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Trunk Exercise Combined with Spinal Manipulative or NSAID Therapy for Chronic Low Back Pain: A Randomized, Observer-Blinded Clinical Trial

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ABSTRACT

Objectives: To study the relative efficacy of three different treatment regimens for chronic low back pain (CLBP). Two preplanned comparisons were made: (a) Spinal manipulative therapy (SMT) combined with trunk strengthening exercises (TSE) vs. SMT combined with trunk stretching exercises, and (b) SMT combined with TSE vs. nonsteroidal anti-inflammatory drug (NSAID) therapy combined with TSE.

Study Design: Interdisciplinary, prospective, observer-blinded, randomized clinical trial with a 1-yr follow-up period. The trial evaluated therapies in combination only and was not designed to test the individual treatment components.

Setting: Primary contact, college out-patient clinic.

Patients: In total, 174 patients aged 20-60 yr were admitted to the study.

Main Outcome Measures: Patient-rated low back pain, disability, and functional health status at 5 and 11 wk.

Interventions: Five weeks of SMT or NSAID therapy in combination with supervised trunk exercise, followed by an additional 6 wk of supervised exercise alone.

Results: Individual group comparisons after 5 and 11 wk of intervention on all three main outcome measures did not reveal any clear clinically important or statistically significant differences. There seemed to be a sustained reduction in medication use at the 1-yr follow-up in the SMT/TSE group. Continuance of exercise during the follow-up year, regardless of type, was associated with a better outcome.

Conclusion: Each of the three therapeutic regimens was associated with similar and clinically important improvement over time that was considered superior to the expected natural history of long-standing CLBP. For the management of CLBP, trunk exercise in combination with SMT or NSAID therapy seemed to be beneficial and worthwhile. The magnitude of nonspecific therapeutic (placebo) effects, cost-effectiveness and relative risks of side effects associated with these types of therapy need to be addressed in future studies. (J Manipulative Physiol Ther 1996; 19:570–82).

Key Indexing Terms: Low Back Pain; Exercise; Manipulation, Orthopedic; Anti-Inflammatory Agents, Nonsteroidal; Chiropractic; Comparative Studies; Randomized Clinical Trial

INTRODUCTION

The incidence and prevalence of low back pain (LBP) in industrialized countries are increasing (1, 2). Although the understanding of the multi-factorial nature of LBP is growing, the cost to society and patients because of this condition is rising exponentially (3, 4). It is estimated that the cost attributable to LBP in the U.S. is presently up to $50 billion yearly, with 75-80% of that amount spent on the nonacute and chronic disabling LBP conditions (5). On a yearly basis, 5-10% of the adult population will experience an acute episode of LBP (6). Approximately half of these patients will recover spontaneously within 2 wk; within 6 wk, an estimated 80% will have recovered without intervention. The remaining 20% will continue to have LBP, which represents a major socioeconomic problem (1).

It is unlikely that there will ever be a single cure for LBP because of its multifactorial nature (3). Exercise is considered an essential part of the management of chronic low back pain (CLBP) (7-9) and may even have a role in primary and secondary prevention of recurring episodes of LBP (10-13). Effective management of LBP calls for changing the patient's role from a passive recipient of treatment to an active participant in health maintenance. Recommendations made by the World Health Organization (WHO) in the Health for All in the Year 2000 campaign echo this sentiment (14). Current knowledge indicates that exercise and motion benefit those joints and soft-tissues that may play an important role in the cause of

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nonspecific mechanical LBP (15-17). Additionally, performance of prescribed exercise can reassure patients that they do not suffer from a serious back disease and that activity will not cause further deterioration (16). Based on reviews of randomized clinical trials (RCTs) on exercise (4, 18-20), extension exercises to strengthen the paravertebral musculature (21), isometric exercises to strengthen the abdominal musculature (22) and stretching exercises to improve overall trunk flexibility (23) have been shown effective for CLBP. However, there is still insufficient evidence to prefer one type of exercise over another (4, 8, 18-20).

Chiropractors are the primary providers of spinal manipulative therapy (SMT) (24). It is estimated that at least 30% of patients seeking care for LBP in the U.S. use chiropractic services (25, 26). Several authors have reviewed RCTs that involve SMT for LBP (24, 27-33). They did not draw uniform conclusions and their methodologies varied from qualitative to meta-analytical. Most of the authors agree, however, that SMT is a relatively safe treatment for acute and nonacute LBP and that it may offer more immediate relief than other forms of conservative care. Long-term benefits of SMT for LBP have not been demonstrated conclusively (24). Two RCTs have shown that combining therapies like SMT or mobilization and exercise can lead to improved outcomes compared with use of the individual treatments (34, 35).

Reviews of RCTs that evaluate different drug regimens for the treatment of CLBP provide evidence of efficacy of both antidepressants and nonsteroidal anti-inflammatory drugs (NSAIDs) (18, 30). A study by Berry et al. that compared naproxen sodium, diflunisal and placebo in the treatment of CLBP showed naproxen sodium to be superior to placebo in relieving global pain, night pain and pain on movement (36). Although side effects are common (37), the use of NSAIDs in the management of nonacute LBP has been advocated (38) and is widely accepted in general medical practice (39).

Purpose

The uncertainty about the role of NSAIDs, SMT and different types of exercise in the management of CLBP led us to conduct this trial to study the relative efficacy of three different combination therapies in adults. Two preplanned comparisons were made: (a) SMT combined with trunk strengthening exercises (TSE) vs. SMT combined with trunk stretching exercises and (b) SMT combined with TSE vs. NSAID therapy combined with TSE.

METHODS

Selection and Evaluation of Subjects

Potential subjects responded to local advertisements in Minneapolis/St. Paul newspapers. Respondents were screened by telephone and scheduled for personal interviews from September 1991 to May 1993. Eligible candidates were evaluated twice during a 1-wk baseline period to establish a reliable baseline assessment, test patient compliance and determine final eligibility. All evaluations and therapeutic interventions took place at the Wolfe-Harris Center for Clinical Studies, a research and outpatient clinic in Bloomington, Minnesota. The study protocol was approved by the Institutional Review Board.

