

OUTCOMES FOR CHRONIC NECK AND LOW BACK PAIN PATIENTS AFTER MANIPULATION UNDER ANESTHESIA: A PROSPECTIVE COHORT STUDY

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ABSTRACT

Background: The purpose of this study was to investigate outcomes of chronic patients unresponsive to previous spinal manipulative therapy subsequently treated with manipulation under anesthesia (MUA).

Methods: A prospective outcome cohort study was performed on 30 patients who had not improved with previous treatment and who underwent a single MUA by a doctor of chiropractic. The numeric rating scale for pain (NRS) and Bourmemouth Questionnaire (BQ) were collected at 2 weeks and 1 day before MUA. At 2 and 4 weeks after MUA, the Patient's Global Impression of Change, NRS, and BQ were collected. The intraclass correlation coefficient evaluated stability before treatment. Percentage of patients "improved" was calculated at 2 and 4 weeks. Wilcoxon test compared pretreatment NRS and BQ scores with posttreatment scores. Mann-Whitney *U* test compared individual questions on the BQ between improved and not improved patients. Logistic regression compared BQ questions to "improvement."

Results: Good stability of NRS and BQ scores before MUA (intraclass correlation coefficient = 0.46-0.95) was found. At 2 weeks, 52% of the patients reported improvement with 45.5% improved at 4 weeks. Significant reductions in NRS scores at 4 weeks ($P = .01$) and BQ scores at 2 ($P = .008$) and 4 weeks ($P = .001$) were reported. Anxiety/stress levels were significantly different at 2 and 4 weeks between improved and not improved patients ($P = .007$). None of the BQ questions were predictive of improvement.

Conclusion: Approximately half of patients previously unresponsive to conservative treatment reported clinically relevant improvement at 2 and 4 weeks post-MUA. (*J Manipulative Physiol Ther* 2014;xx:1-6)

Key Indexing Terms: *Spinal Manipulation; Chiropractic; Outcomes Research; Anesthesia*

Chronic low back pain (CLBP) and chronic neck pain (CNP) are enormous burdens on today's health care system due to a lack of definitive knowledge about the

process of chronification and superior treatment methods.¹⁻⁷

Chronic low back pain and CNP are complex, multifactorial problems that are best understood by the biopsychosocial model of pain.⁸⁻¹² Several recent studies have investigated outcomes of CLBP and CNP patients who received chiropractic treatment, including patients with confirmed symptomatic cervical or lumbar disc herniations.¹³⁻¹⁷ All disk herniation patients and most of the other chronic patients received spinal manipulation as at least part of their treatment.¹⁶⁻¹⁸ Most of even these chronic patients reported clinically relevant "improvement" at medium- and long-term data collection time points. However, a small percentage of patients did not improve in those studies, and it is these therapy-resistant chronic patients who challenge the health care system. Research focusing on identifying reasons for their failure to improve or more invasive therapeutic procedures is ongoing.

Manipulation under anesthesia (MUA), although not a new treatment and not widely practiced internationally, appears to show some promise for certain types of these CLBP and CNP patients.¹⁹⁻²⁷ Manipulation under anesthesia is a technique that allows the physician to treat the patient

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with chronic and resistant nonspecific mechanical musculoskeletal disorders by applying a selection of treatment methods at a higher intensity due to anesthesia than would be possible to replicate in the normal practice setting. Manipulation under anesthesia is typically reserved for patients who have not responded to a variety of conservative treatments or for patients who have reached a therapeutic plateau and further improvement is not likely.²⁸ For example, chronic pain patients who have been suffering for years with musculoskeletal pain may have articular or myofascial adhesions that cannot be resolved in the normal office setting. This is where MUA may show potential to improve these patients that otherwise remain unimproved.²⁵ It has been estimated that approximately 3% of patients who do not respond to traditional chiropractic care may benefit from MUA treatment.²⁶

Although the current evidence for MUA is sparse, a few studies suggest that the procedure may be safe and helpful when patients are carefully selected.^{20,28} However, precise data on outcomes of chronic patients receiving this treatment are still lacking.^{20,22,24} Therefore, the purpose of this study was to investigate the outcomes of chronic patients who were unresponsive to conservative treatments including chiropractic spinal manipulative therapy (SMT) and who subsequently were treated with manipulation under anesthesia.

