Combining Spinal Manipulation With Standard Counseling for Tobacco Cessation: Results of a Feasibility Randomized Clinical Trial

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ABSTRACT

Objective: The purpose of this study was to test the feasibility of a randomized clinical trial on the effectiveness of combining spinal manipulation (SM) with standard tobacco cessation counseling.

Methods: A randomized clinical trial was conducted. Participants in the intervention group received 2 months of counseling plus SM delivered by doctors of chiropractic, whereas control group participants received counseling alone. Primary outcome measures were smoking decreases and 7-day smoking abstinence as measured by a tobacco diary and urinary cotinine. Descriptive statistics were calculated.

Results: Recruitment proved to be difficult because of reluctance of participants to commit to a 2-month course of care. Ten participants completed this pilot study. Counseling plus SM group participants had greater improvement in the number of cigarettes smoked and urinary cotinine. Three participants achieved at least 7 days of tobacco abstinence, all in the counseling plus SM group.

Conclusions: In this feasibility study, doctors of chiropractic appeared to be capable of conducting effective smoking cessation counseling. The preliminary information indicated that there may be some benefit for including chiropractic care in addition to counseling. Researchers conducting future studies that are adequately powered should consider using multiple locations and incentives adequate to recruit participants. (J Chiropr Med 2017;16:41-48)

Key Indexing Terms: *Smoking Cessation; Manipulation, Spinal; Chiropractic*

INTRODUCTION

Tobacco use is the single largest cause of preventable illness and death in the United States. Eighteen percent of American adults smoke, causing an estimated 480 000 deaths per year, millions living with smoking-related diseases, and \$280 billion annually in treatment costs.¹ Tremendous headway in halting the smoking epidemic has been made in the last 50 years since the first surgeon general's report on the dangers of smoking. However, progress in recent years has been very slow, and new approaches need to be explored.¹

National guidelines recommend that all health care providers should advise smoking patients about the importance of tobacco cessation. The United States Preventive

Services Task Force and the Healthy People guidelines suggest that smoking cessation counseling be a routine part of primary health treatment in this country.² Doctors of chiropractic are considered as holistic practitioners and are philosophically well suited to deliver health promotion and prevention messages. Because doctors of chiropractic see approximately 8% of the U.S. population annually, many of whom do not receive regular treatment from a medical doctor, they could be an important source of counseling for smokers. Smoking is also a risk factor for low back pain, and more than 30% of a typical chiropractic practice consists of patients with low back pain.³ Hamm et al⁴ found that 7.8% of current smokers had used chiropractic care during the past 12 months and 17.9% of current chiropractic patients were smokers. The World Federation of Chiropractic began a Chiropractors Against Tobacco campaign in 2003 and recommends that doctors of chiropractic routinely inquire of their patients about smoking and the presence of smokers in their environment.⁵ Gordon et al⁶ found that private practitioner chiropractors could deliver effective smoking cessation counseling to their patients.⁶

Spinal manipulation (SM) is a therapeutic modality used by a variety of health care professionals, the majority in the United

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States being doctors of chiropractic. Although it is primarily used for the treatment of neuromusculoskeletal conditions, some practitioners use SM to help with a variety of other types of conditions.⁷ No articles could be found in the literature on the effect of SM on those who are attempting to quit smoking. Smoking cessation can be very difficult because of the associated withdrawal symptoms, such as irritability, anxiousness, and nervousness.⁸ Spinal manipulation may potentially support smoking cessation by reducing the severity of these symptoms.^{9,10}

The primary objective of this study was to determine the feasibility of conducting a randomized controlled trial of adding SM to a standard counseling program for smoking cessation delivered by doctors of chiropractic. The secondary objective was to collect preliminary data on the effectiveness of this intervention.

METHODS

Trial Design

This feasibility study consisted of a randomized single-site clinical trial. This study was registered in the Clinical Trials Registry as: NCT01689168.