Inclusion Criteria

Candidates between 20 and 60 yr of age with nonspecific LBP of at least 6 wk duration with or without radiating pain to one or both legs to the level of the knee. LBP was not classified according to diagnostic criteria because expert panels have concluded that a diagnosis regarding the specific cause cannot be made for most LBP subjects (40). In this study, LBP is defined as pain that is localized to an area limited superiorly by a horizontal line through the spinous process of the first lumbar vertebra, laterally by the midaxillary lines and inferiorly by the iliac crests, including the sacrum. Leg pain is defined as pain in any aspect of the lower extremity including the gluteal region, the upper borders being the iliac crest, sacrum and inguinal regions.

Exclusion Criteria

Patients were excluded if any of the following conditions were met: LBP caused by specific identifiable pathology in the spine and lower extremities; organic diseases with referred pain to the lumbar spine; severe osteopenia; previous back surgery; severe arterial hypertension or existing cardiovascular diseases requiring medical treatment; poor general health; obesity; history of duodenal or stomach ulcers; previous hypersensitivity to NSAID therapy; and pregnancy. Potential candidates were also excluded if they were unable to keep appointments during the baseline period or if there was evidence of other risks of noncompliance, such as pending litigation, plans for change of residence, inaccessibility by phone or difficulties with the English language.

To minimize confounding by carry-over effects of previous treatment, subjects were excluded if they had received either prescribed NSAIDs or spinal manipulation or had performed prescribed exercise for their LBP $<$ 3 months before study entry. All candidates without recent radiographs had new spinal imaging studies performed and, if indicated, laboratory evaluations. The random allocation into three treatment groups took place when complete eligibility was established at the end of the 1-wk baseline period.

Random Treatment Allocation

The study participants, who all provided signed informed consent, were randomly assigned to one of three groups: (a) SMT plus strengthening exercise (SMT/TSE); (b) NSAID therapy plus strengthening exercise (NSAID/TSE); or (c) SMT plus stretching exercise (SMT/Stretching). Because, by design, the SMT/TSE group served as the comparison in both of the planned contrasts, according to a principle advocated by Dunnett (41), more subjects were allocated to this group (ratio 3:2:2). The random group assignments were drawn from sealed opaque envelopes. The allocation process was verified by an independent, professional agent.

Treatment Descriptions

The 11-wk treatment protocol for the three groups consisted of 5 wk of combination therapy followed by 6 wk of exercise therapy alone, totaling 20 1-hr sessions.

The SMT Treatments

SMT treatments were provided by five licensed chiropractors whose practice experience varied from 5-25 yr. A total of 10 treatment sessions were provided, all during the first 5 wk of the trial, each lasting 10-15 min. Manual palpatory findings were used to identify the spinal segments to be manipulated. The choice of specific manual treatment technique and spinal segment(s) to be manipulated was made by the participating chiropractors. No adjunctive physiotherapy was allowed, except for brief pretreatment heat and manual muscle relaxation techniques. The manual spinal thrusting technique employed a specific contact over a vertebral osseous process, muscle or ligament and introduced a force into the selected vertebral or sacroiliac joint. This manual spinal treatment was carried out with a high-velocity, low-amplitude thrust, most commonly by a short-lever technique. In this technique, the patient is placed on a chiropractic treatment table either seated, prone, supine, or in side-lying posture. The chiropractor places the contact hand in appropriate contact with the patient and, once the end of physiological range of motion is achieved passively, applies a thrust to the joint, carrying it slightly beyond the normal physiological range of motion (42).

Pharmaceutical Therapy

Naproxen sodium, a long-acting NSAID, was prescribed by the participating medical doctor who also monitored the side effects. Patients assigned to NSAID treatment took one 500-mg capsule every morning and evening. This dosage was tested in the placebo-controlled trial by Berry et al. and was shown to be efficacious (36). Each patient started taking the drug on day 1 of the 5-wk intervention phase. No other prescription NSAIDs or analgesics were allowed during the study.

Exercise Protocols

Research assistants that were specifically trained and certified by the principal investigator supervised all 20 exercise sessions. During the first 5 wk of treatment, 10 exercise sessions were done in combination with either SMT or NSAID intervention. For the subsequent 6 wk, patients came solely for the 10 supervised exercise sessions. The dynamic trunk strengthening protocol consisted of trunk and leg extensions as described by Manniche (21), plus abdominal muscle strengthening. Trunk extensions were done with the patient in the prone position with the lower body stabilized and the upper body unsupported; leg extensions were done with the patient's upper body stabilized and the lower body unsupported. The abdominal strengthening was done with the patient lying supine, knees bent at 45°. The patient performed a "crunch-up" that was held for 2 sec, with every other "crunch-up" rotated to the left or right. Twenty repetitions of each of the three types of strengthening exercises were carried out with a 1-min rest between sets. During the 1-hr session, this training cycle was repeated as many times as the patient could tolerate. The series of stretching exercises used in this study were previously used by Deyo (23). These exercises were designed to improve the flexibility of the spine, hips and lower extremities. The individual stretching exercises were maintained for 1 min and the series of stretches repeated twice during each 1-hr session. At completion of the study, all patients were encouraged to continue independently with the exercises they performed in the trial.

Compliance and Cointerventions

Repeated instruction, feedback and written information were given to all subjects to maximize understanding and compliance. All exercise sessions occurred under supervision in the clinical setting to ensure compliance. Patients receiving medication kept a diary indicating the number of tablets taken each day during the first 5 wk of therapy. All patients were asked to record any cointerventions they received during the study and during the follow-up period.