METHODS

Ethics approval was obtained from the Canton of Zürich and Balgrist hospital before the start of the study, and signed informed consent was obtained for all patients. This is a prospective outcome study on a cohort of CLBP and CNP adult patients from a single chiropractic practice in Switzerland who had either reached a less than satisfactory clinical plateau or not improved with a variety of conservative treatments (including SMT). Subsequently, each patient received a single MUA treatment.

Exclusion criteria for MUA included malignancy, certain benign tumors, infection, trauma, fractures, dislocation, excessive osteoporosis or osteopenia, unstable spinal anomalies, neurological, vascular and inflammatory diseases, and psychological disorders.

Manipulation Under Anesthesia Procedure

The MUA procedure consists of 3 stages. First, the patient is sedated by a certified anesthesiologist.²⁸ The patient is connected to monitoring equipment measuring the blood oxygenation, electrocardiogram, blood pressure, and respiration rate before the anesthetic medication being given by an intravenous catheter in the dorsum of the hand.¹⁹ The most common drug used is propofol.²⁸ It is a lipophile, fast-acting derivate of alkyphenol. Its main effects are sedation of the patient and amnesia. The main advantage of propofol is that patients regain consciousness quickly because

Table 1. Intraclass Correlation Coefficients for the Stability of the Condition Before MUA

	ICC	95% CI
Neck pain (NRS)	.76	0.52-0.88
Arm pain (NRS)	.95	0.88-0.97
BQ 1 average pain past week	.46	-0.06 to 0.73
BQ 2 activities of daily living	.78	0.56-0.90
BQ 3 recreational/social activities	.90	0.79-0.95
BQ 4 anxiety/stress	.77	0.53-0.89
BQ 5 depression	.83	0.65-0.91
BQ 6 work	.85	0.69-0.92
BQ 7 locus of control	.68	0.35-0.84
BQ total score	.88	0.75-0.94

BQ, Bournemouth questionnaire; CI, confidence interval; NRS, numerical rating scale for pain.

there is a rapid clearance by the blood into fatty tissues and a fast metabolic clearance in the liver. As the level of sedation used for MUA in Switzerland is not as deep as typically used in other countries and the anesthesia is only administered intravenously, there is no need for intubation during the procedure. Other possible drugs used include sufentanyl, which is a fast-acting opiate; midazolam, a fast-acting benzodiazepine; or methohexital, a fast-acting barbiturate.

After sedation and patient stabilization are complete, the patient is ready for the second stage of the procedure. This involves the manual treatment performed by a specially trained and certified MUA physician.²⁸ In each case for this study, the manipulation was performed by a doctor of chiropractic. The MUA procedure begins with maximal passive stretching of the myofascial tissues of the neck or low back in all planes and axes of movement. Each position is held for 4 to 6 seconds. Then axial traction is applied to the cervical or lumbar spine. These maneuvers are primarily what distinguish MUA from chiropractic treatment without anesthesia. With the patient anesthetized and the muscles relaxed, much larger ranges of movement and soft tissue stretching are possible compared with what can be accomplished in the conscious patient. Finally, SMT is administered, which consists of high-velocity, low-amplitude thrusts in the main areas of the spine that are restricted. During the procedure, an assistant is available to stabilize the sedated patient if needed as well as the anesthesiologist who monitors the patient's vital functions.

Once the treatment is complete, the patient is transferred to the recovery area for the third stage of the procedure where he/she is monitored until conscious and then sent home when cleared to do so.^{19,28}

Baseline and Outcome Measures

Patient age and sex information was collected before the MUA treatment. In addition, the numeric rating scale for pain (NRS) intensity where 0 is no pain and 10, the worst pain imaginable, and the Bournemouth Questionnaire (BQ) for low back or neck pain (German) were collected at 2 weeks

Table 2. Baseline and Outcome Results for Chronic Neck and Low Back Pain Patients Treated With MUA

	Baseline: 2 wk Before MUA	Baseline: 1 d Before MUA	2 wk Post-MUA	4 wk Post-MUA
PGIC			52% Improved	45.5% Improved
NRS mean (SD)	4.33 (2.13)	4.00 (2.06)	3.50 (2.43)	3.18 (2.46) ^a
BQ mean (SD)	26.39 (20.38)	24.17 (13.42)	20.38 (14.25) ^a	19.45 (15.79) ^a

BQ, Bournemouth questionnaire; NRS, numerical rating scale for pain; PGIC, patients global impression of change; SD, standard deviation.