Participants

Approval by the Southern California University of Health Sciences Institutional Review Board was obtained for the conduction of this study. Participants for the study were recruited through on-campus announcements and advertising in 2 county weekly newspaper publications. Compensation of \$100 was offered for the completion of the study. Potential participants were screened by phone by a research assistant to determine if they met the inclusion and exclusion criteria.

Inclusion criteria were age of 18 years or older and a current cigarette smoker with a desire to quit. Exclusion criteria included (1) having received SM within the last month; (2) having received any therapy for smoking cessation during the last month; (3) diagnosis of visceral, systemic, or joint inflammatory disease; (4) history of spinal surgery; (5) presence of osteoporosis; (6) prolonged use of systemic corticosteroid medication; (7) current pregnancy; and (8) recent spinal fracture.

Participants who met the inclusion criteria were examined by a chiropractic clinician for any contraindication to SM. Faculty chiropractic clinicians delivered all study examinations and treatments at an on-campus health center. Each clinician was licensed and had a minimum of 5 years of practice experience. Informed consent was obtained from those participants who passed the screening.

Interventions

A group session was held with the primary investigator, coinvestigators, and clinicians before the study began to present the standardized protocols to follow.

The participants were directed to not use any nicotine replacement therapy or other smoking cessation aids during the course of the study. Clinicians asked at every visit if the participant had followed these directions.

Smoking Cessation Counseling

Both treatment groups received a standard counseling program for smoking cessation. Two sessions with a smoking cessation counselor trainer based on the Treating Tobacco Use and Dependence guidelines were held for clinicians before the start of the trial.¹¹

The smoking cessation counseling program for study participants consisted of 5 sessions over an 8-week period. The clinicians were given a set of worksheets with instructions to be followed each counseling session. They were instructed not to provide any counseling if a participant visit was for any other reason than one of the scheduled counseling sessions.

Spinal Manipulation

Participants in the intervention group received smoking cessation counseling and a course of SM. Spinal manipulation treatments were delivered twice a week during the first 4 weeks of the study and then once a week during the following 4 weeks. When the participant was due for a counseling session, both therapies were delivered during the same visit by the same practitioner.

The SM was pragmatic as the clinicians decided what areas of the spine to manipulate and what technique to use. All clinicians in the study primarily used motion palpation to determine which spinal segments to adjust and performed diversified chiropractic SM technique. Soft tissue therapy could also be administered at the discretion of the clinician to enhance the effectiveness of the SM. No active or passive physical therapy was used.

Clinicians asked the participants at each visit if there had been any adverse effects from the prior visits SM.

Outcomes

The primary outcome measures were (1) a patient-completed tobacco diary and (2) urinary measure of cotinine, a nicotine metabolite.¹² Participants were asked to record in the diary how many cigarettes they smoked in the morning and in the afternoon and evening of each day through the entire 60-day treatment period. Both continuous (number of cigarettes smoked per day) and point-prevalence (7-day abstinence from smoking) analysis were performed.¹³

Urinary cotinine levels are considered to be a validated method to confirm self-reports of tobacco use.^{12,14} Urine tests were conducted by an independent laboratory (Quest Diagnostics, Madison, NJ), which was blinded to which group the participants were assigned. Samples were obtained at baseline and at 14, 30, and 60 days. Seven-day abstinence is often used as a point-prevalence measurement for smoking

cessation trials because it is congruent with the washout period for cotinine.¹²

Three secondary outcome measures were used:

1. The Minnesota Nicotine Withdrawal Scale (MNWS) was administered to participants at 14, 30, and 60 days. This instrument asks participants to rate 15 common symptoms of nicotine withdrawal on a scale ranging from 0 (none) to 4 (severe). The MNWS has been found to be a reliable and valid measure of the symptoms of nicotine withdrawal.⁸ Although the MNWS can be divided into subscales, this study analyzed results from all items combined as recommended by Toll et al.¹⁵
2. Blood pressure was to be recorded as a measure of stress from nicotine withdrawal.
3. Weight was to be recorded, as weight gain is a commonly perceived consequence of smoking cessation.¹⁶

Both physical measurements were to be performed at baseline and 14, 30, and 60 days by office staff who were blinded to the group that the participant was enrolled in.

