ORIGINAL ARTICLES

LONG-TERM FOLLOW-UP OF A RANDOMIZED CLINICAL TRIAL ASSESSING THE EFFICACY OF MEDICATION, ACUPUNCTURE, AND SPINAL MANIPULATION FOR CHRONIC MECHANICAL SPINAL PAIN SYNDROMES

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ABSTRACT

Objective: To assess the long-term benefits of medication, needle acupuncture, and spinal manipulation as exclusive and standardized treatment regimens in patients with chronic (>13 weeks) spinal pain syndromes.

Study Design: Extended follow-up (>1 year) of a randomized clinical trial was conducted at the multidisciplinary spinal pain unit of Townsville's General Hospital between February 1999 and October 2001.

Patients and Methods: Of the 115 patients originally randomized, 69 had exclusively been treated with the randomly allocated treatment during the 9-week treatment period (results at 9 weeks were reported earlier). These patients were followed up and assessed again 1 year after inception into the study reapplying the same instruments (ie, Oswestry Back Pain Index, Neck Disability Index, Short-Form-36, and Visual Analogue Scales). Questionnaires were obtained from 62 patients reflecting a retention proportion of 90%. The main analysis was restricted to 40 patients who had received exclusively the randomly allocated treatment for the whole observation period since randomization.

Results: Comparisons of initial and extended follow-up questionnaires to assess absolute efficacy showed that only the application of spinal manipulation revealed broad-based long-term benefit: 5 of the 7 main outcome measures showed significant improvements compared with only 1 item in each of the acupuncture and the medication groups.

Conclusions: In patients with chronic spinal pain syndromes, spinal manipulation, if not contraindicated, may be the only treatment modality of the assessed regimens that provides broad and significant long-term benefit. (J Manipulative Physiol Ther 2005;28:3-11)

Key Indexing Terms: *Acupuncture; Chiropractic; Medicine; Spinal; Pain*

Chronic spinal pain is commonly triggered by an injury or disease,[1] and mechanical spinal pain presents a diagnostic and treatment challenge because reaching a specific diagnosis is often impossible.[2] A pathological cause cannot be identified for most episodes of spinal pain[3] with only approximately 15% of patients being given a definitive diagnosis.[4]

The search for effective conservative treatments for acute and chronic nonspecific low-back pain has been largely inconclusive,[5,6] as is the case with neck and thoracic spine pain. Conflicting claims exist for nearly every form of conservative therapy for low-back disorders, probably because studies have been performed among widely differing types of patients with back pain or because of methodological problems.[7] Thus, there is still sparse conclusive knowledge about the absolute efficacy of any intervention for chronic spinal pain syndromes, although Giles et al[8] found a high level of patient satisfaction with a multidisciplinary team approach to spinal pain syndromes. A review of the conflicting literature on the efficacy and effectiveness of medication, acupuncture, and spinal manipulation for chronic uncomplicated spinal pain treatment can be found in Giles and Muller.[9]

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What is not disputed is that chronic spinal (ie, neck and "back") pain syndromes have an immense impact on public health, pose an enormous financial strain on the health systems in developed countries, and affect the economy by lost working time through illness. The high incidence of back pain, its chronic and recurrent nature in many patients, and its contribution as a main cause of absence from work are well known.[10] Furthermore, the rise in the use of nontraditional health care providers partly reflects the large number of patients with chronic pain, especially spine-related disorders, who feel they must go outside mainstream medicine to find help.[11]

The immense burden of chronic spinal pain syndromes, in terms of suffering as well as in financial terms, stands in stark contrast to the paucity of evidence-based knowledge about their diagnosis and treatment. It is against this background that the Giles and Muller[9] randomized clinical trial was designed with a rigorous protocol and a broad range of outcome measures in an attempt to overcome the above-mentioned methodological problems and to add much-needed evidence-based knowledge to this important area.

In their 109-patient randomized clinical trial, Giles and Muller[9] included both neck and "back" (ie, low back and thoracic spine) pain patients as it would have been unethical to treat only 1 painful spinal level and to ignore a concurrent additional painful spinal level, particularly when 47 (68%) of 69 patients presented with pain at more than 1 spinal level.

