

Summary

Chronic tension-type headache and manual therapy

Chronic tension-type headache (CTTH) is a complaint with a prevalence of 2-5% that can lead to psychosocial problems, absenteeism and excess use of pain medication. The social and economical impact of CTTH on individuals and society necessitates an effective treatment of this form of headache. Two previously published randomised studies of manual therapy (MT) for CTTH provide insufficient evidence to make at a scientifically sound judgment regarding the effectiveness of MT. Because of the insufficient effectiveness of physiotherapy, the guideline for headache for general practitioners in the Netherlands advises caution regarding referrals to physiotherapy. However, patients with headache are frequently treated by manual therapists.

Research has demonstrated a relationship between functional disorders of the cervical spine and CTTH. This has led to the development of a multimodal manual therapeutic treatment of CTTH, and the design of a pragmatic randomised controlled trial to investigate the effectiveness of this MT intervention for CTTH. This thesis reports the design and results of research into the effectiveness, working mechanisms and predictors of outcome of MT in the treatment of CTTH.

Chapter 1 gives a description of CTTH and provides an overview of the literature and background of the research into the effectiveness of manual therapy in CTTH. The aims and objectives of the research are presented along with an outline of the thesis.

Chapter 2 focuses on the design of the pragmatic randomised controlled trial (RCT) to compare the effectiveness of MT with the usual care provided by general practitioner (GP) to patients with CTTH. Furthermore, this chapter explores the feasibility of the trial and treatment protocols for the research assistant, manual therapist and the GP.

The trial was designed as a pragmatic RCT with two intervention groups. A pilot study with 20 patients was conducted before the start of the full trial to ensure feasibility of trial procedures. The patients were selected in 8 general practises and fulfilled the diagnostic criteria of CTTH according to the International Headache Society. The baseline assessment was carried out by a research assistant who was blinded for the allocation of treatment. Participants with a

strong preference for manual therapy were invited to participate in a parallel cohort study. Following the baseline measurement, another independent research assistant offered each participant a closed envelope with a computer-generated allocation to one of the interventions.

MT was performed by 4 experienced manual therapists in 3 different treatment centers over a period of 8 weeks. The treatment protocol was taught in two sessions and included: mobilisation of the cervical and thoracic spine, muscle strengthening exercises of the neck flexors and giving advice on posture.

The control group received usual care by a GP, according to the national guideline for headache.

The follow-up measurements, consisting of questionnaires and physical examinations, were carried out by a research assistant who was blinded to treatment allocation. Data entry and data processing were carried out by an independent administrator.

The primary outcome measures consisted of the frequency of headache days per 2 weeks (assessed using a headache diary) and the use of pain medication. The secondary outcome measures included mobility of the cervical spine, isometric muscle strength of the neck flexors and local pressure pain of the muscles. Additional secondary outcome measurements included questionnaires completed by participants to assess global perceived recovery, restrictions in activities, and psychosocial wellbeing.

Chapter 3 describes the methods and results of the RCT of MT in patients with CTTH. The research involved 82 patients who were randomly allocated to the two intervention groups (MT and usual care provided by the GP). The mean age of the population was 40 years; mean number of years with headache was 12 years; the mean frequency of headache days was 12 days/per 2 weeks. The two groups showed good baseline similarity in terms of baseline values of outcome measures and prognostic characteristics.

The primary outcome measures showed a statistically significant difference in the reduction of headache days in the MT group. The results after 8 weeks of treatment demonstrated a difference of -6.4 days [95CI%: -8.3 to -4.5]; effect size 1.6. The assessment at 26 weeks showed a difference in the reduction of headache days of -4.9 [95CI%:-6.95 to -2.98] with an effect size of

1.2. The reduction in the use of pain medication was not significantly different between both groups.

Two secondary outcome measurements aimed at indicating psychosocial wellbeing (Headache Impact Test-6, Headache Disability Index) showed a significant difference in favour of the MT group when measured at 8 and 26 weeks. The changes in other secondary outcome measures (cervical range of motion, neck flexor endurance and algometry) showed a significant difference in favour of the MT group at 8 weeks, but at 26 weeks this difference was not significant.

The study concludes that MT offers an effective treatment for patients seen in primary care with CTTH compared to usual care provided by the GP.

