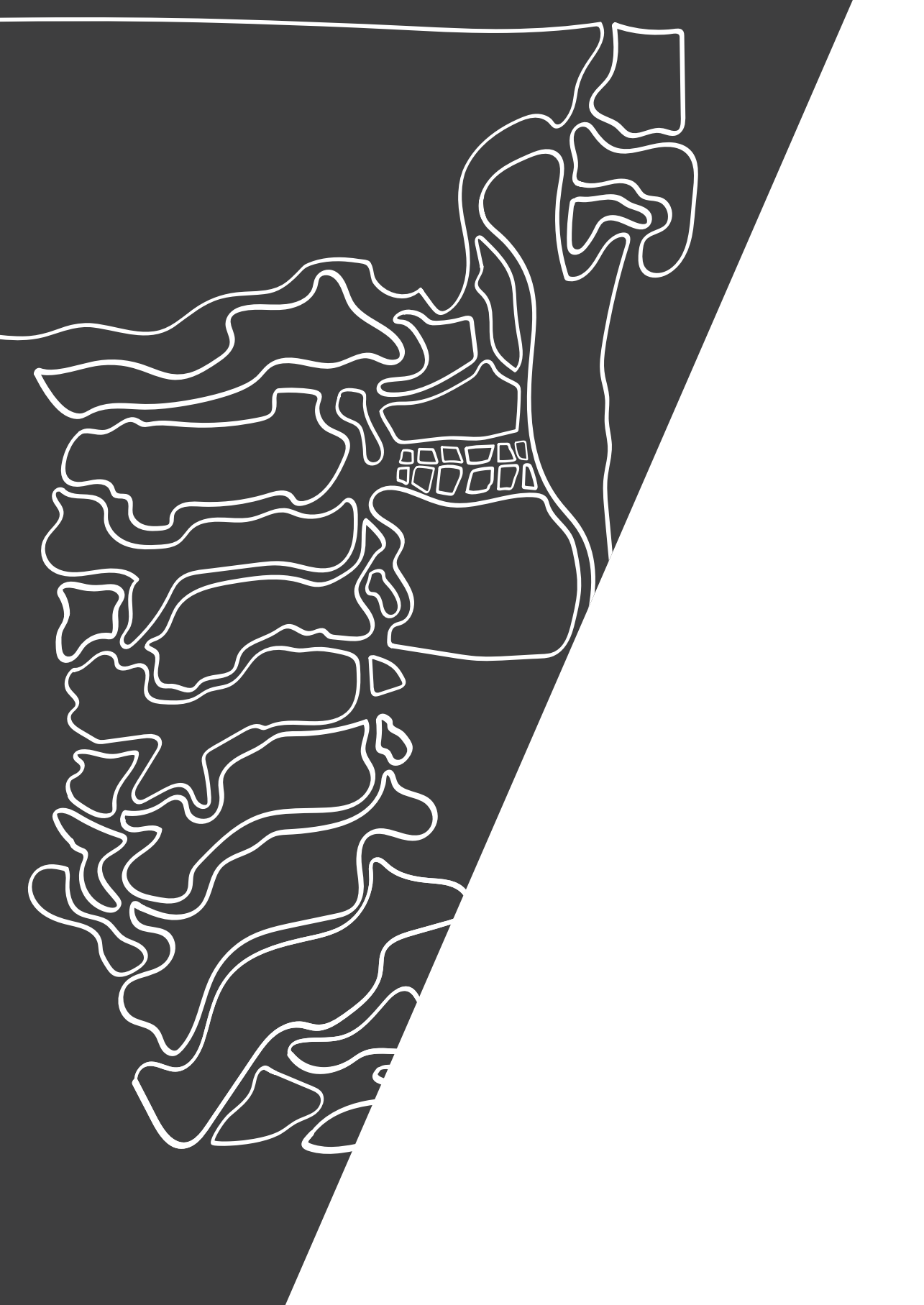
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**CAROTID AND VERTEBRAL ARTERIAL
DISSECTIONS AFTER
MANUAL PHYSICAL THERAPY:
A CASE CONTROL STUDY**

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Submitted

ABSTRACT

Introduction: Neck pain and headache are common health problems for which manual physical therapy is an effective treatment. Treatment techniques that are frequently used are mobilizations and thrust joint manipulations. In some cases, adverse events (AE) occur following these treatments. Factors influencing AE are not fully understood, but may be related to patient characteristics, clinician or the applied techniques. Thereby, incidence rates of AE have a large variation. Therefore, the objective of this study is to determine the number, type and predictors of AE following cervical treatments performed by Dutch manipulative therapists.