Assessments of Outcomes, Blinding and Follow-up

Physical examinations and trunk performance tests were repeated twice during the 1-wk baseline period and once after 5 and 11 wk of intervention. Patients were given outcome questionnaires in the clinical setting twice during the baseline period and after 3, 5 and 11 wk of intervention. Approximately 1 yr after completing the study, all participants who had complied with at least 5 wk of study intervention received a brief follow-up questionnaire by mail. All primary outcome measures were patient-rated, and the trunk performance and range of motion data were obtained by study-certified clinicians blinded to group allocations. The time points chosen before the study began for analysis of the three main outcomes were 5 and 11 wk. The three main outcome measures assessed LBP, low back disability and general health status. Mean weekly LBP severity was recorded on an ordinal 11-box scale (43), shown to have reliability and validity similar to the 10-cm visual analog scale (44). The Roland-Morris index was used to assess low back disability (45). This 24-item questionnaire has measures of reliability, validity and sensitivity to change that are equal to the much longer sickness impact profile from which it was derived and that was previously shown to be highly reliable and valid (46).

Functional health status was evaluated by a patient-rated questionnaire called the Dartmouth Primary Care Cooperative Information Project (COOP) chart system, with nine different scales, covering physical, social and role functions, emotional status, overall health and quality of life. The COOP charts, tested on several thousand patients in various primary care settings in the U.S., Europe and Japan, have appropriate sensitivity to the effects of disease and were shown to be reliable and valid (47-51).

The presence of clinical depression was assessed by a patient-administered questionnaire that was designed to be used in nonpsychiatric populations. This instrument, the Community Epidemiologic Scale-Depression, was developed by the National Institutes of Health and is reliable and valid (52). The weekly use of analgesics and difficulty and inability to perform normal daily work was assessed at baseline, 3, 5 and 11 wk and 1 yr later.

Trunk performance tests measured trunk muscle strength, endurance and range of motion. A computerized digital myograph (DM2000; Myotech Corp., Florida) was used to assess the isometric muscle strength with the subject lying on a couch with the pelvis and legs fixed, supine for trunk flexors and prone for trunk extensors. The load cell of the myograph measures pounds of force with a resolution of 0.1 pounds, and repeatability within 3% according to the manufacturer's specifications. When examining reliability of the isometric strength tests in a pilot study, in contrast to recent reports on low reliability (53), we found intraclass correlation coefficients above 0.8 and method error coefficients of variation between 0.15 and 0.17.

Muscle endurance of trunk extensors was measured by the length of time in seconds (maximum 240 sec) the subject was able to maintain the unsupported upper part of the body horizontally when placed prone on a couch with legs and buttocks fixed. This method has been validated by other investigators (54-56). For measuring muscle endurance of trunk flexors, the subject, in a supine position, knees bent 45°, feet fixed and arms crossed on the chest, performed a "crunch-up" to the point where only the inferior angles of the scapulae would touch the couch. The test is continued until muscle failure or to the limit of pain tolerance (max. 240 seconds). In our pilot study, we assessed the reliability of both endurance tests and found that intraclass correlation coefficients varied from 0.8-0.9.

Assessment of lumbar range of motion employed the modified Schober's test for flexion and extension (57). Additionally, the CA6000 3-dimensional computerized spine motion analyzer (OSI Inc., Hayward, California) (5, 58) was used to assess primary and coupled range of motion of the trunk. The results of this assessment will be reported in a future publication. The straight leg raising test (SLR) was performed on the supine patient using a Reglus inclinometer with 1°-increment scale (CH-8134-Adliswill-1; Switzerland), mounted on an adjustable base. The inclinometer was placed just proximal to the patella and zeroed with the leg in the neutral position. The leg was moved passively into extension and raised off the table until a pull on the quadriceps was felt or the patient indicated pain. The SLR reading was performed at that point.

Patient Bias

Patient attention bias was minimized by using similar therapeutic procedures in the three groups and an equal time commitment for each patient at each visit. The expectation of treatment outcome, according to group, was rated by patients on an ordinal scale at baseline and was later employed as a covariate in the secondary analysis of outcomes.

Statistical Analysis

Statistical power calculations were done initially based on the three primary response variables. The power was set, so the chance of overlooking a difference of 10 percentage points between the interventions on the three primary outcomes (59) was less than 20%. The overall alpha level was set at 0.05, but with adjustment of the level at which each of the multiple primary response variables was declared significant given the number of tests (0.05/6) (Bonferonni's correction). The mean differences between outcome measures and corresponding 95% confidence intervals were calculated. Because SMT/TSE served as the "control group" in the two planned intervention contrasts, Dunnett's t tests and analysis of covariance (ANCOVA) were used, incorporating baseline values (41, 60, 61). A supplementary multivariate ANCOVA was used as an overall test for differences between the three types of treatment, including the three primary and four secondary response variables (62). To evaluate potential predictors of outcome hierarchical, stepwise multiple linear regression analysis was performed. Subgroup analyses were done with t tests (or nonparametric tests where assumptions for parametric testing were violated). If subgroup analyses involved comparing outcomes that incorporated baseline values, ANCOVA was used. All analyses were performed with SPSS for Windows, version 6.0 (SPSS, Chicago, Illinois) and Statistica for Windows, version 4.5 (Statsoft, Inc., Tulsa, Oklahoma).

RESULTS

Study Sample

There were 617 responses to our recruitment efforts. Of these, 272 subjects could not be reached or did not wish to participate, 85 did not attend their intake appointments and 286 were excluded. The most common reasons for exclusion included inability to commit to the 12-wk study period (85 subjects), age (69 subjects) and use of prescription NSAIDs or chiropractic treatment within the 3 months before study entry (78 subjects). Nineteen subjects were excluded because of coexisiting medical conditions, obesity and/or spinal pathology, and 35 subjects were excluded because of intolerance to NSAIDs. In total, 174 patients were admitted to the study and randomly allocated to the three treatment groups: 71 subjects to receive SMT combined with TSE (the SMT/TSE group), 52 to receive NSAIDs combined with TSE (the NSAID/TSE group) and 51 to receive SMT combined with stretching exercises (the SMT/Stretching group). The random allocation process was successfully concealed from the participants in the screening process.