Chapter 4 describes an investigation into the working mechanism of MT in patients with CTTH in comparison with usual care provided by the GP. We studied the following potential mediators of the effects of MT treatment: cervical range of motion, neck flexor endurance and forward head posture.

The baseline and 8 weeks measurements of 186 patients who participated in the RCT or cohort study were used. In total, 145 patients received the MT treatment, of whom 104 patients participated in the cohort group and 41 in the trial. The number of patients in the RCT receiving usual care provided by their GP was 41. The 2 step-model of Baron & Kenny was applied to assess the mediating effect of cervical range of motion, neck flexor endurance and forward head posture. The first step represented the total effect of the MT intervention compared to usual care by the general practitioner on the outcome ($\geq 50\%$ reduction in headache days). In the second step the mediating effect of each of the three mediators on the total effect of MT and the outcome ($\geq 50\%$ reduction in headache days) was calculated.

The analysis showed that as a result of MT the neck flexor endurance significantly increased compared to usual care provided by the GP. This increase in neck flexor endurance contributed 24.5% to the total effect of MT on reduction in headache days. Changes in cervical range of motion and change in forward head posture did not significantly contribute to the total effect of MT on reduction in headache days.

Based on these results, the recommendation was made to include training of isometric muscle strength of neck flexors in the treatment of CTTH.

Chapter 5 describes a study into the course of symptoms in patients with CTTH receiving MT, and identifies factors that are associated with recovery following MT. We used data from all participants who received the MT treatment in RCT (n = 41) or in the parallel cohort group (n = 104). All patients completed identical baseline and follow-up measurements. To define a participant as 'recovered' a definition was used, that required a $\geq 50\%$ reduction in headache days, and a score of 6 'much improved' or 7 'very much improved' on a 7-point Likert scale for perceived recovery.

Prior to the analysis 12 predictive variables were selected on the basis of relevant literature and clinical expertise, while keeping in mind the sample size.

At 8 weeks, 78% of 142 patient were classified as 'recovered' and at 26 weeks this was 73% of 128 patients. Upon univariable regression analysis for each of these follow-up periods, potential prognostic variables ($p < 0.15$) were selected for multivariable regression analysis.

The following combination of prognostic variables was significantly associated with recovery at 8 weeks after the start of MT: presence of migraine, absence of multi-site pain, greater mobility of the cervical spine and high intensity of headache.

For long term outcome (26 weeks) significant prognostic factors for recovery were: greater neck flexor endurance and greater mobility of the cervical spine.

This study demonstrated a favourable course of CTTH both in the short and in the long term. The likelihood of recovery in the short and long term is influenced by the presence or absence of several prognostic factors. Migraine, greater mobility of the cervical spine and greater neck flexor endurance predict a higher likelihood of recovery while the presence of multi-site pain reduces the likelihood of recovery.

Chapter 6 reports on the minimum clinically important change (MCIC) of the HIT-6 in primary care patients with CTTH.

The HIT-6 has a good reliability and validity for the evaluation of headache, and is frequently used in clinical practice and research. The questionnaire includes 6 questions, each representing an area of pain, social and cognitive function, daily activities, vitality and psychological distress.

The HIT-6 has a minimum score of 36 and a maximum score of 78 points.

We used data from patients in the cohort study (n = 104) and the RCT (n = 82) to determine the MCIC of the HIT-6. We defined 'recovery' by combining a clinical measure for evaluation of headache ($\geq 50\%$ reduction in headache days) with a self-reported score from the patient (6 'much improved' or 7 'very much improved' on a 7 points Likert scale). The analysis was undertaken by conducting a Receiver Operant Curve (ROC) analysis to identify the optimal cut off point on the HIT-6 upon which patients defined as 'recovered' are distinguished from 'not recovered' patients.

The MCIC on the HIT-6 was 8 points. The smallest detectable change of the HIT-6 in this study was 5 points. We concluded that a decrease of at least 8 points on the HIT-6 constitutes a MCIC that distinguishes 'recovered' from 'not recovered' patients. This score falls outside the measurement error of the measuring instrument.

In **chapter 7** the main findings of this thesis are summarized and discussed. This chapter concludes with a list of recommendations for future research, and implications for the management of CTTH by general practitioners and manual- and physical therapists.