Giles and Muller,[12] using a "fastidious"[10] approach (ie, standardized treatment regimens of medication, needle acupuncture, or spinal manipulation with respect to the type, frequency, and duration of each treatment regimen), showed in a public hospital-based multidisciplinary spinal pain unit pilot study and in the subsequent larger study[9] that in patients with chronic (ie, >13 weeks' duration) spinal pain, spinal manipulation, if not contraindicated, seems to result in greater short-term (9 weeks) improvement than acupuncture and medicine. There were no particular distinguishing features for pain other than pain of "mechanical" origin in all of the 3 spinal areas. In addition, there were no mechanisms of injury that were distinct enough to warrant separate investigation or management, and all patients were considered to have mechanical joint dysfunction after extensive investigations (ie, physical examination and various forms of imaging with or without laboratory tests as indicated by the history).

A thorough systematic review of the literature indicates that evidence-based knowledge (ie, originating from randomized clinical trials using standardized treatment regimens) about the short-term efficacy of different conservative treatment regimens for chronic spinal pain syndromes is scarce, and it is virtually nonexistent with respect to long-term benefit.

Very few long-term (ie, of at least 1-year follow-up) clinical trials of treatment(s) of patients with various spinal problems could be located for low-back pain[13-15] and chronic neck pain.[16] Moreover, these trials deliberately followed a pragmatic methodology (ie, details of the type, frequency, and duration of each treatment were at the discretion of the treating clinician) as opposed to a fastidious approach (ie, exclusively standardized treatment regimens) and consequently lacked the methodological scientific rigor necessary to be able to attribute an observed effect to only 1 specific standardized treatment modality.

The present study assesses the extended follow-up (of at least 1 year) efficacy of medication, needle acupuncture, and spinal manipulation, as standardized and exclusive treatment regimens. Patients with chronic spinal pain syndromes from the fastidious approach of the Giles and Muller[9] randomized clinical trial were eligible for this study if they adhered to the study protocol for their treatment period.

Methods

Study Protocol

A randomized clinical trial using exclusive and standardized treatment modalities (ie, using a "fastidious" as opposed to "pragmatic" approach) was conducted at the multidisciplinary spinal pain unit of Townsville's General Hospital from February 1999 to October 2001. Patients with chronic (>13 weeks) spinal pain syndromes were randomly allocated to 1 of 3 exclusive and standardized treatment regimens: medication, needle acupuncture, or spinal manipulation. A range of validated subjective questionnaires and objective measurements were taken initially and at the end of the study treatment period. Detailed methods of this trial were published[9] and are only summarized in this extended follow-up paper. The same validated subjective instruments were used again as the extended follow-up questionnaires that were sent out to patients 12 months after their inception into the study.

Inclusion and exclusion criteria for this extended follow-up study are the same as for the short-term study.[9] Inclusion criteria were having "mechanical" spinal pain syndrome for a minimum of 13 weeks and being at least 17 years of age. Exclusion criteria were nerve root involvement, spinal anomalies other than sacralization or lumbarization, pathological conditions other than mild to moderate osteoarthrosis, greater than a grade 1 spondylolisthesis of L5 on S1, previous spinal surgery, or leg length inequality of >9 mm with postural scoliosis. The only additional criterion of this long-term study was that only those were included who received exclusively their randomly allocated treatment regimen during the 9-week treatment period.

Randomization

Patients satisfying the inclusion and exclusion criteria and giving their informed consent were subsequently randomly allocated by drawing 1 envelope from a box of well-shuffled sealed envelopes containing 1 of 3 possible

treatment codes as detailed in the short-term study[9] in a balanced way to 1 of 3 exclusive and standardized treatment regimens: medication, acupuncture, or manipulation.