Dropouts

By the end of the 5-wk combined intervention period, 26 subjects (15%) had dropped out of the study, 9 (13%) from the SMT/TSE group, 8 (15%) from the NSAID/TSE group, and 9 (18%) from the SMT/Stretching group. The most common reasons for attrition were: missed appointments, change in residence, lack of continued motivation and adverse reactions to NSAIDs (two subjects). By the completion of 11 wk of intervention, an additional 16 patients had dropped out, 6 from the SMT/TSE group, 4 from the NSAID/TSE group, and 6 from the SMT/Stretching group, leaving 132 (76%) who completed the intervention part of the study (11 wk) and were available for all main outcome assessments. Statistical analysis revealed that the dropouts and remaining subjects were comparable in demographic and baseline clinical characteristics except for gender, depression scores and smoking. Neither gender, depression, smoking nor the other variables that showed a potential difference between drop-outs and completers were predictors of outcome when analyzed in a multiple regression model. We investigated the means, standard deviations, and minima and maxima for all patients, including dropouts, for all primary outcomes at the three times of assessment. We were unable to identify any patterns that suggested anything except that the data were missing completely at random (6, 63). Missing completely at random is the term used to indicate that the missingness is like a random sample, hence analysis of the completers has reduced power but should not be biased. This means the dropouts represent a random sample of patients in this trial, and it is unlikely that data from these patients would have changed the main results of the study.

At the 1-yr follow-up, questionnaire responses were obtained from 126 patients, 72% of the original study group and 83% of the participants who had complied with at least the first 5 wk of study intervention.

Compliance and Cointervention

Compliance was measured during the first 5 wk of the trial by the number of treatment and exercise sessions that subjects attended and the number of prescribed NSAIDs taken by the NSAID/TSE group. Except for dropouts, all patients had a better than 85% compliance rate with the medication, SMT sessions and exercise sessions during the 3 months of the study. Two patients sought nonstudy treatment for LBP during the study. All statistical tests were performed on the basis of intent-to-treat analysis (64).

Characteristics of the Subjects

Demographic and clinical characteristics of all subjects are summarized in Table 1. Ninety-three percent of the subjects were white, 2% were black and 5% belonged to other ethnic or racial groups. Ninety-one percent had high-school educations, and 55% held college or other professional degrees. Sixty-three percent had jobs outside the home, 23% were self-employed and 2% were unemployed. Twenty-nine percent had manual labor occupations. Thirty-six percent reported suffering from muscle/joint disorders other than LBP and 13% reported having been diagnosed with rheumatism/arthritis.

Therapeutic Outcomes

The main research questions of the trial were predicated on individual group comparisons after 5 and 11 wk of intervention on all three major outcome measures, which were analyzed with Dunnett's t tests. Because the baseline differences among groups, although not statistically significant, could slightly alter the results, the analyses of the three primary outcome measures were done using the baseline values as covariates. These tests did not reveal any clear clinically important differences or statistically significant differences between the groups (Table 2 and 3). Figure 1 displays the change in pain over time, Figure 2 shows low back disability over time and Figure 3 shows general health status over time. In addition, multivariate repeated-measures ANCOVA was performed that incorporated all three primary outcome variables and analgesic medication use. This analysis also did not reveal any statistically significant differences between groups. For descriptive purposes, four different levels of magnitude of clinically important reduction in pain after 11 wk of treatment were calculated for each of the three groups together with associated relative risk (chance) ratios (Table 4).

It may be argued that summary measures, such as area under the curve (65), may be a more relevant analysis of serial measurements than separate group comparisons at each time point. We supplemented our primary analysis with area under the curve comparisons of groups by computing the product of time difference between the measurement points (baseline, week 3, week 5 and week 11) and the mean of these four measurements. The cumulative scores for the SMT/TSE, NSAID/TSE and SMT/Stretching groups respectively were 39.5, 40.4 and 42.7 for pain, 217.3, 252.0 and 252.3 for low back disability and 793.4, 785.4 and 814.4 for functional health status. This analysis showed no clear clinically important or statistically significant differences and thus corroborated our other statistical analyses. A tendency toward group difference in pain between the SMT/TSE and NSAID/TSE groups (at 3 wk favoring the NSAID/TSE group and at 11 wk favoring the SMT/TSE group) was observed, with p values approaching the .05 level in both instances.

The proportion of patients using over-the-counter analgesic medication was reduced over time during the 11 wk intervention phase in all three groups at different rates (no statistically significant group differences). At 1-yr follow-up, however, there was a clinically important advantage in this outcome for the SMT/TSE group (a difference in proportions of 24%, (CI: 3.8%, 44.2%)) over the NSAID/TSE group (Figure 4).

The mean depression (Community Epidemiologic Scale-Depression) scores improved slightly during the 11-wk intervention phase compared with baseline values (10-15%, $p <$ .05), but no significant group differences were observed.

A substantial increase in trunk flexion/extension strength and endurance was observed after 11 wk of exercise in both the SMT/TSE and NSAID/TSE groups but not in the SMT/Stretching group (Table 5). Range of lumbar motion as assessed by Schober's modified tests showed no important change in flexion at week 11 in any of the groups. However, the SMT/TSE group showed an increase in extension of 20% compared with negligible change in the other two groups (p = .05). Five patients had positive SLR tests at baseline (< 60°), which normalized by week 11. Compared with baseline, the mean

Table 1. *Demographic and baseline clinical characteristics (Values are means and standard deviations [SD] unless otherwise noted.)*