Sample Size

Because this was a feasibility study, no power analysis was conducted. A sample of 10 participants was recruited based on available resources, including funding, space at the treatment facility, and clinician schedules.

Randomization

The participants were randomly assigned to either (1) the counseling or (2) the counseling plus SM group by a research assistant using a computer program that stratified the sample by age, gender, and the number of cigarettes smoked per day. Because of the small size of the sample, an adaptive randomization scheme was implemented. The program queried the number of current participants in each treatment group with the same stratification classifications as the new participant. If the numbers in each group were uneven, the participant was assigned to the one with fewer members. If the groups were even, a random-number generator was used to choose a group. Allocation was concealed from the research assistant until after the group assignment had been made.

Blinding

Participants and clinicians were not blinded to the treatments performed. Because the tobacco diary and MNWS were completed by the participants who were not blinded, these outcomes were not considered blinded. The urinary cotinine level was blinded because the laboratory did not know which group the participant was enrolled in, and the 2 physical outcomes were to be blinded as the staff performing them did not know which group the participant was enrolled in.

Statistical Methods

All data were entered into a Microsoft Access database for cleanup, and descriptive statistics, including percentages, medians, and interquartile ranges (IQRs), were calculated. Inferential statistics were not calculated because of the small number of participants.

RESULTS

Participant Flow

One hundred and forty-nine prospective participants contacted the research assistant, of whom 17 enrolled in the study (Fig 1). Most called after seeing one of the advertisements but did not wish to participate because of the need to travel to the study location for 2 months. Nine participants were randomized to the treatment group, of whom 6 completed the study (67%), whereas 8 participants were randomized to the control group, of whom 4 completed the study (50%). The most commonly cited reason for dropping out of the study was deciding that the incentive was not enough to justify driving to the study site 1 or 2 times per week.

The most common spinal levels reported treated by SM were C2, C3, T4, T5, and T6. No participant reported receiving any other treatment for smoking cessation during the course of the study.

Recruitment

Recruitment and treatment took place between April 16, 2012, and September 11, 2013. The trial ended when funds were exhausted.

Baseline Data

Baseline characteristics of the participants in the 2 groups were similar (Table 1).

Numbers Analyzed

Six participants were analyzed in the counseling plus SM group and 4 in the counseling group. All analysis was performed by original assigned group.

Outcomes and Estimation

During the first week of treatment, the counseling group participants reported a higher median number of cigarettes smoked per day in their tobacco diaries than the counseling plus SM group did (median = 14.0, IQR = 9.8 vs median = 10.5, IQR = 7.3). Although there was a reduction in the number of cigarettes smoked per day in both groups by the 60-day end of treatment period (Fig 2), this was more pronounced in the counseling plus SM group (median = 1.0, IQR = 4.3 vs median = 9.0, IQR = 12.0).

Three participants in the treatment group (50%) and zero participants in the control group (0%) reported complete

Fig 1. Participant flow chart.

Table 1. Participant Baseline Characteristics

	Counseling + SM ^a	Counseling ^a
Gender	Male: 56% Female: 44%	Male: 50% Female: 50%
Age	46.8 ± 9.9	44.3 ± 6.2
Years smoking	19.4 ± 10.7	21.2 ± 8.6
Cigarettes/day	18.0 ± 5.0	20.5 ± 4.0

SD, standard deviation; SM, spinal manipulation.

^a Continuous variables are reported as mean ± SD.

smoking abstinence for at least 7 days at the end of the treatment period (Fig 3).

Average urinary cotinine level also started somewhat higher in the counseling group (median = 1230, IQR = 2497 vs median = 980, IQR = 1847). Levels dropped by the 60-day end point in both groups (Fig 4), more so in the treatment group (median = 305.5, IQR = 1594.5 vs median = 746, IQR = 2620.5). There appeared to be good congruence between the tobacco diary and urine cotinine measures (Fig 3).