^a $P \leq .01$.

and 1 day before MUA by telephone interview to determine the stability of the patients' condition before MUA. At 2 and 4 weeks after MUA the Patient's Global Impression of Change (PGIC) (primary outcome measure), the NRS for low back pain/neck pain and the BQ were collected by telephone interview. All telephone interviews were conducted by a chiropractic medicine masters student unknown to the patients. Data were entered into a computer database and statistically analyzed using the SPSS version 21.0 software (Chicago, IL, USA).

Statistical Analysis

The stability of the patients' condition at the 2-week and 1-day time points before treatment (NRS and BQ scores) was evaluated using the intraclass correlation coefficient (ICC). The proportion (percentages) of patients reporting clinically relevant improvement (PGIC responses of "much better" or "better") was calculated for the 2- and 4-week post-MUA time points. The χ^2 test was used to assess for differences in the proportions of "improved" low back pain patients compared with neck pain patients. Numeric rating scale for pain and BQ change scores were compared between males and females using the unpaired Student *t* test.

The Wilcoxon test for matched pairs compared pretreatment NRS and BQ median scores with the 2 posttreatment scores to determine statistically significant differences. The paired *t* test was also performed to obtain the mean NRS and BQ scores for ease of reporting. Numeric rating scale for pain and BQ change scores were compared between improved and "not improved" patients at the 4-week time point using the unpaired *t* test. Individual questions on the BQ were compared between these same 2 groups using the Mann-Whitney *U* test. $P < .05$ was considered statistically significant. Logistic regression analysis was also done to compare the various questions on the BQ to improvement.

RESULTS

Thirty chronic low back ($n = 17$) and neck ($n = 13$) pain patients were included with an equal sex distribution. Of the 30 patients, there were no drop outs from the study. The mean patient age was 44.25 years (SD, 12.70). Both the NRS and BQ scores showed good stability before MUA. The specific ICC scores and 95% confidence intervals for neck pain, arm pain, the BQ total score, and the scores for all 7 questions on the BQ compared at 2 weeks and 1 day

before MUA are shown in Table 1. At 2 weeks post-MUA, 52% reported clinically relevant improvement with 45.5% improved at 4 weeks. There were no significant differences in the proportion of neck pain patients reporting clinically relevant improvement compared with patients with low back pain at either 2 or 4 weeks posttreatment. No significant differences in NRS or BQ scores between the sexes were found at any time point.

Statistically significant reductions in NRS low back pain/neck pain scores at 4 weeks ($P = .01$) and BQ scores at both 2 weeks ($P = .008$) and 4 weeks ($P = .001$) were reported (Table 2). Comparing improved with not improved patients found a significant difference in NRS and BQ change scores at the 4-week time point ($P = .018$ and $P = .012$, respectively) (Table 3). Responses to question number 4 on the BQ (anxiety/stress) between improved and not improved patients were significantly different at 2 weeks ($P = .007$) and 4 weeks ($P = .011$) post-MUA. Patients not improved had significantly higher (ie, worse) mean scores of 4.13 (SD, 2.39) compared with a mean score of 1.94 (SD, 1.44) for patients reporting clinically relevant improvement at 2 weeks. Patients reporting improvement at 4 weeks had mean scores of 1.71 (SD, 1.49) compared with 3.79 (SD, 2.42) for those not improved. However, logistic regression analysis found that none of the questions on the BQ were predictive of improvement at either 2 or 4 weeks post-MUA, although question 5 (depression) had a significance of $P = .06$ at 4 weeks. There were no reported adverse events as a result of treatment.