Method: A prospective cohort study was performed during 12 months in The Netherlands amongst clinicians using manipulative techniques. Characteristics of patients, clinicians and therapy were inventoried. Additionally, the Health and Youth Care Inspectorate (IGJ) and professional associations were asked to share reported major AE. An independent privacy monitoring board supervised the study. Descriptive techniques and robust binominal regression were applied to analyze the data.

Results: Fifty-five clinicians delivered data of 392 patients. Clinicians were averagely treating 3.5 patients per day with 0.99 manipulations, 2.86 mobilizations and 1.76 exercises during a session. No major AE were reported in our sample. Two major AE were reported at the IGJ. Minor AE were reported in 28.1% of the sessions. The indication headache and female gender of the clinician were considered significant predictors for minor AE.

Discussion: Most AE following cervical TJM are minor, the incidence for major AE is estimated at 1:2.869.020 cervical TJMs. There were no strong predictors for AE indicated.

INTRODUCTION

Neck pain is a common health problem which ranks 4th on the global burden for disability.(Hoy et al., 2014) Neck pain is considered to be a multidimensional condition that includes physical, affective, cognitive, and social aspects. A serious medical pathology is rarely the cause of neck pain (<1%).(Blanpied et al., 2017) In most cases, the pathoanatomical basis for neck pain is unclear and the pain is labeled as being nonspecific or mechanical.(de Vries et al., 2016) Clinical characteristics of neck pain can be categorized as 1] neck pain with mobility deficits; 2] neck pain with impaired movement coordination; neck pain with headache; neck pain with radiating pain; and neck pain with migraine.(Blanpied et al., 2017; Dunning et al., 2016; Gross et al., 2015) The incidence of neck pain in the general population is 16% (Kim et al., 2018) and overall prevalence is estimated around 23.1%.(Hoy et al., 2010) The latter is generally higher in woman, high income countries and rural areas.(Hoy et al., 2010) Physical manual therapy can be indicated and is an effective treatment for patients with neck pain and headache.(Coulter et al., 1996; Gross et al., 2015; Rist et al., 2019) Physical manual therapy may include mobilizations and thrust joint manipulations (TJM). The TJM is characterized by a quick thrust aiming to achieve a joint cavitation. (Beeton et al., 2010)

In some cases, mobilizations and TJM may lead to unintended Adverse Events (AE). Adverse Events following cervical mobilization or TJM, can be divided into minor or major AE.(Kranenburg et al., 2017a) Minor AE are more common following cervical physical manual therapy, and involve the onset of new symptoms or a temporary worsening of symptoms that last for 24 to 48 hours. Major AE following cervical treatments, and especially cervical TJM, have been described anecdotally, but are frequently discussed due to their serious clinical consequences such as spinal cord injury or stroke.(Hutting et al., 2018; Nielsen et al., 2017; Swait and Finch, 2017) Although TJM has been described as a risk factor for major AE, causality have not been proven. Incidence rates for major AE following TJM vary between 1 to 20.000 and 1 to 5,7 million TJM. (Assendelft et al., 1996; Haldeman et al., 2002; Nielsen et al., 2017) Minor AE are described more often and fluctuate from 23% up to 83% after a treatment session.(Chaibi et al., 2017; Rajendran et al., 2015) The large variation of incidence rates is challenging when discussing the 'risk-benefit ratio' during a shared decision making process.(Rushton et al., 2014) Moreover, the unpredictability of the risk of AE following cervical treatment, might make clinicians doubtful and unconfident when choosing techniques or performing cervical physical manual therapy. Although all Dutch Manual Physical Therapy programmes are fulfilling the International Federation of Orthopaedic Manipulative Therapists (IFOMPT)