Minnesota Nicotine Withdrawal Scale scores were higher in the counseling plus SM group at 14 days (median = 13, IQR = 10.5 vs median = 7, IQR = 10.5). Scores improved in the counseling plus SM group between the 30- and 60-day outcomes but remained flat in the counseling group throughout the study period (Fig 5).

The physical measurements to be performed by office staff were not completed because of logistical factors.

Harms

No adverse events were reported by any of the study participants.

DISCUSSION

Interpretation

This feasibility study can help inform future endeavors in the study of using SM to help with smoking cessation. First and foremost, in agreement with Gordon et al,⁶ it was found that with minimal training, doctors of chiropractic can be effective at promoting smoking cessation among cigarette smokers with a desire to quit. This may be attributed to the skills that doctors of chiropractic have in empathy and communication, and it is aligned with the profession's emphasis on health promotion and prevention.¹⁷⁻¹⁹

It was also learned that the logistics for conducting a trial on smoking cessation requiring multiple clinic visits is challenging. Participant recruitment and retention turned out to be particularly difficult. Limited funding prevented advertising beyond 2 countywide weekly publications. Most of the responders to these ads lived more than 20 miles from the study site. Other smoking cessation studies advertised in these publications typically offered similar incentives for 1 visit, whereas this study required multiple visits over 2 months. This

Fig 2. Median number of cigarettes smoked per day. SM, spinal manipulation.

Counseling + SM Group

Counseling Group

Fig 3. Tobacco diary and urine cotinine outcomes. SM, spinal manipulation.

resulted in most of the ad respondents declining to participate, citing the inconvenience. The participants who began the study and then dropped out also most often cited the long drives to the study site as the reason. Future researchers should consider using multiple sites, advertising in local publications for each site, and offering generous incentives for recruitment.

The participants in the intervention group had good response to an 8-week program of combined smoking cessation counseling and SM. The participants in this study were chronic smokers (average 19.3 cigarettes per day for 20.3 years), yet by the end of the study, 50% of the counseling plus SM group participants reported at least 7 consecutive days of

Fig 4. Median urine cotinine levels. SM, spinal manipulation.

Fig 5. Median Minnesota Nicotine Withdrawal Scale scores. SM, spinal manipulation.

complete smoking cessation. At this point, the average cigarettes smoked for the other 3 participants in this group was down to 2.1 per day. Although at the onset of the study, the participants in the counseling group had somewhat worse outcome measures than the counseling plus SM group, this difference was small compared with the difference between groups seen by the end of the treatment period and does not change our conclusions of the apparent benefit of adding SM to the counseling protocol.

The results of this study compare favorably to the 28.4% abstinence rate achieved by following standard tobacco cessation counseling guidelines.¹¹ Stead et al²⁰ conducted a meta-analysis of clinical trials that used a combination of counseling and pharmacotherapy, and found that 15% of participants were tobacco abstinent at the last data collection point. Most of the included studies had last data collection points at 6 to 12 months, compared with only 2 months for the

current study. Although this current study was primarily a feasibility analysis and its findings have to be interpreted with caution, it can be useful, as an initial examination into the use of counseling and SM for tobacco cessation, for practitioners who treat smokers until more rigorous studies are conducted.

Although it was speculated that SM would help study participants quit smoking by decreasing the common symptoms of nicotine withdrawal, this was not borne out by the MNWS scores. It is possible that by the time the first outcome measurement was completed at day 14, the participants were already past their peak symptoms of nicotine withdrawal.

There is some research support for mechanisms by which SM may help smokers who are attempting to quit. Niedermaier et al²¹ found that cigarette smoke in habitual smokers reduced both parasympathetic and sympathetic activity. There is evidence that anxiety, such as is commonly experienced on tobacco withdrawal, also leads to an

imbalance in the autonomic nervous system.^{22,23} The most common areas treated with SM in this study were in the upper cervical and midthoracic spine. These correspond to the areas where Welch et al²⁴ reported that SM can cause sympathetic and parasympathetic responses, respectively, potentially restoring autonomic balance and enhancing participant's wellbeing.¹⁰ Vernon et al²⁵ reported an 8% increase in plasma β -endorphin levels 5 minutes after SM, which may help promote relaxation.