Interventions

Medication patients were normally given celecoxib (Celebrex) (200 to 400 mg/d; 27 patients) unless celecoxib had previously been tried; the next drug of choice was rofecoxib (Vioxx) (12.5 to 25 mg/d; 11 patients), followed by acetaminophen (paracetamol) (500-mg tablets 2-6 per day; 5 patients). These doses were typical of those used in daily practice and conformed to the MIMS Australia (www.mims.com.au) pharmaceutical product information publication and to the manufacturer's Consumer Medicine Information leaflet. In addition, doses were related to patients' weight with the severity of symptoms playing a minor role. In 4 cases where celecoxib was prescribed at 200 mg/d, the medical physician increased the dose to 400 mg/d, when indicated by symptoms at review and if there had been no adverse reaction. Because all patients had already tried some form of medication, it was necessary to have a choice of 3 drugs from which to choose one that had not already been tried by a patient. Additional fortnightly 20-minute office visits defined this intervention until patients became asymptomatic or achieved a status of feeling that they had achieved acceptable pain relief.

Acupuncture was performed using sterile HWATO Chinese Acupuncture Guide Tube Needles (50 mm long; 0.25-mm gauge) for 20-minute appointments. For each patient, 8 to 10 needles were placed in local paraspinal intramuscular maximum pain areas, and approximately 5 needles were placed in distal acupuncture point meridians according to the "near and far" technique (upper limb, lower limb, or scalp).[17] Once patients could satisfactorily tolerate the needles, needle agitation was performed by turning or 'flicking' the needles at approximately 5-minute intervals. Two 20-minute office visits per week defined this intervention until patients became asymptomatic or achieved a status of feeling that they had achieved acceptable pain relief.

High-velocity low-amplitude spinal manipulative thrust to a joint[10,18] was performed as judged safe and usual treatment by the treating chiropractor for the spinal level of involvement to mobilize the spinal joints at that level. Two 20-minute office visits per week defined this intervention until patients became asymptomatic or achieved a status of feeling that they had achieved acceptable pain relief.

Ethical Approval

Ethical approval for all parts of the study was granted by the Northern Regional Health Authority's Hospital Institutional Ethics Committee (reference 32/94).

The patient flow chart is detailed in Fig 1: Out of the initially randomized 115 patients, a subsample of 69 patients

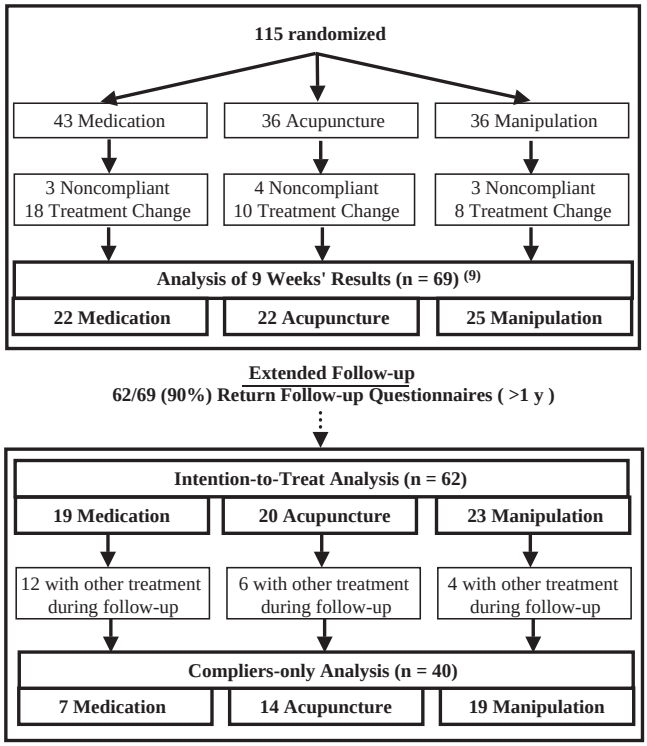

Fig 1. *Patient flow chart for the original short-term (9-week) treatment study followed by the extended follow-up study.*

received exclusively the randomly allocated treatment regimen during the short-term study treatment period[9] and was therefore eligible for the extended follow-up study period.

Outcome Measures

The extended follow-up questionnaire comprised the identical validated subjective measurement instruments as used at the initial visit and at the end of the 9-week treatment period: pain frequency scores; Visual Analogue Scale (VAS) for pain intensity,[19] the Oswestry questionnaire (Oswestry)[20] for low-back and thoracic spine pain ("back" pain), the Neck Disability Index for neck pain,[21] and the Short-Form-36 Health Survey questionnaire (SF-36).[22,23] For details, please refer to Giles and Muller.[9] The bending and extension measurements were not available for the extended follow-up because the wide catchment area and a mobile population impeded the physical reexamination of patients.

