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The long-term course of patients undergoing alternative and integrative therapy for lumbar disc herniation: A prospective observational 3-year follow-up study

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ABSTRACT

Objectives: This study aimed to (1) assess the efficacy and safety of an integrative complementary and alternative medicine (CAM) approach in management of lumbar disc herniation (LDH) with sciatic pain and (2) investigate pain relapse and use of medical care and surgery rate in patients who actively chose non-surgical CAM treatment for LDH.

Study design/Setting: This prospective observational study was undertaken at a Korean medicine hospital outpatient setting in Korea.

Participants: A total of 128 consecutive LDH patients with a numeral rating scale for leg pain of ≥5 completed 6 months of CAM treatment after recruitment from November 2006, and 73/128 participants (57%) attended follow-up 3 years later.

Interventions: Six months of CAM treatment (herbal medicine, acupuncture, bee-venom pharmacopuncture, and Chuna manipulation).

Primary outcome measures: Visual analogue scale (VAS) for low back and leg pain, Oswestry Disability Index (ODI), and SF-36 Health Survey.

Secondary outcome measures: Neurological impairment (muscular weakness, sensory loss, straight leg raise test), MRIs, recurrence of low back pain and/or radiating pain, and use of medical care.

Results: Ninety-one patients could be assessed for surgical state, of which 4 replied they had received surgery. Seventy-three patients attended the 3 year follow-up. The baseline VAS of back pain (4.37±2.70) decreased after treatment (0.90±1.01; P<0.001) and was maintained at 3 years (1.12±1.64; P=0.19). Baseline VAS of leg pain (7.57±1.40) also decreased upon treatment (0.82±1.18; P<0.001) and was sustained at 3 years (0.99±1.58; P=0.34). ODI scores declined from 40.74±16.15 to 9.84±9.67 (P<0.001), then further to 6.30±7.19 (P<0.01). SF-36 scores increased from 34.96±13.30 to 69.20±14.96 (P<0.001), reaching 76.19±14.45 (P<0.001) at 3 years. Thirty-seven patients reported recurrence of pain, and most chose CAM treatment for management of relapse symptoms.

Conclusions: Although absence of a control group prevents validation of effectiveness, many patients showed favorable long term outcomes.

TRIAL REGISTRATION

ClinicalTrials.gov Identifier: NCT01989403.

KEYWORDS

Lumbar herniated disc; Sciatica; Complementary and alternative medicine; Integrative treatment

Article summary: Strengths and limitations of this study

*The first strength of this study is that it is a rigorous cohort observation on CAM treatment over a period of three years.

*The second strength of the study is the high compliance of treatment and low adverse reaction rate (1 case of mild allergic reaction to bee venom).

*The most important limitation of this study is that our findings provide no insight into which intervention(s) have the greatest impact on improvement. The comparative effectiveness of overall treatment and individual treatment modalities cannot be verified due to the integrative treatment modality and observational design.

*The second limitation is the low long term compliance rate(57%) due to strict follow-up inclusion criteria.

INTRODUCTION

Sciatica associated with lumbar herniated disc (LHD) is the most common cause of sciatica in working populations.[1] Based on several RCTs on LHD patients with sciatica that report no significant difference in long-term clinical outcomes between surgery vs. non-surgery,[2, 3] guidelines generally agree that in the absence of symptoms requiring emergency surgery the first line of treatment should be conservative treatment, yet there is lack of consensus regarding the type of treatment.[4] Recently, conservative approaches for low back pain (LBP) are being evaluated multidimensionality, and options are not limited to conventional treatment but also include complementary and alternative medicine (CAM).[5] A 2004 survey by Brunelli and Gorson reported that 43% of patients with peripheral neuropathy used CAM to manage their symptoms, and the main reason for seeking CAM was due to unsatisfactory management of symptoms with standard care.[6]

Korea has a dual medical system where western and Korean traditional medical doctors have equal individual treatment rights, and the patient usually decides the means of primary health care. We recruited participants from consecutive outpatients visiting for treatment purposes and administered CAM treatment, excluding conventional treatment (e.g. analgesics, physical therapy, injections), and the 6 month results have been published.[7] The participants had severe leg pain, and 60% had previously been diagnosed as needing surgery for LHD at other hospitals or clinics.