Generalizability

The study participants were generally chronic, 1-pack-a-day cigarette smokers, as are typically found in the US population. These findings could potentially be applicable to other populations of smokers, although the small sample size makes this conclusion uncertain.

Limitations

Because this was a feasibility study with several limitations, caution must be taken when interpreting the findings on the effectiveness of combined smoking cessation counseling and SM performed by doctors of chiropractic. The dropout rate was high, and it is possible that those who did not complete the study did not experience the same positive results. Nicotine replacement therapy was not used in this study because of the increased cost and complexity it would entail. Although potential participants were excluded if they had used any smoking cessation therapy within the previous month, we did not inquire about any previous attempts to quit or participation in any previous trials.

The counseling plus SM group had a greater number of scheduled clinic visits, and this may have contributed to the better results in this group. Although the clinicians were instructed not to discuss smoking cessation during visits scheduled for SM only, it is possible that some unscheduled counseling did occur. Future studies may consider evening out the number of clinic visits between groups by either incorporating a sham SM therapy for the counseling group or by delivering SM on the same schedule as counseling sessions in the counseling plus SM group.

Blinding of participants and practitioners is a common challenge for trials of manual therapies such as SM, and this was not attempted in this study. Having separate practitioners deliver counseling and SM could have helped mitigate possible bias by these clinicians who were all doctors of chiropractic, but a lack of available personnel prevented this.

CONCLUSIONS

This feasibility study indicated that it is possible to conduct a randomized clinical trial examining the effectiveness of smoking cessation counseling and SM for helping smokers quit, albeit with some logistical challenges. It also

presents some preliminary evidence that combining these therapies may be more effective than counseling alone. The mechanism of this possible effect remains unclear. Adequately powered randomized clinical trials should be conducted to more definitively study this treatment method and possible mechanisms of action. Researchers of future studies should consider using multiple treatment sites, local advertising at each site, and larger financial or other incentives for participants.

Practical Applications

- This study found that it was feasible to conduct a randomized clinical trial of a novel method to assist smokers who desire to quit.
- Therapy consisted of standard tobacco cessation counseling and SM delivered by chiropractors.
- Difficulties were encountered in participant recruitment, which could be remedied by using multiple sites for future studies, local advertising for each site, and sufficient financial incentives.
- The small group of participants who completed the trial reported good results after receiving the combined therapies.