The extended follow-up questionnaires were routinely mailed out to patients 12 months after their treatment period concluded. An additional final effort was made at the end of the overall study period (November 2002) to locate the few patients that had changed their address or had not returned their extended follow-up questionnaires at 12 months after their study treatment period.

Potential Confounders

Sex, socioeconomic status, age, body mass index (BMI), and duration of pain syndromes before inception were identified as potential confounders and consequently recorded.

Data Handling and Statistical Analysis

Color coding of patients' data (different to the 9-week study) was used to ensure that no one involved with data analysis would be aware of the treatment provided. Data were analyzed using SPSS version 10 (SPSS, Inc).

Because the frequency distributions of the main outcome measures proved to be skewed, medians were used as measures of central tendency and quartiles as measures of dispersion. Consequently, nonparametric test procedures were used for testing numerical variables. Preintervention follow-up changes within the 3 treatment groups were tested using an exact version of the paired Wilcoxon signed rank test. For comparisons between the 3 treatment groups at inception, an exact version of the Mann-Whitney U test was used. All tests relating to categorical variables were assessed with exact χ^2-type tests. Additional checks for potential confounders (including sex, age, socioeconomic status, BMI, and the duration of the pain syndromes before inception to the study) and possible interactions of these confounders were performed by multiple regression models and logistic regression approaches. For all tests, a P value of below .05 was regarded as statistically significant.

This study was concerned with an area where no accepted "gold standard" exists and where very little is known about the absolute benefit of the different treatment regimens. Consequently, the main emphasis of analysis relates to paired precomparison/postcomparison to assess absolute efficacy and was performed in 2 blocks: the "intention-to-treat" (ITT) and the "compliers-only" analysis, respectively.

Dissatisfied patients who had to change treatment modalities or were otherwise noncompliant before the 9 weeks' follow-up proved to have no distorting effect on the outcome as reported in the respective ITT analysis of the short-term study.[9] The present ITT analysis (n = 62) is consequently based on all patients eligible for this extended follow-up study (n = 69) who returned the extended follow-up questionnaire (n = 62). Only 7 patients not returning the long-term follow-up information (ie, all of them left the area went "missing" for reasons unrelated to the outcome, eg, relocated) had to be treated as "missing." Patients analyzed in the ITT analysis therefore received only their randomly allocated treatment regimen during the initial 9-week study treatment period, however, could have received treatments other than the randomized regimen during the extended follow-up period but were still analyzed within the randomized group according to the ITT principle.

The public hospital's computer patient-booking system was monitored to track patients and to determine whether any of these patients actually had re-presented to the multidisciplinary spinal pain unit or to another clinic within the public hospital for spinal pain treatment during the extended follow-up period. During patient tracking, it was found that 22 patients received, at some stage after their study treatment period but within the extended follow-up period, a different type of treatment from the randomized regimen. Consequently, a compliers-only analysis (n = 40) was performed that was restricted to those patients who never (including the extended follow-up period of at least 1 year) received any treatment other than the randomly allocated regimen through the free public hospital system (Fig 1).

Results

Participants and Follow-up

Overall, a total of 62 extended follow-up questionnaires were obtained from 69 patients eligible for this extended follow-up study reflecting a retention proportion of 90%. One person had left Australia, 3 army members were relocated and could not be traced for confidentiality reasons, and 3 patients left the area without any trace. The overall median extended follow-up period was 12 months (with a minimum of 12 months and a maximum of 36 months) with most (75.8%) of these questionnaires returned at exactly 12 months after the commencement of treatment. The median follow-up time for all groups was identical (12 months).

Table 1 details initial characteristics of the 62 extended follow-up patients and the respective groups in the 3 treatment modalities. None of the comparisons of the initial measurements between the 3 treatment groups revealed any significant differences.

Main Analysis

Intention-to-Treat Analysis. Table 2 details the findings of the initial status (T1) and the extended follow-up measurements (TE) of at least 1 year for all 62 patients who returned the long-term follow-up questionnaire and adhered to the randomized treatment during the study treatment period, although may thereafter have received other than the randomized treatment during the extended follow-up period.