The purpose of this study is to evaluate the feasibility of this model of integrative treatment as a valid alternative option for LHD patients with sciatica. In an attempt to answer this question, we report the 3 year follow-up results of a prospective cohort observational study on CAM treatment.

METHODS

Design & Ethics Statement

LHD patients with a main complaint of sciatica were recruited at Jaseng Hospital of Korean Medicine, Seoul, Korea, an integrative hospital that offers both western and Korean traditional medical services, from November 2006 to April 2007. A prospective cohort study with a follow-up period of 3 years was conducted. This study is

a follow-up analysis of a previous trial[7] and the protocol has been registered at ClinicalTrials.gov under the registration number NCT01989403.[8] The interviewer was not given any prior information about a participant before the interview, and all participants provided written consent to participate in the study.

Participants

The participants were recruited from outpatients who had not previously been treated for LBP at this hospital. The inclusion criteria were: (1) LBP with sciatica, with a numeral rating scale (NRS) leg pain intensity of 5 or higher and onset within 1 year; (2) sciatica due to LDH as confirmed by MRI and neurological examinations; (3) age 18 to 60 years; (4) written consent to attend 6 months of integrative CAM treatment and following assessment visits.

The exclusion criteria were: (1) other treatment regarding current LBP and/or sciatica (e.g. surgery, nerve blocks, analgesic medication); (2) non-spinal or soft tissue problems potentially related to back pain or sciatica (e.g. pregnancy, spinal tumor, rheumatoid arthritis); (3) history of spinal surgery, vertebral dislocation, or fracture; (4) severe neurological symptoms (e.g. cauda equina syndrome).

Follow-up sessions were conducted annually through hospital visits on participants who had completed the 6 months of treatment and previous assessments, including MRI scans, physical examinations and surveys.

Interventions

Participants received integrative CAM treatment for back pain and sciatica. The contents of the treatment package were decided from LHD treatment frequently used in current clinical practice.[9] The treatment package included herbal medicine, acupuncture, bee-venom pharmacopuncture and Chuna therapy (Korean spinal manipulation). Treatment was conducted once a week for 24 weeks, except herbal medication which was taken twice daily for 24 weeks; (1) Acupuncture: frequently used acupoints (BL23, BL24, BL25, BL31, BL32, BL33, BL34, BL40, BL60, GB30, GV3, and GV4)[10, 11] and the site of pain were selected, and the needles were left in situ for 20 minutes. Sterilized disposable needles (stainless steel, 0.30x40mm, Dong Bang Acupuncture Co. Korea) were used; (2) Chuna therapy[12, 13]: Chuna is a Korean spinal manipulation that includes high-velocity, low amplitude thrusts to spinal joints slightly beyond the passive range of motion for spinal mobilization, and manual force to joints within the passive range; (3) Bee-venom pharmacopuncture[14]: 0.5-1cc of diluted bee-

venom solution (saline:bee-venom ratio, 1,000:1) was injected into 4-5 acupoints around the lumbar spine area to a total amount of 1cc using disposable injection needles (CPL, 1cc, 26Gx1.5 syringe, Shinchang medical co. Korea); (4) Herbal medicine was taken twice a day in dry powder (2g) and water extracted decoction form (120ml) (Ostericum koreanum, Eucommia ulmoides, Acanthopanax sessiliflorus, Achyranthes bidentata, Psoralea corylifolia, Peucedanum japonicum, Cibotium barometz, Lycium chinense, Boschniakia rossica, Cuscuta chinensis, and Atractylodes japonica). These herbs were selected from herbs frequently prescribed for LBP (or nerve root pain) treatment in Korean medicine and traditional Chinese medicine[15] and the prescription was further developed through clinical practice at Jaseng Hospital of Korean Medicine.[9] In addition, recent investigations report that compounds of Cibotium barometz inhibit osteoclast formation in vitro,[16] and Atractylodes japonica extracts protect osteoblast cells from oxidative stress.[17] Eucommia ulmoides has been reported to have osteoclast inhibitive,[18] osteoblast-like cell proliferative, and bone mineral density enhancing effects.[19]

Outcome measures

All assessments were conducted by trained physicians at visits to the hospital for follow-up purposes. The 1st follow-up period consisted of assessments performed at baseline, 4, 12, 16, 20 and 24 weeks for the duration of treatment. Further results were obtained through the 2nd follow-up period with annual follow-up visits at 1, 2 and 3 years.