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REFERENCES

1. U.S. Department of Health and Human Services. The Health Consequences of Smoking—50 Years of Progress: A Report of the Surgeon General. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health; 2014.
2. Levy DT, Nikolayev L, Mumford E, Compton C. The Healthy People 2010 smoking prevalence and tobacco control objectives: results from the SimSmoke tobacco control policy simulation model (United States). *Cancer Causes Control*. 2005;16(4):359-371.
3. Johnson C, Rubinstein SM, Côté P, et al. Chiropractic care and public health: answering difficult questions about safety, care through the lifespan, and community action. *J Manip Phys Ther*. 2012;35:493-513.
4. Hamm E, Muramoto ML, Howerter A, Floden L, Govindarajan L. Use of provider-based complementary and alternative medicine by adult smokers in the United States: comparison from the 2002 and 2007 NHIS survey. *Am J Health Prom*. 2014;29(2):127-131.
5. World Federation of Chiropractic. Chiropractors against tobacco. Available at: https://www.wfc.org/website/index.php?option=com_content&view=article&id=91%3Achiropractors-against-tobacco&catid=63%3Achiropractors-against-tobacco&Itemid=89&lang=en [Accessed August 5, 2014].
6. Gordon JS, Istvan J, Haas M. Tobacco cessation via doctors of chiropractic: results of a feasibility study. *Nicotine Tob Res*. 2010;12(3):305-308.
7. Hawk C, Khorsan R, Lisi AJ, Ferrance RJ, Evans MW. Chiropractic care for nonmusculoskeletal conditions: a systematic review with implications for whole systems research. *J Altern Complement Med*. 2007;13(5):491-512.
8. Cappelleri JC, Bushmakina AG, Baker CL, Merikle E, Olufade AO, Gilbert DG. Revealing the multidimensional framework of the Minnesota nicotine withdrawal scale. *Curr Med Res Opin*. 2005;21(5):749-760.
9. Williams NH, Hendry M, Lewis R, Russell I, Westmorland A, Wilkinson C. Psychological response in spinal manipulation (PRISM): a systematic review of psychological outcomes in randomised controlled trials. *Compl Ther Med*. 2007;15(4):271-283.
10. Brockman S. The role of chiropractic manipulation in promoting an individual's perception of psychological well being. *Clin Chiropr*. 2007;10(1):8-23.
11. Fiore MC, Jaén CR, Baker TB, et al. Treating Tobacco Use and Dependence: 2008 Update. Clinical Practice Guideline. Rockville, MD: U.S. Department of Health and Human Services. Public Health Service; 2008.
12. Vartiainen E, Seppälä T, Lillsunde P, Puska P. Validation of self reported smoking by serum cotinine measurement in a community-based study. *J Epidemiol Community Health*. 2002;56(3):167-170.
13. Hughes JR, Keely JP, Niaura RS, Ossip-Klein DJ, Richmond RL, Swan GE. Measures of abstinence in clinical trials: issues and recommendations. *Nicotine Tob Res*. 2003;5(1):13-25.
14. World Health Organization, International Agency for Research on Cancer. Methods for evaluating tobacco control policies. In: IARC Handbooks of Cancer Prevention. Tobacco Control. Vol. 12. Lyon, France: IARC;78-80.
15. Toll BA, O'Malley SS, McKee SA, Salovey P, Krishnan-Sarin S. Confirmatory factor analysis of the Minnesota Nicotine Withdrawal Scale. *Psychol Addict Behav*. 2007;21(2):216-225.
16. Farley AC, Hajek P, Lycett D, Aveyard P. Interventions for preventing weight gain after smoking cessation. *Cochrane Database Syst Rev*. 2012;1CD006219.
17. Oths K. Communication in a chiropractic clinic: how a D.C. treats his patients. *Cult Med Psychiatry*. 1994;18(1):83-113.
18. Hennius BJ. Contemporary chiropractic practice in the UK: a field study of a chiropractor and his patients in a suburban chiropractic clinic. *Chiropr Man Therap*. 2013;21(1):25.
19. Davis MA, Bove GM. The chiropractic healer. *J Manip Phys Ther*. 2008;31(4):323-327.
20. Stead LF, Koilpillai P, Fanshawe TR, Lancaster T. Combined pharmacotherapy and behavioural interventions for smoking cessation. *Cochrane Database Syst Rev*. 2016;3CD008286.
21. Niedermaier ON, Smith ML, Beightol LA, Zukowska-Grojec Z, Goldstein DS, Eckberg DL. Influence of cigarette smoking on human autonomic function. *Circulation*. 1993;88(2):562-571.
22. Pistorio E, Luca M, Luca A, Messina V, Calandra C. Autonomic nervous system and lipid metabolism: findings in anxious-depressive spectrum and eating disorders. *Lipids Health Dis*. 2011;10:192.
23. Friedman BH, Thayer JF. Autonomic balance revisited: panic anxiety and heart rate variability. *J Psychosomatic Res*. 1998;44(1):133-141.
24. Welch A, Boone R. Sympathetic and parasympathetic responses to specific diversified adjustments to chiropractic vertebral subluxations of the cervical and thoracic spine. *J Chiro Med*. 2008;7(3):86-93.
25. Vernon HT, Dhami MS, Howley TP, Annett R. Spinal manipulation and beta-endorphin: a controlled study of the effect of spinal manipulation on plasma beta-endorphin levels in normal males. *J Manip Phys Ther*. 1986;9(2):115-123.