Compliers-only Analysis. Table 3 displays the same type of information but only for the subgroup of 40 patients who never received any other than the randomized treatment during the study treatment period and within the extended follow-up period. However, of these 40 compliers, some received additional treatments in their randomized treatment regimen after their treatment period: 2 required 1 to 4 acupuncture follow-up visits, 3 required 1 to 4 medical follow-up visits, and 3 required 1 to 4 spinal manipulation follow-up visits.

In both Tables 2 and 3, the displayed P values refer to statistical tests comparing the initial measurements before the study treatment period (T1) and the extended follow-up

Table 1. *Initial assessments and control of randomization of those with extended follow-up*

Variable	Total (n = 62)	Manipulation (n = 23)	Acupuncture (n = 20)	Medication (n = 19)	*P* value
Sex, men	53.2%	47.8%	55.0%	57.9%	.81
Socioeconomic					
Tradesmen	22.6%	17.4%	25.0%	26.3%	.70
Pensioner/unemployed	19.4%	30.4%	5.0%	21.1%	
Manager/clerk/sales	24.2%	26.1%	25.0%	21.1%	
(Para) Professional	17.7%	13.0%	25.0%	15.8%	
Other	16.1%	13.0%	20.0%	15.8%	
Age (quartiles)	39 (29-46)	39 (29-53)	38 (27-47)	39 (26-43)	.54
BMI	25.8 (22.8-29.2)	25.7 (21.4-29.6)	24.9 (23.8-28.7)	26.0 (22.1-29.5)	.94
Pain duration (y) back	3 (0.63-10)	3 (0.15-11)	2.5 (0.63-6)	4 (2-11)	.21
Pain duration (y) neck*	2 (0.02-6)	3 (0.02-8.5)	2 (0.3-6.5)	1.5 (0.3-4.5)	.74
Time since first treatment (mo)	12 (12-12.5)	12 (12-12)	12 (12-36)	12 (12-12)	.08

Displayed are percentages for categorical variables and medians with interquartile ranges for numerical variables. *P* values refer to tests between the treatment groups.

* Analysis restricted to those who had a neck problem at least once (n = 47).

Table 2. *Results of ITT analysis (n = 62)*

Variable	Total (n = 62)	Manipulation (n = 23)	Acupuncture (n = 20)	Medication (n = 19)
Pain frequency, back				
T1	4 (4-5)	5 (4-5)	4 (4-5)	4 (3-5)
TE	4 (2-5)	4 (2-5), *P* = .001	4 (1-5), *P* = .04	4 (2-5), *P* = .26
Pain frequency, neck*				
T1	4 (2-5)	4 (3.5-5)	4 (2.5-4.5)	2 (1-5)
TE	3 (1-4)	2 (1-4), *P* = .03	3 (0.5-4), *P* = .09	4 (2.5-4.5), *P* = .36
Pain scale (VAS), back				
T1	5 (3.8-8)	5 (3-8)	6 (4.3-8)	5 (3-7)
TE	3.8 (2-6.4)	3.7 (1.4-6.8), *P* = .05	3.9 (1.8-6.1), *P* = .01	3.9 (2-6.4), *P* = .94
Pain scale (VAS), neck*				
T1	6 (3-8)	6 (3.5-7)	7 (4.5-9)	4 (2-8)
TE	3.5 (0.4-6)	2.8 (1-8), *P* = .04	2.5 (0.1-4.8), *P* = .006	4.7 (3.3-6.5), *P* = .70
Oswestry Back Pain Index				
T1	26 (16-38)	24 (10-32)	27 (18-41)	28 (20-42)
TE	20 (6-37)	16 (6-30), *P* = .09	13 (2-33), *P* = .003	24 (8-42), *P* = .27
NDI*				
T1	36 (20-48)	28 (18-44)	36 (22-50)	42 (12-50)
TE	24 (6-44)	20 (8-40), *P* = .045	24 (0-32), *P* = .005	36 (16-50), *P* = .26
SF-36				
T1	47 (32-63)	57 (38-67)	46 (32-56)	39 (25-65)
TE	65 (38-80)	77 (54-86), *P* = .007	55 (40-76), *P* = .02	66 (29-78), *P* = .004

Displayed are medians with interquartile ranges. *P* values refer to tests between initial (T1) and extended assessments (TE). For all variables except SF-36, a decrease in the score indicates improvement; for SF-36, an increase indicates improvement. *NDI*, Neck Disability Index.