educational standards, there are differences in educational programmes worldwide. (Thoomes-de Graaf et al., 2017) This might also contribute to the explanation of the difference in numbers of AE and might limit the generalizability of results worldwide. Factors which are influencing the occurrence of AE are not completely understood but can be divided into patients' related factors and clinicians related factors. Patient related factors are age, gender, history of smoking, and recent neck trauma. (Debette, 2014; Rushton et al., 2014; Thomas, 2016) Clinicians' related factors are work experience, level of education, educational programme, and applied treatment techniques. Knowing patients' and clinicians' characteristics and the type and frequency of treatment could be helpful in understanding risk factors for AE following cervical mobilizations and joint thrust manipulations.

The primary purpose of reporting AE is to learn from experience and monitoring progress in the prevention of errors. In the Netherlands, it is obligatory for clinicians to report all major AE to the Health and Youth Care Inspectorate and are also strongly advised report to their professional association. However, underreporting may be the case. (Kranenburg et al., 2017b; Leape, 2002) This may due to time pressure, fear of punishment, shame, fear of liability, loss of reputation and fear disapproval. (Leape, 2002; Mick et al., 2007) Thereby, if symptoms not immediately occur after treatment, clinicians could be unaware of the occurrence of AE.

Although TJM seem to be less often applied in the upper cervical spine than in the mid and lower cervical spine, the frequency of applied TJM in the Netherlands is currently unknown. Therefore, calculating the incidence of AE following cervical mobilizations and joint thrust manipulations in The Netherlands is not possible. The first step towards reduction the risk of the occurrence of AEs following CSM, is to understand its magnitude and determinants. Therefore, the objective of this study is to determine the number, type and predictors of AE following cervical treatments performed by Dutch manipulative clinicians.

METHOD

STUDY DESIGN AND SETTING

A prospective cohort study was performed in The Netherlands. Data were collected from September 2016 to September 2017. The Medical Ethical Committee of the University Medical Center Groningen, The Netherlands, deemed this study exempt and approved a waiver.

PARTICIPANTS

Potential participants were manual physical therapists, chiropractors, osteopaths and manual practitioners working in a primary care setting. Manual therapists were required to be graduated by an IFOMPT recognized university. Other professionals had to be recognized by their own national professional association. Recruitment was done using newsletters of professional associations (national and regional), alumni networks, snowballing, and by online recruiting on social networks.

To enhance compliance, the reporting system as to be used in this study, was based on the following criteria: 1] non-punitive, 2] confidential, 3] independent, 4] systems orientated, 5] simple to use, 6] voluntary and 7] has clear definitions. Additionally, related to compliance, participants could attend to a free conference before the study started. During this conference, participants received state of art information on the topic of adverse events after CSM. Also, participants received practical information and instructions about the study. The conference was recorded and published in an online environment which was only be available for participants.

CLINICIAN, PATIENT AND TREATMENT CHARACTERISTICS

Characteristics of the clinicians (profession, years of working experience and level and type of education) were registered. Every three months participants provided general clinical information and patient information during a day they chose as a representative average workday for them. The number of CSM applied on that day, the number of cervical patients treated with TJM that day, as well as demographic information of the patients who received TJM, and all minor AE were registered.

ADVERSE EVENTS

Participants were asked to define and classify adverse events according the classification by Kranenburg et. al.(Kranenburg et al., 2017a)

MAJOR ADVERSE EVENTS

When a major AE occurred, the clinician was asked to -anonymously- report the major AE and specific information regarding the patient and the treatment. Reporting could be done using a code which could trace back to the reporting profession but not to the clinician. A major AE had to be reported when it: 1] complied to the definition of a major AE and 2] the first symptoms started within four weeks after the CSM was applied. Additionally, to collect data on a national scale the Health and Youth Care Inspectorate and the professional associations were asked for major AE reports during that period.