Characteristic	Group A SMT + strength exercise	Group B NSAID + strength exercise	Group C SMT + stretch exercise	All subjects
No of subjects	71	52	51	174
Age (yr)	41.3 [10.5]	40.3 [8.9]	41.4 [9.3]	41.0 [9.7]
Gender (% female)	53.5	44.2	39.2	46.6
Living with significant other (%)	85.5	79.6	78.2	81.7
Height (inches)	66.8 [4.1]	66.3 [10.1]	68.4 [4.0]	67.1 [6.5]
Weight (pounds)	167.1 [32.7]	174.3 [38.8]	178.2 [36.2]	172.5 [35.7]
Working at full capacity at study entry (%)	76.1	80.8	74.5	77.1
Duration of current episode of low back pain (yr) (median)	3.0	2.0	2.3	2.5
Pain radiation to leg (%)	54.9	53.8	64.0	57.3
Use of analgesics for back pain during past week (%)	43.7	50.0	45.1	47.0
Three or more previous episodes of low back pain (%)	56.3	37.3	50.0	48.8
Depression score (CES-D, 0–60 scale)	10.0 [9.0]	9.3 [8.2]	8.6 [8.8]	9.4 [8.7]
Low back pain score (0–10 scale)	5.3 [1.5]	5.5 [1.7]	5.4 [1.4]	5.4 [1.5]
Global general health score (COOP Charts, 0–100 scale)	63.8 [12.0]	61.6 [13.3]	66.4 [14.0]	63.0 [13.1]
Global general health score (SF-36D, 0–100 scale)	63.9 [14.3]	63.1 [14.9]	66.6 [14.0]	64.5 [14.4]
Low back disability score (Roland-Morris, 0–100 scale)	33.3 [17.8]	35.0 [16.9]	34.7 [17.9]	34.2 [17.4]
Previous hospitalization for low back pain (%)	8.6	7.7	7.9	8.1
MMPI raw scores				
Hysteria-scale	26.8 [4.5]	25.8 [4.9]	25.2 [5.1]	26.1 [4.9]
Hypochondriasis-scale	9.3 [5.0]	8.3 [4.1]	8.2 [4.3]	8.7 [4.6]
Lie-scale	5.3 [1.8]	5.4 [2.1]	4.9 [1.9]	5.2 [1.9]
Waddell's score (0–5 scale)	0.2 [0.4]	0.3 [0.8]	0.1 [0.4]	0.2 [0.6]
Smoker (%)	16.9	15.4	27.5	19.5

values for the SLR tests increased by 3-5° ($p < .008$) at week 11, with no group differences observed.

Clinically important improvement over time was shown in all three major outcome measures at similar rates in each of the three study groups. Improvement was progressive from week 3 to week 11. A reduction was noted from baseline levels in patient-rated mean weekly pain of 27-33% at week 3, 35-37% at week 5 and 35-50% at week 11. At the 1-yr follow-up, a reduction in pain of 35-40% compared with baseline levels was still evident. LBP disability (Roland Morris Scale scores) was reduced by 32-35% at week 3, by 43-47% at week 5 and by 37-53% at week 11. Global General Health Status (COOP Chart scores) was improved by 8-12% at week 3, 14-16% at week 5 and 15-17% at week 11. All within group changes over time were statistically significant at or below a probability level of 0.000001.

Side Effects

Despite screening for increased risk of gastrointestinal intolerance to NSAIDS, two patients developed severe nausea/vomiting without evidence of gastrointestinal bleeding after 1-2 wk use of the prescribed NSAID medication, necessitating discontinuation of study participation. Eight additional patients reported substantial nausea and dyspepsia while taking the

Table 2. *Group differences in primary outcome measures after 5 wk of intervention/exercise (means are adjusted for baseline values for comparability)*

	Group A SMT + strength. exercise (Adjusted means and [SD]) $n = 62$	Group B NSAID + strength. exercise (Adjusted means and [SD]) $n = 43$	Group C SMT + stretch. exercise (Adjusted means and [SD]) $n = 42$	Group differences (95% CI) (analyzed with Dunnett's t tests) A/B	A/C
Pain (11-box scale)	3.4 [1.9]	3.6 [2.2]	3.9 [2.1]	0.2 (−0.6, 1.0)	0.5 (−0.3, 1.3)
Low back disability (Roland-Morris)	19.1 [19.3]	20.8 [17.8]	20.8 [17.3]	1.7 (−5.6, 9.0)	1.7 (−5.6, 8.9)
General health status (COOP Charts)	71.9 [14.3]	74.3 [14.6]	72.0 [16.5]	2.4 (−2.3, 7.1)	0.1 (−4.6, 4.8)

Table 3. *Group differences in primary outcome measures after 11 wk of intervention/exercise (means are adjusted for baseline values for comparability)*

	Group A SMT + strength. (Adjusted means and [SD]) n = 56	Group B NSAID + strength. (Adjusted means and [SD]) n = 40	Group C SMT + stretch. (Adjusted means and [SD]) n = 36	Group differences (95% CI) (analyzed with Dunnett's t tests)	
				A/B	A/C
Pain (11-box scale)	2.7 [2.0]	3.5 [2.2]	3.3 [2.3]	0.8 (−0.02, 1.6)	0.6 (−0.2, 1.4)
Low back disability (Roland-Morris)	15.1 [17.4]	20.9 [17]	18.4 [17.1]	5.8 (−1.1, 12.7)	3.3 (−3.6, 10.2)
General health status (COOP Charts)	75.4 [12]	75.6 [11.1]	74.8 [16.3]	0.2 (−4.2, 4.6)	−0.6 (−4.8, 4.0)

prescribed NSAID medication, but this was partially or totally relieved when nonprescription antacids were taken simultaneously. One patient developed severe tinnitus for the first time in his life 4-5 wk after entering the trial in the group that received the prescription NSAID. The medical physician prescribing the medication attributed the onset of the condition to the study NSAID use. The tinnitus did not resolve during the subsequent 12 months. One patient dropped out after 5 wk of SMT and strengthening exercise because she could not tolerate the exercise. Seven patients developed considerable muscle soreness and stiffness, including neck pain, from the TSE during the first month. Their symptoms gradually abated and did not prevent any of them from completing the study. One patient in the SMT/TSE group developed symptoms of myocardial infarction unrelated to the performance of exercise. The patient was subsequently hospitalized but later returned and completed the study. Overall, both strengthening and stretching exercise and SMT were well tolerated.