* Analysis restricted to those who had a neck problem at least once (n = 47).

questionnaires (TE). Not a single comparison between the results obtained at the end of the study treatment period (9 weeks) and the results obtained for this extended follow-up observations (TE) study returned any significant result neither for the ITT nor the "compliers-only analysis" (data not displayed).

In the ITT analysis (Table 2), in both the manipulation and the acupuncture groups, improvements in each of the 7 examined measurements are observed when the extended follow-up findings (TE) are descriptively compared with the pretreatment measurements (T1). Subsequent statistical testing revealed that, in both groups, 6 of the 7 variables were at or below the significance level. The medication group, in contrast, descriptively deteriorated in 2 of the 7 variables (pain frequency neck, and pain scale [VAS] neck), and only a single variable (SF-36) displayed a significant improvement.

In the compliers-only analysis (Table 3), improvements were observed in all variables in both the manipulation and the acupuncture group when the TE findings are descriptively compared with the T1 measurements. The medication arm descriptively deteriorated in 2 items. Statistical testing

Table 3. *Results of compliers only analysis (n = 40)*

Variable	Total (n = 40)	Manipulation (n = 19)	Acupuncture (n = 14)	Medication (n = 7)
Pain frequency, back				
T1	4 (4-5)	4 (4-5)	5 (3.5-5)	4 (3-5)
TE	4 (1.3-4.8)	3 (1-4), $P = .002$	4 (1.8-5), $P = .13$	4 (1-4), $P = .44$
Pain frequency, neck*				
T1	4 (3.5-5)	4 (4-5)	4 (2-5)	4 (1-5)
TE	2 (1-4)	2 (1-4), $P = .006$	2 (0-5), $P = .24$	4 (2.5-4), $P = .75$
Pain scale (VAS), back				
T1	5 (3-7.8)	5 (3-7)	5.5 (4-8)	3 (0-8)
TE	3.4 (1.9-6.1)	2.8 (0.7-6.2), $P = .06$	4.5 (2.4-5.7), $P = .13$	3.1 (1.9-3.6), $P = .47$
Pain scale (VAS), neck*				
T1	6 (3.5-8.5)	6 (3.5-7)	6 (4-9)	6 (1.5-8.5)
TE	2.7 (0.2-5.7)	2.3 (0.4-4.8), $P = .004$	2.5 (0-7.9), $P = .1$	3.9 (2.9-5.7), $P = .44$
Oswestry Back Pain Index				
T1	26 (14-31)	22 (10-30)	29 (21-46)	24 (14-30)
TE	16 (5-28)	9 (4-24), $P = .12$	19 (5-37), $P = .02$	20 (4-42), $P = .5$
NDI*				
T1	36 (20-47)	28 (18-40)	42 (20-50)	47 (21-55)
TE	20 (4-35)	18 (6-27), $P = .02$	24 (0-36), $P = .06$	30 (13-49), $P = .31$
SF-36				
T1	47 (33-64)	57 (38-68)	45 (31-52)	41 (23-74)
TE	70 (49-83)	80 (59-88), $P = .006$	53 (38-75), $P = .1$	70 (50-85), $P = .02$

Displayed are medians with interquartile ranges. *P* values refer to tests between initial (T1) and extended (TE) assessments. For all variables except SF-36, a decrease in the score indicates improvement; for SF-36, an increase indicates improvement.

* Analysis restricted to those who had a neck problem at least once (n = 29).

revealed that only in the manipulation group, 5 of the 7 observed improvements were statistically significant which compares with only 1 item in each of the acupuncture and the medication groups, respectively.

The percentages of those who received, at any time after randomization, a treatment other than the allocated regimen (because of side effects or because it was considered that the allocated treatment showed no effects) differed significantly ($P < .05$) between the treatment groups. The respective percentages were manipulation 38.7%, acupuncture 53.3%, and medication 81.2%, respectively. For these calculations, 10 noncompliers during the 9-week study treatment period and 7 patients who did not return the extended follow-up questionnaires in the present study were excluded (Fig 1).