MINOR ADVERSE EVENTS

Every three months clinicians were reporting patient and treatment information about all their cervical patients for a full working day. Clinicians could choose any day within a period of two weeks they felt was most representable for their average working day. During that registration day, all minor AE were inventoried from the last treatment and the treatment session itself.

DATA ANALYSES

Descriptive techniques were used to characterize the sampled data. Incidence was estimated by dividing the total number of new reported major AE by the total registered CSM applied. The number of AE over the total number of sessions was taken as outcome for binominal generalized linear models with the logit link using the explanatory variables for: 1] patient characteristics; 2] clinician characteristics, 3] treatment characteristics, and 4] AE characteristics. When a logistic analysis yielded influential data points according to Cook's distance or testing of studentized residuals, the analyses was replaced by robust binominal regression was applied using the statistical programming language R, version 3.5.3. (Cantoni and Ronchetti, 2001; R Core Team, 2019). Throughout the significance was set at .05.

PRIVACY MONITORING BOARD (PMB)

An independent supervisory board (PMB) was founded for this study in order to guarantee participants and patients their privacy when reporting a major AE. Also, the PMB could be contacted by participants when questions arose, and they did not wish to contact the research group. The PMB had two members which were executive board members of the two largest participating groups of clinicians (i.e. manual therapists and chiropractors) and was chaired by an independent non-clinician.

RESULTS

Of the 131 clinicians who signed up for the study, 55 clinicians (54 manual physical therapists and 1 chiropractor) delivered data of 392 patients. The remaining 76 clinicians did not send patient data, but did deliver their characteristics such as experience, age, gender and average working hours. The manual physical therapists reported data of 357 sessions. The chiropractor reported data on 35 sessions. Participating clinicians had a mean (SD) age of 38.8 (8.5) years with a mean (SD) working experience of 7.3 (6) years and 38 of them were male. On average, clinicians were seeing 3.5 patients each day during an average working week of 32.2 (SD6,9) hours. The 392 included patients had a mean (SD) age of 45.5 years (14.7) ranging

from 18-87 years; 251 were female. Most patients were treated with the indication neck pain (78.6%), restricted range of motion (42.6%), headache (34.9%), dizziness (6.6%) and 28.6% had another not further specified indication. Exercise was the most applied intervention (n=298), followed by mobilizations (n=249), and TJM (n=207) during all sessions. This resulted in an average of 0.99 TJM, 2.86 mobilizations and 1.76 exercises during one session.

ADVERSE EVENTS

Major AE were not reported by the participating clinicians in this study. Two cases of major AE were reported at The Health and Youth Care Inspectorate during that same period. One case of Major AE occurred during the treatment of a manual physical therapist and one case after a treatment by a chiropractor. Both cases were also reported to their own professional associations and were not included in our results.

Minor adverse events were reported in 28.1% of the treatment sessions. Minor AE that occurred were pain, muscle tenderness, aggravated headache, stiffness, fatigue, dizziness, radiation, radiation into the arm, a heavy arm, nausea, new headache, a thick throat, an uncomfortable feeling and puking. In sessions where only one intervention was applied TJM recorded the least minor AE with 6.1%, mobilizations scored 23.5% and exercises scored 44.3%. Sessions in which a TJM was applied, without additional mobilization, scored less minor AE (8.3%) than sessions in which a mobilization without additional manipulation was applied (29.4%). When analyzed per indication, the most minor AE were recorded for headache (40.1%), followed by a non-specified indication (28.8%), neck pain (27.9%), restricted cervical range of motion (25.1%) and dizziness (23.1%). Details for minor AE can be found in table 1.