DISCUSSION

The purpose of this study was to evaluate outcomes of CNP and CLBP patients after a single MUA treatment. These were all patients who had previously (and recently) undergone a series of SMT treatments but who had failed to demonstrate clinically relevant improvement. The patients and procedure used in this study are consistent with the consensus guidelines recently published.²⁸ The results of this study are encouraging as more than half of the patients reported improvement at 2 weeks post-MUA and 45.5% were improved at 4 weeks. *Improvement* was defined as responses of much better or better on the PGIC scale. The response of "slightly" better was not considered improved in line with other recent outcome studies.¹⁴⁻¹⁷ In addition, statistically significant decreases in disability scores were found at both 2 and 4 weeks posttreatment as well as

Table 3. Comparison of the NRS Change Scores and BQ Change Scores at 4 weeks Post-MUA Between Patients Reporting Improvement and Those not Improved

	4-wk NRS Change Scores (SD)	4-wk BQ Change Scores (SD)
Improved patients	2.29 (1.90)	12.39 (10.95)
Not improved patients	0.32 (2.45)	2.92 (9.41)

BQ, Bournemouth questionnaire; SD, standard deviation.

significant decreases in pain scores at 4 weeks post-MUA. When statistically significant improvement is found in a sample size of only 30 patients, this is likely to be clinically relevant. This is much better than the figure reported by Morey²⁶ where it was estimated that 3% of patients who did not respond to traditional chiropractic care improved after MUA. However, that is a very old reference, dating from 1976.

Importantly, no adverse events occurred due to the MUA treatment. Rarely may a patient experience laryngospasm during the anesthesia. If this should happen, the patient is temporarily intubated. In the several year experience of the treating clinician in this study, this has happened only once.

The proportion of patients reporting improvement in this current study is certainly less than the results published for chronic patients after traditional chiropractic treatment in recent outcomes studies where more than 70% of chronic lumbar disk herniation patients and 58% of chronic cervical disk herniation patients were improved at 1 month, and 59% of chronic low back pain patients and 62% of chronic neck pain patients reported clinically relevant improvement at 1-month post-chiropractic treatment.¹⁴⁻¹⁷ However, this current study using MUA only included patients who would not have improved after traditional chiropractic treatment as provided in the above-cited studies, and thus, the fact that approximately half of these previous therapy-resistant patients improved after a single MUA treatment is noteworthy. However, 4 weeks is a relatively short period to assess outcomes, and further studies should assess longer term outcomes as well as whether additional MUA treatments are of any value.

Outcome studies do not prove whether a treatment is responsible for any changes in patient condition. Randomized controlled trials are needed for this. However, the fact that 2 different baseline data collection time points were used to assess pain and disability levels before the MUA treatment and that there was a high correlation between their scores strongly suggests that the condition of these patients before treatment was stable and unimproved. Furthermore, all patients had previously been treated with chiropractic therapy and failed to respond sufficiently, if at all. Therefore, it could be argued that these patients served as their own control group.

Chronic neck and low back pain patients were combined in this study to achieve an adequate sample size of 30 patients.

Comparing the outcomes of these 2 groups separately did not reveal any statistically significant differences in baseline or outcome results, and therefore, it was felt that combination of the data was justified. However, it should be noted that when analyzing the 2 groups separately with sample sizes of 17 low back and 13 neck pain patients, the outcome results did not achieve statistical significance for either group, although trends were noted. However, the proportion of improved patients in the 2 groups was nearly identical to the results for the combined data reported here. This highlights the importance of sample size in searching for clinically meaningful results. Sample sizes that are too small may hide clinically relevant information, whereas very large sample sizes may lead to results that are statistically significant but clinically meaningless.