Outcome measures of back pain and referred pain were assessed using the Visual Analogue Scale (VAS, 0-10),[20] Oswestry Disability Index (ODI)[21] and SF-36 Health Related Quality of Life Questionnaire.[22, 23] Levels of neurological damage were evaluated through assessments of muscular weakness and sensory loss. A Straight Leg Raise test (SLRT) of 60 degrees or lower in the leg with radiating pain was considered a positive test result. Lumbar Range of Motion (ROM) was also checked to assess pain occurring within normal range of motion. MRI scans were conducted at baseline, 24 weeks, 1, 2 and 3 years. Changes in size and severity of the main herniated disc causing radiating pain were evaluated by radiology specialists and KMDs and categorized into 3 groups (improved, worse or no discernible change) in comparison with the immediate previous MRI image. Recurrence of pain and use of medical care (type, frequency) were also investigated.

Statistical analysis

Descriptive analyses were performed using SPSS software for Windows (Version 18.0, SPSS Corp., Chicago, IL, USA) for all data. Confirmatory analyses of single primary outcomes were not included in this study. Instead, changes from baseline for primary outcome measures were presented as mean differences with a 95% confidence interval. The paired t-test was conducted to assess whether the 24 week outcome results were sustained after completion of treatment.

RESULTS

A total of 4,184 LBP and leg pain patients were screened and 150 eligible patients were enrolled in the study and started treatment. A hundred and twenty-eight patients completed the 6 months of treatment and 1st follow-up. 22 patients discontinued treatment and participation due to surgery or personal reasons.

The mean duration of treatment for the 22 patients who prematurely terminated treatment was 6.91±4.59 weeks. Of these patients, 8 underwent lumbar operations at an average of 6.75±4.30 weeks after participating in the study. The remaining 128 patients who completed treatment did not receive any treatment other than that assigned in the protocol and were followed up annually and 73 patients completed the 2nd follow-up period to 3 years post-baseline. The participants' demographic characteristics and medical history were assessed at baseline **<Table 1>**.

Table 1. Patient characteristics at baseline

Characteristics[a]	**Follow-up** (n=73) **% (n)**	**Drop-out** (n=55) **% (n)**	**p-value**
Age (yr), mean (SD)	35.38 (8.09)	33.25 (8.60)	0.154
Gender, male	58% (42)	58% (32)	0.941
Smoking status			0.076
Yes	37% (27)	53% (29)	
No	63% (46)	47% (26)	
Drinking[b]			0.756
Yes	85% (62)	88% (21)	
No	15% (11)	12% (3)	
Body Mass Index, mean (SD)	23.88 (2.91)	23.94 (2.97)	0.905
Length of current episode (month), mean (SD)	2.71 (3.13)	2.49 (2.98)	0.686

Positive history of prescription medication intake regarding current episode	67% (49)	78% (43)	0.168
Recommendation of surgery[c]	62% (45)	62% (34)	0.984
Previous back pain			0.347
None	93% (68)	98% (54)	
Disc herniation	4 % (3)	2% (1)	
Others	3% (2)		
Comorbid illnesses[d], yes	5% (4)	4% (2)	0.625
Positive physical examination findings[e]			
Muscular weakness	47% (34)	49% (27)	0.778
Sensory loss	25% (18)	29% (16)	0.574
Abnormal Deep Tendon Reflex (DTR)	37% (27)	42% (23)	0.579
Straight Leg Raise test < 60°	63% (46)	69% (38)	0.474
Limited range of lumbar motion with pain[f]	80% (59)	87% (48)	0.329
Low back pain VAS score, mean (SD)	4.37 (2.70)	4.35 (2.65)	0.968
Radiating leg pain VAS score, mean (SD)	7.57 (1.39)	7.09 (1.21)	0.043
Oswestry disability index (0–100), mean (SD)	40.74 (16.15)	41.75 (12.84)	0.705
SF-36 score (0–100), mean (SD)	34.95 (13.30)	33.12 (12.38)	0.428
Magnetic Resonance Imaging (MRI) reading[g]			0.587
Protrusion	59% (43)	64% (35)	
Extrusion	41% (30)	36% (20)	
Number of degenerative discs, mean (SD)[h]	1.92 (0.92)	1.84 (0.98)	0.631