Table 1. Indications, interventions and adverse events

Indication	Patients (n)	Ae (%)	Ae (n)	Ae (%)	Pain (n)	Muscle tenderness (n)	Headache (n)	Stiffness (n)	Fatigue (n)	Dizziness (n)	Radiation (n)	Radiation (n)arm	Heavy arm (n) (n)	Nausea (n)	Headche other (n)	Thick throat (n)	Unfomfortable feeling (n)	Puking (n)
Neck pain	308	78,6	86	27,9	24	19	13	7	8	5	3	2	1	0	1	1	1	1
Rom	167	42,6	42	25,1	11	11	6	5	1	3	2	1	1	0	0	1	0	0
Headache	137	34,9	55	40,1	15	11	13	2	6	2	1	1	1	1	1	0	1	0
Dizziness	26	6,6	6	23,1	2	0	3	0	0	1	0	0	0	0	0	0	0	0
Other	111	28,3	32	28,8	9	8	1	5	4	0	2	2	1	0	0	0	0	0
All	392	100,0	110	28,1	31	24	15	10	10	6	4	3	2	1	1	1	1	1
Intervention																		
Only manipulation	33	8,4	2	6,1	1	1	0	0	0	0	0	0	0	0	0	0	0	0
Only mobilization	17	4,3	4	23,5	1	1	1	0	0	1	0	0	0	0	0	0	0	0
Only exercises	61	15,6	27	44,3	11	4	4	1	1	1	2	1	0	1	0	0	1	0

Table 1. Continued

<i>Indication</i>	<i>Patients (n)</i>	<i>Ae (%)</i>	<i>Ae (n)</i>	<i>Ae (%)</i>
<i>Pain (n)</i>	60	15,3	5	8,3
<i>Muscle tenderness (n)</i>				
<i>Headache (n)</i>			0	0
<i>Stiffness (n)</i>			1	1
<i>Fatigue (n)</i>			0	0
<i>Dizziness (n)</i>			0	0
<i>Radiation (n)</i>			0	0
<i>Radiation (n)arm</i>			0	0
<i>Heavy arm (n) (n)</i>			0	0
<i>Nausea (n)</i>			0	0
<i>Headche other (n)</i>			0	0
<i>Thick throat (n)</i>			0	0
<i>Unfomfortable feeling (n)</i>			0	0
<i>Puking (n)</i>			0	0
Man = y & mob = n	60	15,3	5	8,3
Man = n & mob = y	102	26,0	30	29,4
Man = y & mob = y	147	37,5	44	29,9

Abbreviations: Man = manipulation, mob = mobilization, exerc = exercises, y= yes, n = no

PREDICTORS

The indication headache ($P = .0092$) and gender of clinician ($P = .0007$) were considered a significant predictor for minor AE after a robust analysis. Other significant results from the classical univariate and multivariate logistic analysis were not confirmed by a robust analysis, not sensible to influential outlying cases in the data. Furthermore, all patient characteristic other than the indication headache (e.g. gender, age), all clinician characteristic (age, work experience and working hours per week) except for gender, or all different treatment techniques, resulted tested not significant by robust analyzes. Due to the relatively limited number of events, predictors could only be simultaneously analyzed by (robust) logistic regression aggregating over all AE's in the sense of taking a "yes" if any of the AE occurred.

Table 2a. Predictors for AE following manual therapy. Model 1: patient characteristics

	<i>Estimate</i>	<i>Std. Error</i>	<i>Z value</i>	<i>P value</i>	
Age	-0.0078	0.0090	-0.8688	0.3849	
Gender	-0.0185	0.2741	-0.0673	0.9463	
Indcation_Neck_Pain	-0.0014	0.3263	-0.0044	0.9965	
Indication_Headache	0.7310	0.2779	2.6303	0.0085	**
Indication_Dizziness	0.0459	0.5103	0.0900	0.9283	
Indication_ROM	0.0132	0.2634	0.0501	0.9600	
Indication_Other	0.1674	0.3246	0.5158	0.6060	

* = $P \leq 0.05$; ** = $P \leq 0.01$; *** = $P \leq 0.001$

Table 2b. Predictors for AE following manual therapy. Model 2: patient and clinician characteristics