1-yr Follow-up Results

A response to a seven-item follow-up questionnaire was received from 126 patients 1.2 yr (mean) after completion of the trial. Group differences in pain and analgesic medication use, the latter being the only variable to show statistically significant group differences, are displayed in Figure 1 and Figure 4, respectively. Eighty percent (groups varied from 73-87%) of all patients reported little or no current interference with daily activities because of LBP. A mean value of 0.7 work days were lost (groups varied from 0.5-1.1 days) during the follow-up year because of LBP. During the same period, 17% of patients in the SMT/TSE group, 18% in the NSAID/TSE group and 9% in the SMT/Stretching group had received additional treatment for LBP. Reduced activity and inability to work because of LBP during the study and the 1-yr follow-up period is described in Table 6. Compared with baseline, improvement in LBP (rated as better, much better or no symptoms) was reported by approximately half of the patients in each of the three groups. Of the 120 patients, for whom information about continuance of exercise and baseline and 1-yr follow-up pain ratings were available, 73% continued

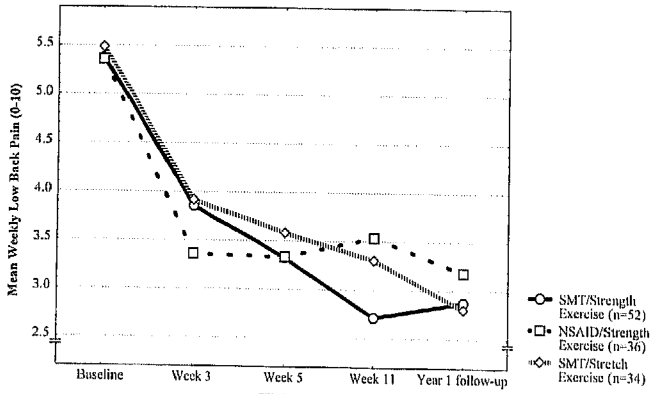

Fig. 1 *Change in pain over time.*

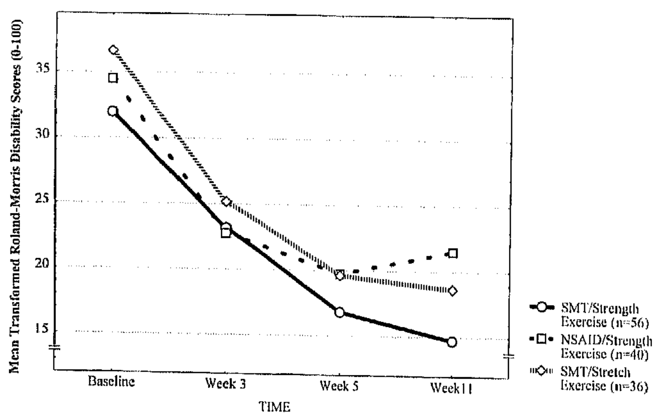

Fig. 2 *Low back disability over time.*

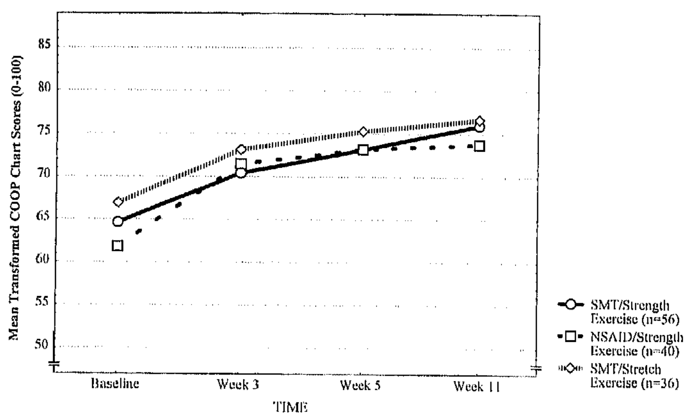

Fig. 3 *Functional health status over time.*

Table 4. *Proportion of subjects achieving four different levels of reduction in patient-rated pain after 11 wk of intervention/exercise by group including relative risks*

Percentage point reduction in pain	Group A SMT + strength. exercise (n = 56) proportion	Group B NSAID + strength. exercise (n = 40) proportion	Relative Risk group B/A	Group C SMT + stretch. exercise (n = 36) proportion	Relative Risk group C/A
	%	%		%	
≥ 10	80.3	70.0	.87	72.2	.90
≥ 20	71.4	47.5	.66	58.3	.81
≥ 30	55.4	30.0	.54	47.2	.85
≥ 40	32.1	15.0	.47	27.7	.86

their prescribed trunk exercise at various frequencies, whereas 27% completely discontinued their exercise, the majority after 1-2 months. Regardless of original group assignment, a higher and clinically important reduction in pain after 1 yr (12% difference, p = .01) compared with baseline was reported by the patients that continued the prescribed back exercise during the 1-yr follow-up compared with the patients that did not (Figure 5). A comparison of these two subgroups of patients regarding sociodemographic factors, severity and duration of LBP and other important clinical characteristics at baseline, as well as rate of improvement after 3 months of study therapy, showed no important differences except on reported frequency of fitness exercise, which was an important predictor of long term adherence to a home back-exercise protocol. Three fourths of the subgroup that continued to perform back-exercises during the 1-yr follow-up period engaged in regular general fitness exercise at study entry, compared with half of the subgroup that did not continue their back exercises. The type of back exercise and frequency of performance during the follow-up year was poorly correlated with outcome.

Prognostic Indicators

In a secondary analysis of possible prognostic indicators of outcomes, a hierarchical, stepwise regression analysis was done entering age, gender, smoking, manual/nonmanual labor, duration of complaint, previous episodes, psychological overlay, level of depression and frequency of fitness exercise as independent variables in an attempt to predict the amount of change in the three major outcomes (pain, disability and general health status) after three months of therapy. Reporting the nature of the LBP as one long continuous episode since debut in contrast to one or more discrete previous episodes was a significant predictor of poorer outcome, whereas the other variables in the model were not significant. Additionally, although a cause-effect relationship cannot be assumed, continued compliance with exercise, regardless of type, was a significant predictor of decreased pain level at the 1-yr follow-up, explaining 20% of the variance (p = .02).