VAS; Visual analogue scale (1-10).
[a]Characteristics of the 73 participants who were available for 3 year follow-up evaluation of the total 128 participants who completed 6 months of integrative CAM treatment. In the mean difference of characteristics between follow-up patients (n=73) and drop-out patients (n=55), there is no statistically significant difference for all characteristics (p-value≥0.05) except radiating leg pain VAS score; [b]Twenty-four missing values in drop-out cases; [c]Surgery recommended by surgeons consulted prior to participation in study; [d]Any self-reported gastritis, tuberculosis poliomyelitis, cardiovascular disease, uterine myoma, or hepatitis B carrier; [e]Number of patients with positive physical examination findings including muscle strength, sensation, and reflex abnormality; [f]Number of patients with restricted physical examination findings including lumbar flexion, extension, right lateral bending, left lateral bending; [g]MRI reading of sciatica as diagnosed by physicians; [h]Based on the classification by *Pfirrmann et al.*,[24] the number of lumbar intervertebral discs with a degeneration level of Grade 4 or higher of 5 grades in each patient. The grade is classified according to the average number of degenerated discs of the 5 lumbar spinal discs from L1/2 to L5/S1.

The authors lost contact with most of the 55 patients who failed to attend the 3 year follow-up. The main reason for failure to attend the 3 year follow-up was loss of contact (n=37), and other personal reasons <**Fig. 1**>.

Fig. 1. Flow diagram of study

We compared the outcomes (VAS, ODI, SF-36 scores) of each follow-up with the immediate previous evaluation over the 2nd follow-up period. The pain intensity of LBP in the 73 patients showed a steady and significant decrease up to 1 year, which slightly increased at the 3 year follow-up. Pain intensity for sciatica showed a stable and significant decrease up to 24 weeks, but no significant change was observed from 1 to 3 years. ODI and SF-36 scores decreased significantly up to 1 year and showed no significant change at 3 years.

Difference in VAS for LBP, leg pain and ODI scores from baseline were maintained above minimal clinically important change (MCIC) at 1, 2 and 3 years <**Table 2**>.

Table 2. **Change in pain, functional status and quality of life at 3 years from baseline**

	Baseline	12 wks	24 wks	1 yr	3 yrs
Low back pain VAS					
Mean (SD)	4.37 (2.70)	2.14 (1.72)	0.90 (1.01)	0.59 (0.74)	1.12 (1.64)
Mean change[a] (95% CI)		2.23 (1.56 to 2.91)	3.47 (2.81 to 4.14)	3.78 (3.15 to 4.42)	3.26 (2.58 to 3.93)
Radiating leg pain VAS					
Mean (SD)	7.57 (1.40)	2.19 (1.82)	0.82 (1.18)	0.62 (2.12)*	0.99 (1.58)*
Mean change[a] (95% CI)		5.38 (4.86 to 5.90)	6.75 (6.33 to 7.17)	6.95 (6.50 to7.39)	6.58 (6.10 to 7.07)
Oswestry disability index					
Mean (SD)	40.74 (16.15)	18.99 (14.56)	9.84 (9.67)	6.47 (6.94)	6.30 (7.19)*
Mean change[a] (95% CI)		21.75 (17.03 to 26.48)	30.90 (26.58 to 35.23)	34.27 (30.19 to 38.36)	34.44 (30.24 to 38.64)
SF-36 total					
Mean (SD)	34.96 (13.30))	57.78 (18.56)	69.20 (14.96)	75.45 (12.64)	76.19(14.45)*
Mean change[a] (95% CI)		-23.09 (-27.31 to -18.33)	-34.37 (-38.55 to -29.96)	-39.58 (-44.70 to -36.28)	-40.38 (-45.72 to -36.75)

VAS, Visual analog scale (1-10); CI, Confidence interval.
[a]Mean difference from baseline.
*Indicates a P value of over 0.05 after the paired t-test on the difference with the immediate previous follow-up.