	<i>Estimate</i>	<i>Std. Error</i>	<i>Z value</i>	<i>P value</i>	
Age	-0.0089	0.0091	-0.9772	0.3285	
Gender	-0.0999	0.2840	-0.3519	0.7249	
Indcation_Neck_Pain	0.1559	0.3389	0.4599	0.6456	
Indication_Headache	0.7478	0.2887	2.5905	0.0096	*
Indication_Dizziness	-0.0125	0.5228	-0.0240	0.9809	
Indication_ROM	0.1200	0.2744	0.4375	0.6617	
Indication_Other	0.2529	0.3342	0.7984	0.4246	
Gender_clinician (female = 1)	0.2669	0.2679	3.4263	0.0006	**
Working_experience_clinician	-0.0226	0.0240	-0.9399	0.3473	

* = $P \leq 0.05$; ** = $P \leq 0.01$; *** = $P \leq 0.001$

Table 2c. Predictors for AE following manual therapy. Model 3: patient, clinician and treatment characteristics

	<i>Estimate</i>	<i>Std. Error</i>	<i>Z value</i>	<i>P value</i>	
Age	-0.0089	0.0096	-0.9270	0.3539	
Gender	-0.0917	0.2883	-0.3182	0.7503	
Indcation_Neck_Pain	0.1479	0.3419	0.4325	0.6654	
Indication_Headache	0.7780	0.2987	2.6041	0.0092	**
Indication_Dizziness	0.0870	0.5340	0.1629	0.8706	
Indication_ROM	0.0747	0.2783	0.2684	0.7884	
Indication_Other	0.2529	0.3401	0.7436	0.4571	
Gender_clinician (female = 1)	0.9153	0.2706	3.3829	0.0007	***
Working_experience_clinician	-0.0228	0.0244	-0.9323	0.3512	
Intervention_Manipulations_session	0.0812	0.1066	0.7621	0.4460	
Intervention_Mobizations_session	0.0194	0.0261	0.7415	0.4584	
Intervention_Exercises	0.0133	0.0780	-0.1703	0.8648	

* = $P \leq 0.05$; ** = $P \leq 0.01$; *** = $P \leq 0.001$

DISCUSSION

The aim of this study was to determine the number, type and predictors of AE following cervical treatments performed by Dutch manipulative clinicians. There were no major AE in our sample. Due to the low incidence, our study group was too small to reliably determine the incidence of major AE. The incidence of minor AE following a treatment session was 28%. Minor AE that occurred were pain, muscle tenderness, aggravated headache, stiffness, fatigue, dizziness, radiation, radiation into the arm, a heavy arm, nausea, new headache, a thick throat, an uncomfortable feeling and puking. Only the indication headache and the gender of the clinician appeared significant predictors for a minor AE. Other indications, work experience of the clinician or interventions gave no significant predictors for minor AE.

Since no major AE was reported, incidence of major AE could not be calculated based on our sample. Furthermore, the number of cervical TJMs per session in our study seemed a little higher (0.99 vs 0.77) when compared to the study of Cagnie e.a. (Cagnie et al., 2004) This number is an essential part of the formula to calculate the incidence estimations. Furthermore, the average manual physical therapist in our study was seeing 3.5 cervical patients per working day, performed 0.99 manipulations per patient session, worked 4 days a week, and works 46

weeks per year. Also, in October 2018 approximately 4500 manual physical therapists were registered in The Netherlands. (Koninklijk Nederlands Genootschap voor Fysiotherapie (KNGF), 2018) Therefore, the estimated number of cervical manipulations per year in The Netherlands is: 3.5 sessions * 0.99 manipulations * 4 days * 46 weeks * 4500 therapists = 2.869.020 manipulations. However, one case was registered by the Health and Youth Care Inspectorate by manual physical therapist that year. Therefore, the incidence for major AE following TJM in The Netherlands is estimated at 1 per 2.869.020 cervical TJMs. Although the causality of major AE following cervical TJM is still debatable, an association has been described. (Church et al., 2016; Hutting et al., 2018; Nielsen et al., 2017) However, the heterogeneity of terminology in literature, the lack of an uniform reporting system and possible underreporting, makes the accuracy of these estimates debatable. (Gorrell et al., 2016; Kranenburg et al., 2017a) Moreover, these estimates should be seen together with the natural estimate to develop a dissection. (Hutting et al., 2018) Spontaneous dissections are estimated to have an annual incidence of 1.0-1.5 per 100.000 people for the vertebral artery and 2.3-3.0 per 100.000 people for the carotid artery. (Debette et al., 2009; Dziewas et al., 2003; Schievink et al., 1994)