For all the main outcome measures, additional analyses were performed to assess potential confounding of variables such as age, sex, BMI, pain duration (of both neck and back), and involvement in litigation. Bivariate analyses proved that none of the assessed variables were significantly correlated with the main outcome measures. Additional multivariate models also disproved any influence of these variables on the outcome measures thus effectively excluding the presence of any relevant confounding bias.

Discussion

This is, to the authors' knowledge, the first report on long-term efficacy of 3 distinct and standardized treatment regimens for patients with chronic spinal pain syndromes using a "fastidious" approach; that is, the only type of study from which potentially valid inferences of cause and effect can directly be drawn.[24] The validity of the study (ie, the absence of different types of bias) is hereby essential and will be discussed first.

Selection Bias

The study sample has a broad socioeconomic background and a wide age range. Quite stringent exclusion criteria guaranteed a pathologically homogeneous sample. It was successfully ascertained that all "dropouts" occurring during the study treatment period, as well as during the extended follow-up period thereafter, occurred for reasons unrelated to the study outcome (ie, moving overseas, being transferred, etc). A high retention proportion of 90% for this extended follow-up study, together with the above stated facts, supports the generalizability of the findings.

Information Bias

Intention-to-treat analyses including noncompliers (1 for the 9-week treatment period[9] and 1 for the presented study) revealed results quite consistent with the respective compliers-only analyses thus effectively diminishing any relevant misclassification bias from noncompliers. A different color code was used from that in the 9-week analysis to ensure successful blinding[25] of data analysis. All data handling and analyses were again performed before the treatment color code was broken. The senior biostatistician was involved

neither in the data collection process nor in any daily business of the center, thus minimizing information bias.

Blinding of the physician was not possible; even if, for instance, a "sham" acupuncture treatment would have been regarded as ethically justifiable, the acupuncturist would still have to know what treatment to perform. Blinding of the patients was not possible because there is, for instance, no known practical way to perform a sham manipulation. The potential for information bias, in this context, however, seems limited by the standardized treatment regimens and the fact that the clinician was not involved in measuring outcome. Information bias arising from a placebo effect or from a self-limiting effect is highly unlikely because patients in this study had chronic spinal pain syndromes (the average duration of having this exceeded 2 years) and had long histories of having sought pain relief. Improvement caused by the abovementioned effects could be expected in cases with acute spinal pain[26] but seems rather unlikely in long-term cases.

Confounding Bias

Table 1 indicates that the 3 groups were very similar in their characteristics at inception. Additional bivariate and multivariate analyses of potential effects of these characteristics on the outcome measures also disproved any relevant confounding bias.

According to Turk and Rudy,[27] no clinical study can be completely valid because of the complexities of extended follow-up trials; however, we have attempted to conduct a well-executed extended follow-up randomized trial with a rigorous protocol, and the overall validity of the reported findings does not seem to be negatively affected by any obvious bias. The main emphasis of this study was to assess absolute efficacy; consequently, within-group comparisons constituted the basis for analysis. Additional across-group comparisons, as often used in clinical trials to assess relative efficacy (eg, when new treatments are compared with an accepted "gold" standard), would have resulted in 2-dimensional testing (ie, determining and validating a gold standard within the same data set) defying any meaningful interpretation. The validation process (ie, the relative comparison) consequently has to be reserved for future trials.

However, the presented trial with successful randomization, thorough concealment, and within-group analyses applied the most powerful design possible to a research area where no accepted gold standard exists and where the emphasis, at this early stage of the research process, has to be on absolute, as opposed to relative, efficacy.

It should be noted that definitions of chronicity for low-back pain have been suggested by various authors such as Nachemson and Bigos[28] and by Skouen et al.[29] For the reported study, the definition for chronic pain duration was more than 13 weeks, so it is against this definition that these results are to be interpreted.