For LBP at 3 years, 65 patients (89%) reported almost no or mild pain (VAS<3), 6 (8%) moderate (3≤VAS<6) and 2 (3%) severe pain (6≤VAS≤10). For sciatica, 66 patients (90%) had almost no or mild pain (VAS<3), 5 (7%) moderate (3≤VAS<6) and 2 (3%) severe pain. In ODI scores, 58 patients (79%) could be considered as having almost no difficulty with daily life (ODI<10), 15 (21%) mild functional disability (10≤ODI<30) and none had severe functional disability (ODI≥30). In SF-36 scores, 35 patients (48%) reported scores of 80-100, 26 (36%) reported scores of 60-80 and 12 (16%) reported scores of 30-60 <**Fig. 2**>.

Fig. 2. Distribution of pain classified by pain severity over time

Observations of change in size of the main herniated disc by MRI at baseline, 24 weeks, 1, 2 and 3 years revealed temperamental changes with many cases showing fluctuation in volume. Of the patients who displayed abnormality in neurological and physical exams, most recovered to normal range in muscular weakness, sensory loss, SLRT and lumbar ROM by week 24 <**Table 3**>.

Table 3. Changes in physical examination findings and herniated disc as assessed by MRI up to 3 years

	Evaluation			
Number of patients (n)	Baseline	24 wks	1 yr	3 yrs
Outcome assessed by MRI[a]				
Similar		36	27	23
Improved		21	37	42
Aggravated		16	9	8
Limited range of motion (ROM)	59	10	7	9
Muscle weakness	34	6	2	2
Sensory loss	18	4	2	3
Straight leg raise test < 60°, mean (SD)	51	11	3	5

[a]Changes in size of the main herniated disc most likely to produce sciatic symptoms were compared by MRI with results from the previous follow-up and classified into three categories as evaluated by a radiologist and Korean medicine doctor: improved, similar and worse.

Twenty-seven (37%) out of 73 patients reported having sought medical care for recurrence of LBP and/or sciatica at 3 years, of which 23 patients (85%) continued with CAM, and the rest opted for conservative treatment such as medication, physical therapy, exercise or nerve block injection <**Table 4**>.

Table 4. Use of health care service by 27 patients with low back pain and/or sciatica recurrence (after the pre-defined 6 months of treatment) at 3 years

Type of treatment	Number of patients[b]	Number of sessions (SD)
CAM therapy[a]	23	21.54 (17.97)
Conventional medication	2	3.00 (1.41)
Korean medicine Physical therapy	8	28.50 (35.74)
Exercise therapy	1	10.00
Nerve block injection	3	4.00 (3.61)

[a]Refers to integrative treatment including acupuncture, Chuna manipulation, bee venom pharmacopuncture and herbal medicine.
[b]Number of patients was tallied allowing for multiple choices.

Ninety-two out of 128 patients answered whether they had undergone surgery at 3 years, and 4 patients reported having received surgical operations.

DISCUSSION

Patients with sciatica due to LHD reported improvement in leg pain and ODI scores above MCIC from week 8 during the 24 weeks of CAM treatment. Clinically significant improvements in LBP also became apparent, and most patients no longer presented neurological disorders from week 24.[7] In additional investigations over 3 years, patients showed further improvement or maintained their improved state. Cases with continuous neurological disability were few.

In cases of recurrent pain, most patients (23 out of 37 patients, 85%) reselected CAM therapy and only a few cases sought conventional treatments. Thirty-six of 73 patients reported minimal levels of pain intensity and functional disability that did not require further treatment at the 3 year follow-up. The fact that a high percentage returned to CAM suggests a high satisfaction rate and these results imply that CAM could be considered an effective treatment option for LHD patients with neurological symptoms.

One of the major strengths of our study is that it is a rigorous cohort observation on CAM treatment over a period of three years. All participants underwent multidimensional pain and functional ability assessments including MRI scans and physical examinations.

The combined approach of integrative treatment is similar to real-world settings and the collected data can be highly informative to clinicians as examinations and treatment were performed under circumstances comparable to typical Korean clinics. During the 24 weeks of treatment, patients were subjected to an intense regimen of integrative treatment, but the high compliance rate of 85.3% (128 out of 150) indicates that patients were highly satisfied with treatment. Additionally, the fact that no side effects other than a mild allergic reaction to bee venom occurred is noteworthy.

However, there are also weaknesses and limitations. One particular limitation is due to the innate nature of a prospective cohort study where we cannot draw any definite conclusions regarding treatment efficacy. Due to

the lack of a control group, we are unable to conclusively comment on the effectiveness of individual treatments or on the comparative effectiveness of this integrative package to conventional treatment modalities.