DISCUSSION

Other studies have shown an advantage in combining similar therapies as were studied in this trial (34, 35, 66). The combination of SMT and exercise in this study was at least as effective as the combination of NSAIDs and exercise and may be preferable, because both SMT and exercise were associated with very few side effects, as has been found in other studies (20, 24), whereas several patients in the NSAID group, despite careful screening, reported side effects from the drug. Twenty-one percent of the patients in the NSAID/TSE group developed symptoms consistent with NSAID-associated toxicity, which seem to be higher than predicted given the results of findings of numerous studies (67, 68). The relative risk of gastrointestinal events in NSAID (naproxen) users has been estimated to be approximately 3 times as high as in nonusers, although the relative risk for NSAID exposure of 1 month or less has been

Table 5. *Change from baseline in trunk muscle performance after 11 wk of exercise*

	Group A SMT + strength. exercise Mean % improvement (95% CI) n = 52	Group B NSAID + strength. exercise Mean % improvement (95% CI) n = 39	Group C SMT + stretch. exercise Mean % improvement (95% CI) n = 33	Group difference A/B	Group difference A/C
Trunk extension strength	32 (15, 49)	15 (2, 28)	1 (−12, 14)	ns[a]	p = .01
Trunk flexion strength	34 (15, 53)	23 (3, 44)	7 (−10, 13)	ns	p = .05
Trunk extension endurance	101 (34, 168)	72 (25, 118)	15 (−10, 33)	ns	p = .05
Trunk flexion endurance	141 (73, 210)	79 (35, 122)	30 (−8, 68)	ns	p = .02

[a] ns = $p \geq .05$.

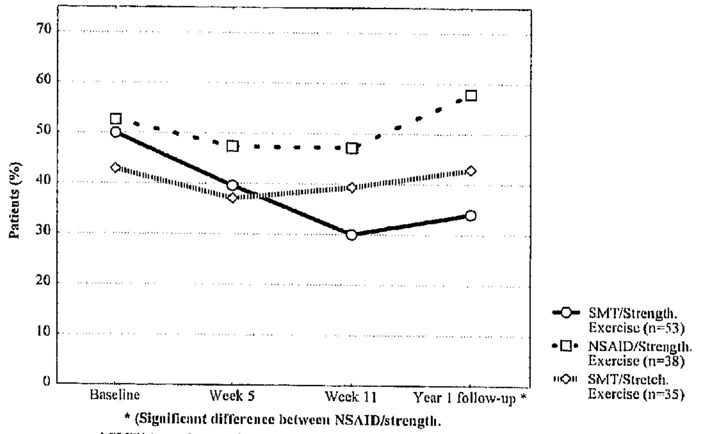

Fig. 4 *Group differences in analgesic medication use.*

estimated to be 8 times has high as in nonusers (68), which may partially explain the high rate of reported side effects in this study. Additional risk factors are age over 60 yr, previous history of gastrointestinal events and concomitant use of corticosteroid medication (68).

This study revealed no advantage of strengthening over stretching exercise in combination with SMT, other than improved trunk muscle performance, which in this study was not a good predictor of outcome. Methods for optimizing dose and level of initial supervision for patient-individualized exercise protocols, possibly including a combination of the two types of exercise evaluated in this study, need to be developed and tested in future clinical trials. This research provides evidence that all three combination treatments for CLBP under investigation were associated with very similar and important improvements in patient-reported outcomes for pain, restriction in daily activities, and psychosocial function. It is noteworthy that the reduction in patient-reported low back pain after three months of treatment was mostly sustained after a year. The reduced use of analgesics in the SMT/TSE compared with NSAID/TSE group at 1-yr follow-up could not be explained by any known mediating variables in a multiple regression analysis.

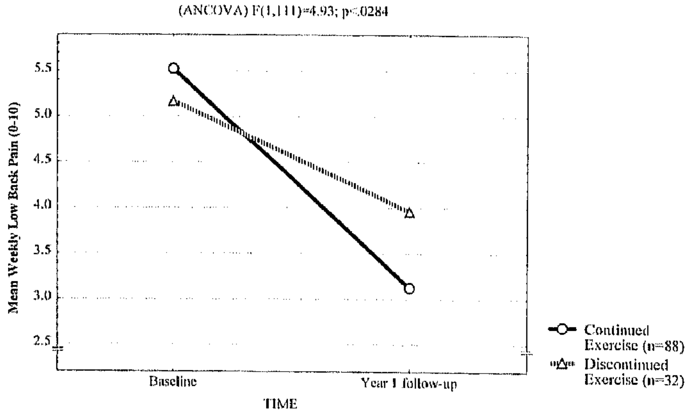

Fig. 5 *Change in pain over time in relationship to continued compliance with exercise.*

We estimated the relative responsiveness of the patient-rated pain by comparing it with an external criteria (the Roland-Morris low back disability scores) that differentiated between improved and nonimproved patients and by calculating a receiver operating characteristic curve. The area under this curve was 0.85 (SE 0.05) with optimal cut-off values of 5 to 10%. The respective sensitivity/specificity of 5 and 10 percentage points were 88%/58% and 88%/60%. The tendency toward a greater reduction in pain of 5% after 3 wk of treatment in the NSAID/TSE group compared with the SMT/TSE group, and 8% greater reduction in pain after 3 months of treatment in the SMT/TSE group compared with the NSAID/TSE group, constitute differences that we consider of borderline clinical importance. No definite conclusions, however, can be drawn regarding these findings, which must be examined in future studies.

The effect of SMT on CLBP has been evaluated in several RCTs, (69-77); these studies collectively provide some evidence of short-term benefits. Four studies have included long-term follow-up in the design (34, 70, 72, 75). Meade et al. employed the longest follow-up and reported reductions in pain after 1 yr in patients with CLBP that were close to the magnitude in our study (72).

One of the aims of this study was to compare effective exercise regimens for CLBP, specifically the stretching exercises reported by Deyo (23), and the dynamic trunk exercises studied by Manniche (21, 78) and Hansen (79). The similarity in demographics and clinical characteristics of patients reported in these studies and the nature of the outcome measures allowed us to make important comparisons. Our study showed a similar reduction in pain but a higher reduction in low back disability (rated on similar and validated scales) in SMT/TSE patients after 3 months of treatment when compared with the findings of Manniche's study. In that study, patients participated in an almost identical exercise program, with approximately twice as many exercise hours, but with no SMT.