The overall results of this extended follow-up efficacy study appear to favor the application of manipulation and suggest that manipulation, if not contraindicated, and, to some extent, also needle acupuncture seem to successfully achieve long-term benefits in chronic spinal pain syndrome patients. However, no such benefit could be observed for medication. These results not only corroborate the findings of the 9-week analysis[9] but also of the smaller pilot study.[12] It seems noteworthy that the comparison of the percentages of those who had to change the treatment modality (because of side effects or unsatisfactory results) also appears to favor manipulation in that manipulation showed by far the lowest proportion (38.7%) of changeovers compared with acupuncture (53.3%) and medication (81.2%). Consequently, spinal manipulation appeared to provide the highest satisfaction. Moreover, both the 9-week findings and the extended follow-up results are consistent with conclusions by Meade et al,[10,13] who, on comparing chiropractic with hospital therapists for treating low-back pain as they would in day-to-day practice ("pragmatic" approach), reported that those treated by chiropractic derived more short-term and long-term benefit and satisfaction than those treated by hospital therapists.

Medication apparently did not achieve an improvement in chronic spinal pain, although the SF-36 indicator of general health status did show an improvement ($P = .02$) for general health status. This may reflect some satisfaction with not having the inconvenience of needing to attend twice weekly for treatment and/or may also suggest that medication did not act as a nocebo.

It is interesting that the application of manipulation and acupuncture seem roughly equally successful in the ITT analysis, but only manipulation seems of broad-based long-term benefit in the compliers-only analysis. A more detailed look at the noncompliers data revealed that 4 of the 6 patients in the acupuncture arm who had some other type of treatment than the randomly allocated regimen during the extended follow-up period were actually treated with manipulation. Therefore, an artificial inflation of the effect of acupuncture treatment in the ITT analysis by additional manipulation therapy seems likely. The compliers-only analysis therefore seems to provide information that is more accurate.

The ITT analysis, however, is per se relevant because it displays the information that would be available from a similar trial in a larger metropolitan setting where the information on additional treatment may not be collected (or at least only less reliably). The setting of the present trial in a small, geographically relatively isolated community which is served by only 1 major public (providing free treatment) hospital rendered it possible to directly collect precise information on possible additional treatments during the extended follow-up period by checking the single public hospital's computer records.

This advantage of the small community setting, however, is partly offset by a long inception period (several years) to

reach the minimum necessary sample size. In this context, it seems noteworthy that because of the necessarily stringent inclusion and exclusion criteria, 533 patients had to be seen (and treated) at the unit to achieve the reported sample sizes, reflecting that only around 1 (22.3%) of 5 patients fulfilled the inclusion /exclusion criteria.

Another general reason for the relatively small sample sizes for the extended follow-up analysis, however, lies in the very nature of this strictly fastidious approach itself: the group of strict compliers necessarily dwindles with increasing period of observation as the likelihood increases that additional treatment (eg, simple pain killers) is used by those in the long-term condition. This consequence of the fastidious approach, however, is easily compensated for by the fact that it is the only approach where an observed effect can be unambiguously attributed to 1 specific treatment modality only (if the study follows an otherwise rigorous methodology). Moreover, it seems worth reiterating that statistical testing takes into account the sample size and the observed effects proved to be both medically relevant and statistically significant.

It should be emphasized that this study was exclusively concerned with chronic spinal pain, and therefore, no statement whatsoever can be made about the potential role of the investigated regimens in treating acute spinal pain syndromes.

Conclusion

Chronic mechanical spinal pain syndromes are prevalent conditions[30] that tend to create a cluster of related problems reaching from withdrawal from social activity to a compromised immune function.[31] The associated resulting direct and indirect costs in industrialized communities are vast.[32] A large community study seems to be the next logical step to address this important problem and to further investigate the reported findings. Consideration should also be given to assessing the efficacy of other treatment modalities. This suggested study should be based on a fastidious approach and incorporate an expanded multidisciplinary team to gain further evidence-based information on the absolute and also the relative efficacy of all forms of available treatments.

The results of this "fastidious" approach were able to add some information regarding the efficacy of treatment regimens in patients with chronic spinal pain syndromes. Overall, patients who have chronic mechanical spinal pain syndromes and received spinal manipulation gained significant broad-based beneficial short-term and long-term outcomes. For patients receiving acupuncture, consistent improvements were also observed, although without reaching statistical significance (with a single exception). For patients receiving medication, the findings were less favorable. Larger studies are now clearly justified.

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