Perhaps the most significant limitation is the low long term compliance rate. The 3 year follow-up was conducted only on patients who had completed the 24 weeks of treatment and 1st follow-up term, leaving 73 of the original 128 participants (57%) who initially completed treatment. The reason for this poor compliance may be partly explained by the strict follow-up inclusion criteria. MRI scans and assessments on both neurological and physical function required regular visits to the hospital as they could not be replaced with phone interviews or online assessments. A large proportion of the study population refused further participation in the study due to personal reasons; some no longer required treatment, others refused to travel long distances after moving.

We lost track of many patients in the course of this study, and this may be due, in part, to the rapidly changing communications industry in Korea. Many Koreans are replacing home phones with internet or personal mobile phones, and frequently changing personal contact information. Also, it cannot be decisively said that the patients that did not attend the 3 year follow-up were necessarily in worse medical states. As seen in Table 1, the baseline characteristics of drop-out patients did not differ greatly from follow-up patients, and as we had made it known to the participants prior to follow-up that the follow-up MRIs and tests were free of charge, it is possible that patients in worse medical conditions would be more committed to follow-ups.

Although integrative treatment may be considered pragmatic, this leads to another limitation. A combined approach makes it difficult to discern the level of contribution of individual factors. Current clinical guidelines[25, 26] suggest composition of integrative treatment should be based on a coherent theoretical basis and evidence-based effectiveness. However, the present study treatment was pre-decided through clinical experience and preferential consensus of KMDs. Therefore, this study requires further consideration of such factors as evidence-based effectiveness and cost-effectiveness in treatment construction for a more organized gradient intervention.

These limitations notwithstanding, the study results show that the herniated disc patients included in the present study were able to control their symptoms using only CAM without the help of conventional treatments[27, 28]

during the treatment period. Only a few people reported need of conventional treatment at the 2nd follow-up also.

This study is one of the few studies and only study conducted in Korea to evaluate the effects of CAM treatment in LHD patients with sciatica multi-dimensionally using standardized imaging and examinations. In the current study, integrative treatments were proven safe and brought about improvement in pain, functional disability, quality of life and neurological disorders. Further investigations and RCTs are required to assess the comparative benefits of integrative CAM treatment to contemporary conventional medicine.

Contributors

IHH drafted the study, and MRK and IHH wrote the final manuscript. JSS, JHL, BCS and MSL contributed to the study design and made critical revisions. All of the authors have read and approved the final manuscript.

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Competing interests

None declared.

Ethics approval

The study protocol was approved by the Institutional Review Board of Jaseng Hospital of Korean Medicine.

Data sharing statement

No additional data are available.