Hansen et al. studied the effects of the exercise program described by Manniche but with less than half the number of exercise hours used in our study. They reported this therapy to be more effective for women, patients with low fitness levels and those individuals with sedentary/light job functions. In our study, we found neither gender differences in any of the groups nor an indication that any of the therapies was more effective for individuals with less physically demanding occupations; however, our study was not designed to test for these effects and had inadequate power to do so.

In Deyo's study, unsupervised stretching exercises were associated with a higher reduction in pain after 1 month of 10 1-hr sessions compared with the SMT/Stretching group in our study. Both studies showed the same amount of improvement in low back disability, assessed with similar modified short versions of the Sickness Impact Profile (46). Two months after the active intervention in Deyo's trial, most patients had discontinued the exercises and the initial improvements were

Table 6. *Reduced activity and inability to work because of low back pain*

Proportion of patients	Group A SMT + strength. exercise	Group B NSAID + strength exercise	Group C MT + stretch. exercise
		%	
During month before study entry	(n = 71)	(n = 52)	(n = 51)
One or more days with inability to work	8.4	9.6	11.8
Proportion of all possible work days lost[a]	1.2	3.2	1.4
One or more days with reduced activity	55.7	53.8	54.1
Proportion of all possible lowered activity days[a]	12.9	17.0	13.8
At study entry			
Sick-listed	0	0	0
Working at full capacity	76.1	80.8	74.5
Working at reduced capacity	11.2	9.6	23.5
Without job	12.7	9.6	2.0
During month before study completion	(n = 56)	(n = 40)	(n = 38)
One or more days with inability to work	5.4	5.0	8.3
Proportion of all possible work days lost[a]	0.9	0.3	1.1
One or more days with reduced activity	33.9	25.0	44.5
Proportion of all possible lowered activity days[a]	7.7	5.0	13.1
At study completion			
Sick-listed	0	0	0
Working at full capacity	82.1	77.5	77.8
Working at reduced capacity	3.6	5.0	11.1
Without job	14.3	17.5	11.1
During year following study completion	(n = 52)	(n = 38)	(n = 35)
One or more days with inability to work	9.6	21.1	11.4
Proportion of all possible work days lost[b]	0.3	0.4	0.2

[a] 22 (days) × number of subjects.
[b] 264 (days) × number of subjects.

diminishing. Twice as many supervised stretching exercise sessions in combination with SMT in our study may explain why the reduction in pain found after 3 months of treatment was sustained at the 1-yr follow-up. When reviewing the trials that have employed exercise in the management or prevention of LBP, it becomes apparent that an exercise dose-response phenomenon may exist, because study patients involved in relatively few hours of exercise (less than 16 hr) tend to have poorer outcomes (10, 11, 20, 23, 34, 78, 79).

Study Limitations

Patients in this study were recruited through newspaper advertising; it may be argued that they differ from patients seeking care in clinics on their own. However, selection of patients based on this study's inclusion/exclusion criteria likely excluded subjects that deviated substantially from an expected clinical population. There is also evidence to suggest that sufficient clinical and demographic similarity may often exist between patients recruited for RCTs through advertising and through clinical settings, making generalization of findings from studies like ours possible (23, 80). Finally, our patients were very similar to the patients studied by Manniche (21, 78), who were recruited through clinics.

Dropouts may significantly bias the outcome of a trial (81). In our study, the number of dropouts was high but varied little among groups, and there is no indication that the dropouts were different from the subjects that remained in the study based on clinical and demographic baseline characteristics and available outcomes data. The improvement in all three groups over time may be explained by the combination of the natural history of CLBP and such phenomena as regression to the mean, expectation of positive therapeutic outcome and the nonspecific effects of patient-provider interaction. Given that the vast majority of patients had long-standing, stable, moderately severe LBP, the changes in outcomes over time seem to be much more favorable than the natural history or the result of the combination of nonspecific effects. The Manniche trial, which most closely resembles ours in terms of patient characteristics, therapeutic intervention and length of follow-up period, supports this contention (21, 78). In the Manniche trial, patients in the group that completed minimal training and were exposed to similar attention as the other study groups had significantly poorer outcomes during the treatment phase and reverted to baseline values in pain and disability at the 1-yr follow-up. In contrast, patients who had completed the most intensive exercise program, and in particular continued to exercise, reported improved ratings for pain both during treatment and at 1-yr follow-up, which is comparable with what was shown in our study.

We have solely examined the relative efficacy of combinations of therapies precluding us from assessing positive or negative interactions between the therapeutic components. We decided not to address the question of whether the combination of SMT and exercise or medication and exercise leads to therapeutic benefits that are superior to no treatment or applying SMT, exercise or NSAID therapy alone, because it would have required a factorial design that involved more subjects to retain the same statistical power and it would not have controlled for nonspecific therapeutic effects.

The optimal dose-response for SMT and NSAID and trunk exercise still remains to be established.

CONCLUSION

We were unable to demonstrate clearly that SMT combined with TSE was superior to NSAIDs combined with TSE or to SMT combined with stretching exercise. A definite tendency toward a sustained reduction of analgesic medication use at the 1-yr follow-up was evident in the group that received the combination of SMT and TSE. The same reduction was not found in the group that received the combination of NSAIDs and TSE. In this study, each of the three therapeutic regimens was associated with a clinically important improvement over time with respect to patient-rated pain, disability and general functional health status. Compared with baseline values, the approximately 50% reduction in LBP and low back disability, plus the 17% improvement in general health status after 3 months of intervention, and the 40% reduction in pain at the 1-yr follow-up in all three groups are considered clinically important and superior to the expected natural history of long-standing CLBP. For the management of CLBP, trunk exercise in combination with SMT or NSAID therapy seems to be beneficial and worthwhile. The magnitude of placebo effects, the cost-effectiveness and the relative risks of side effects associated with these types of therapy need to be addressed in future studies.

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