Our finding that most AE following TJM are minor, and among these the most frequent reported are increased pain, tenderness, stiffness and headache, fatigue and dizziness and radiation, which is consistent with the literature. (Cagnie et al., 2004; Swait and Finch, 2017) The percentage of reported minor AE (28.1%) falls in the lower quartile when compared with other studies where occurrence percentages of 23-83% have been reported. (Chaibi et al., 2017; Rajendran et al., 2015) Senstad et al. suggested that during the first session more minor AE are reported. (Senstad et al., 1996) The cases in our sample were cervical patients on a random chosen workday. Therefore, it seems unlikely that most patients were included during their first session and might contribute to the lower percentage.

Headache seemed a predictor for minor AE, as seen in other studies. Specific therapeutic interventions such as TJMs were not or working experience. Contrary what one might expect was our finding that female clinicians seemed to be a predictor for minor AE as well. Our results therefore strengthen the impression that predictive factors for AE currently appear poorly understood due to inconsistent findings reported in the literature. (Swait and Finch, 2017) However, the comparisons of predictors should be interpreted with some caution since some studies surveyed the interventions to the whole spinal region instead of only the cervical region and

the possible influence of outlying observations is not explicitly ruled out.(Cagnie et al., 2004; Rajendran et al., 2015; Swait and Finch, 2017).

LIMITATIONS

Notation and interpretation of AE was done by the reporting therapists. Therefore, is it not possible to check whether the reporting clinician correctly interpreted and reported all AE's. To enhance clinician interpreting and uniformity of reporting and to increase compliance, a symposium was organized at the start of the study and making it online available participants afterwards. Also, major AE could be reported anonymously. However, major AE could only be reported for their own profession. Unfortunately, not all manipulating professions were represented well in this study. Before the start of the study, all professional associations were contacted to inform them and to stimulate the participation of their members. Two professional associations were not interested in distributing information about this study and one professional association advised their members not to participate. The manual physical therapists appeared to be most dominant among 55 participants in total. Furthermore, the interventions during the treatment sessions were reported sufficiently explicit. However, elements outside the session (e.g. neck trauma, sports injuries or changes in work setting) which could have influenced the AE, were not reported. All results should therefore be interpreted with caution, within the perspective of this sample and might not be representable for other clinicians or settings.

STRENGTHS

The transparency and openness of the study was a major strength of this study. The independent privacy monitoring board with a delegation of different professional associations and an independent chair was valuable in gaining trust of the participants. Also, the web-based reporting system was user friendly and compatible for mobile devices as well. It fulfilled all our 7 predefined criteria, and therewith treatments could be reported accurate and fast. Furthermore, using advanced robust statistical methods results were corrected for outliers and repetitive testing. The self-selection of a representable workday every quarter for a therapist, should minimize selection bias and give a good insight in the treatment of a cervical patient. Therefore, it gives a better representation of an 'average' treatment session instead of the first session.

FUTURE RESEARCH

It is advisable to repeat these measurements about treatments for a longer period, on a regularly base and interdisciplinary supported by their professional associations. A larger sample measured over a longer period would give better insights and might familiarize clinicians with reporting systems. However, a reporting system should primarily have the purpose to gain insight, and therewith enhance prevention, and be based on a non-punitive character. Measuring should be performed uniformly, and worldwide so cultural and professional differences can be compared as well.

CONCLUSION

The incidence of major AE seems low. Based on the frequency of applied manipulations per session and the case reported at the Health and youth care inspectorate, major AE incidence following CSM is estimated at 1 per 2.869.020 cervical manipulations in The Netherlands. The incidence of minor AE is considerable with 28% and is more frequent in case of headache indication and female clinicians. However, there were no strong predictors indicated for minor AE.

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