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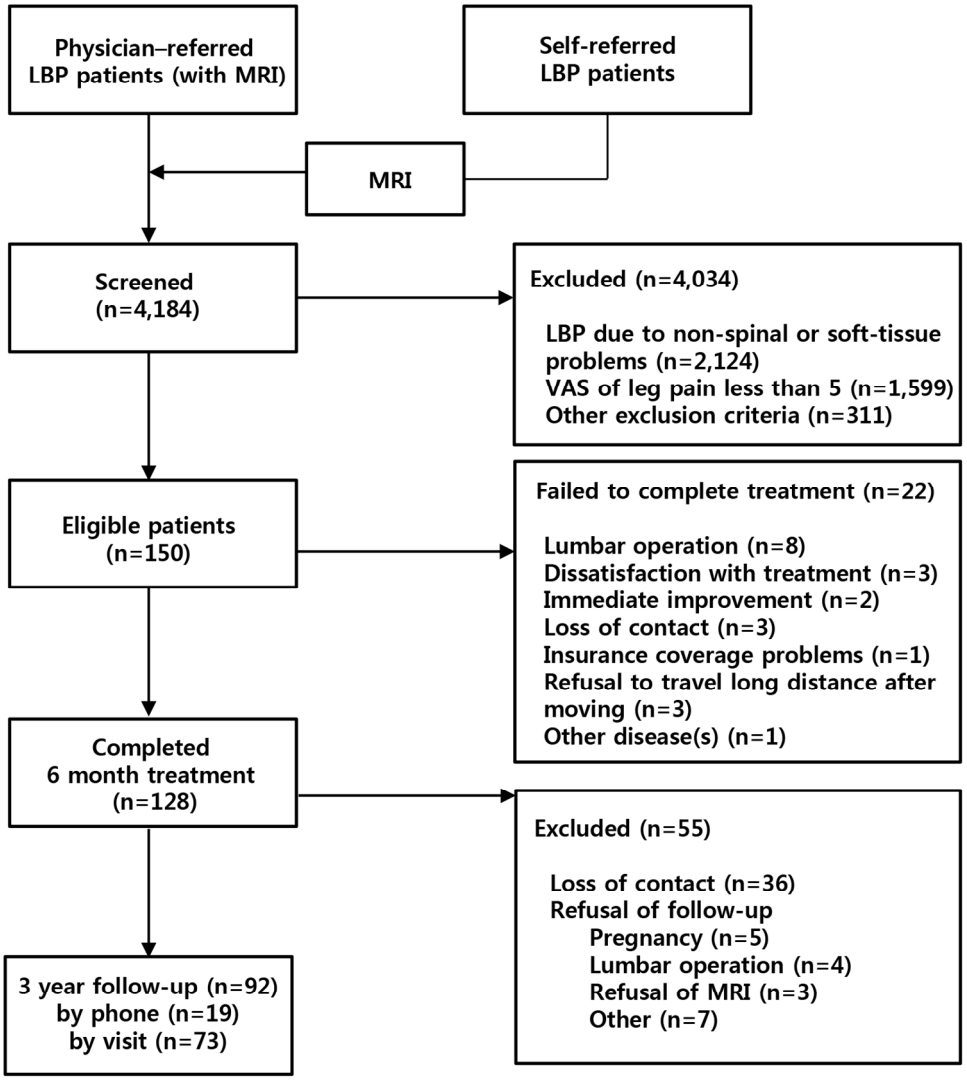

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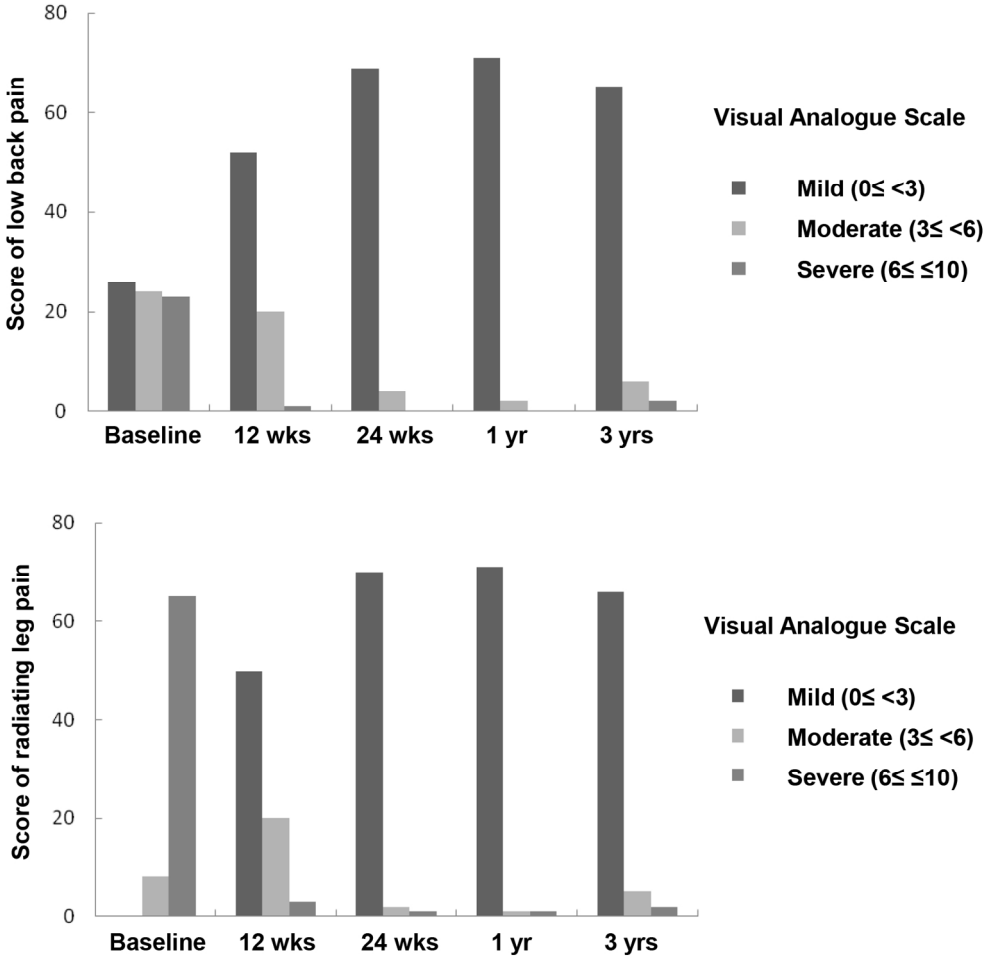