It was not surprising that the question concerning anxiety and stress levels on the BQ found statistically significant differences between patients improved and those not improved with patients who were not improved reporting higher levels at both 2 and 4 weeks posttreatment. This is consistent with other studies looking for factors associated with failure to improve.²⁹⁻³¹ However, this question was not predictive of improvement when placed into the logistic regression model. Question 5 on the BQ (depression) was nearly significantly predictive of improvement at 4 weeks, however, with a *P* value of .06. A larger sample size may indeed find this to be predictive, similar to other studies.²⁹

Limitations

There are several limitations to this study. The first is the relatively small sample size and the need to combine the chronic neck and low back pain cohorts to achieve 30 patients. Manipulation under anesthesia is not a commonly available treatment worldwide, although a few specially trained and certified chiropractic physicians in Switzerland do practice this technique when indicated. It is only done if other treatments have failed however, and therefore, obtaining a large sample size is challenging. The relatively short period for collecting outcomes is another limitation as well as the fact that this is an outcome study and not a randomized controlled trial as discussed above.

CONCLUSIONS

This small cohort study found that approximately half of chronic patients previously unresponsive to conservative chiropractic treatment that included SMT reported clinically relevant improvement at 2 and 4 weeks after a single session of MUA. Patients who did not improve had significantly higher levels of anxiety and stress compared with improved patients. No moderate or serious adverse events were reported for treatment in this cohort.

Practical Applications

- Approximately half of previously therapy-resistant chronic nonspecific low back or neck pain patients reported clinically relevant improvement after a single treatment of MUA.
- Patients who did not improve reported higher levels of anxiety and stress.
- There were no adverse events reported from treatment in this cohort.

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Concept development (provided idea for the research): RN, BKH

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Supervision (provided oversight, responsible for organization and implementation, writing of the manuscript): CP, BKH

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REFERENCES

1. Cagnie B, Danneels L, Van Tiggelen D, De Loose V, Cambier D. Individual and work related risk factors for neck pain among office workers: a cross sectional study. *Eur Spine J* 2007;16:680-5.
2. Hogg-Johnson S, van der Velde G, Carroll LJ, et al. The burden and determinants of neck pain in the general population: results of the bone and joint decade 2000-2010 task force on neck pain and its associated disorders. *J Manipulative Physiol Ther* 2009;32(2 Suppl):53-5.
3. Bot SD, van der Waal JM, Terwee CB, et al. Incidence and prevalence of complaints of the neck and upper extremity in general practice. *Ann Rheum Dis* 2005;64:118-23.
4. Fejer R, Kyvik KO, Hartvigsen J. The prevalence of neck pain in the world population: a systematic critical review of the literature. *Eur Spine J* 2006;15:834-48.
5. Haldeman S, Carroll L, Cassidy JD. Findings from the bone and joint decade 2000 to 2010 task force on neck pain and its associated disorders. *J Occup Environ Med* 2010;52:425-7.
6. Shekelle PG, Markovich M, Louie R. Factors associated with choosing a chiropractor for episodes of back pain care. *Med Care* 1995;33:842-50.
7. Walker BF. The prevalence of low back pain: a systematic review of the literature from 1966 to 1998. *J Spinal Disord* 2000;13:205-17.
8. Carroll LJ, Hogg-Johnson S, van der Velde G, et al. Course and prognostic factors for neck pain in the general population: results of the bone and joint decade 2000-2010 task force on neck pain and its associated disorders. *J Manipulative Physiol Ther* 2009;32(2 Suppl):S91-4.
9. Carroll LJ, Holm LW, Hogg-Johnson S, et al. Course and prognostic factors for neck pain in whiplash-associated disorders (WAD): results of the bone and joint decade 2000-2010 task force on neck pain and its associated disorders. *J Manipulative Physiol Ther* 2009;32(2 Suppl):S97-S107.
10. Carroll LJ, Hogg-Johnson S, Côté P, et al. Course and prognostic factors for neck pain in workers: results of the bone and joint decade 2000-2010 task force on neck pain and its associated disorders. *J Manipulative Physiol Ther* 2009;32(2 Suppl):S108-16.
11. Foster NE, Thomas E, Bishop A, Dunn KM, Main CJ. Distinctiveness of psychological obstacles to recovery in low back pain patients in primary care. *Pain* 2010;148:398-406.
12. Sieben JM, Vlaeyen JW, Portegijs PJ, et al. A longitudinal study on the predictive validity of the fear-avoidance model in low back pain. *Pain* 2005;117:162-70.
13. Humphreys BK, Peterson C. Comparison of outcomes in neck pain patients with and without dizziness undergoing chiropractic treatment: a prospective cohort study with 6 month follow-up. *Chiropr Man Therap* 2013;21:3.
14. Peterson C, Bolton J, Humphreys BK. Predictors of improvement in patients with acute and chronic low back pain undergoing chiropractic treatment. *J Manipulative Physiol Ther* 2012;35:525-33.
15. Peterson C, Bolton J, Humphreys BK. Predictors of outcome in neck pain patients undergoing chiropractic care: comparison of acute and chronic patients. *Chiroprac Man Therap* 2012;20:27.
16. Peterson C, Schmid C, Leemann S, Anklin B, Humphreys BK. Outcomes from MRI confirmed symptomatic cervical disc herniation patients treated with high velocity, low amplitude, spinal manipulative therapy. A prospective cohort study with 3 month follow-up. *J Manipulative Physiol Ther* 2013;36:461-7.
17. Leemann S, Peterson C, Schmid C, Anklin B, Humphreys BK. Outcomes of acute and chronic patients with MRI confirmed symptomatic lumbar disc herniation receiving high velocity, low amplitude, spinal manipulative therapy. A prospective observational cohort study with one year follow-up. *J Manipulative Physiol Ther* 2014;37:155-63.
18. Humphreys BK, Peterson CK, Muehleman D, Haueter P. Are Swiss chiropractors different than other chiropractors? Results from the Swiss job analysis survey 2009. *J Manipulative Physiol Ther* 2010;33:519-35.

19. Cremata E, Collins S, Clauson W, Solinger AB, Roberts ES. Manipulation under anesthesia: a report of four cases. *J Manipulative Physiol Ther* 2005;28:526-33.
20. Gordon RC. An evaluation of the experimental and investigational status and clinical validity of manipulation of patients under anesthesia: a contemporary opinion. *J Manipulative Physiol Ther* 2001;24:603-11.
21. Kohlbeck FJ, Haldeman S. Medication-assisted spinal manipulation. *Spine J* 2002;2:288-302.
22. Davis CG, Fernando CA, da Motta MA. Manipulation of the low back under general anesthesia: case studies and discussion. *J Neuromusculoskel Syst* 1993:126-34.
23. Palmieri NF, Smoyak S. Chronic low back pain: a study of the effects of manipulation under anesthesia. *J Manipulative Physiol Ther* 2002;25:E8-E17.
24. West DT, Mathews RS, Miller MR, Kent GM. Effective management of spinal pain in one hundred seventy-seven patients evaluated for manipulation under anesthesia. *J Manipulative Physiol Ther* 1999;22:299-308.
25. Siehl D, Olson DR, Ross HE, Rockwood EE. Manipulation of the lumbar spine with the patient under general anesthesia: evaluation by electromyography and clinical-neurologic examination of its use for lumbar nerve root compression syndrome. *J Am Osteopath Assoc* 1971;70:433-40.
26. Morey LW. Osteopathic manipulation under general anesthesia. *J Am Osteopath Assoc* 1976:S61-72.
27. Kohlbeck FJ, Haldeman S, Hurwitz EL, Dagenais S. Supplemental care with medication-assisted manipulation versus spinal manipulation therapy alone for patients with chronic low back pain. *J Manipulative Physiol Ther* 2005;28:245-52.
28. Gordon R, Cremata E, Hawk C. Guidelines for the practice and performance of manipulation under anesthesia. *Chiroprac Man Therap* 2014;22:7.
29. Reme SE, Lie SA, Eriksen HR. Are two questions enough to screen for depression and anxiety in chronic low back pain? *Spine* 2014;39:E455-62.
30. Schiltenswolf M, Akbar M, Hug A, et al. Evidence of specific cognitive deficits in patients with chronic low back pain under long-term substitution treatment of opioids. *Pain Physician* 2014;17:9-20.
31. Esteves JE, Wheatley L, Mayall C, Abbey H. Emotional processing and its relationship to chronic low back pain: results from a case-control study. *Man Ther* 2013;18:541-6.