Distribution of pain classified by pain severity over time
148x145mm (300 x 300 DPI)

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cohort studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	Title page #1 Abstract #1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	Abstract #1
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	#1
Objectives	3	State specific objectives, including any prespecified hypotheses	#1
Methods			
Study design	4	Present key elements of study design early in the paper	#1
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	#1-2
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	#2-3
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	-
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	#3
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	#3
Bias	9	Describe any efforts to address potential sources of bias	#2
Study size	10	Explain how the study size was arrived at	-
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	#4
		(*b*) Describe any methods used to examine subgroups and interactions	-
		(*c*) Explain how missing data were addressed	-
		(*d*) If applicable, explain how loss to follow-up was addressed	-
		(*e*) Describe any sensitivity analyses	-

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	#4
		(b) Give reasons for non-participation at each stage	#5
		(c) Consider use of a flow diagram	#5
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	#4-5
		(b) Indicate number of participants with missing data for each variable of interest	-
		(c) Summarise follow-up time (eg, average and total amount)	-
Outcome data	15*	Report numbers of outcome events or summary measures over time	#4-6
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	#6
		(*b*) Report category boundaries when continuous variables were categorized	#4,5,7
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	-
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	-
Discussion			
Key results	18	Summarise key results with reference to study objectives	#9-10
Limitations			
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	#8-10
Generalisability	21	Discuss the generalisability (external validity) of the study results	#8
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	#10

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

The long-term course of patients undergoing alternative and integrative therapy for lumbar disc herniation: 3-year results of a prospective observational study

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The long-term course of patients undergoing alternative and integrative therapy for lumbar disc herniation: 3-year results of a prospective observational study

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Lumbar herniated disc; Sciatica; Complementary and alternative medicine; Integrative treatment

Objectives: This study aimed to (1) assess the efficacy and safety of an integrative complementary and alternative medicine (CAM) approach in management of lumbar disc herniation (LDH) with sciatic pain and (2) investigate pain relapse, use of medical care and surgery rates in patients who actively chose non-surgical CAM treatment for LDH.

Study design/Setting: This prospective observational study was undertaken at a Korean medicine hospital outpatient setting in Korea.

Participants: A total of 128 consecutive LDH patients with a numeral rating scale for leg pain of ≥5 completed 6 months of CAM treatment after recruitment from November 2006, and 73/128 participants (57%) attended follow-up 3 years later.

Interventions: Six months of CAM treatment (herbal medicine, acupuncture, bee-venom pharmacopuncture, and Chuna manipulation).

Primary outcome measures: Visual analogue scale (VAS) for low back and leg pain, Oswestry Disability Index (ODI), and SF-36 Health Survey.

Secondary outcome measures: Neurological impairment (muscular weakness, sensory loss, straight leg raise test), MRIs, recurrence of low back pain and/or radiating pain, and use of medical care.

Results: Ninety-two patients could be assessed for surgical state, of which 4 replied they had received surgery. Seventy-three patients attended the 3 year follow-up. The baseline VAS of back pain (4.37±2.70) decreased after treatment (0.90±1.01; P<0.001) and was maintained at 3 years (1.12±1.64; P=0.19). Baseline VAS of leg pain (7.57±1.40) also decreased upon treatment (0.82±1.18; P<0.001) and was sustained at 3 years (0.99±1.58; P=0.34). ODI scores declined from 40.74±16.15 to 9.84±9.67 (P<0.001), then decreased further to 6.30±7.19 (P<0.01). SF-36 scores increased from 34.96±13.30 to 69.20±14.96 (P<0.001), reaching 76.19±14.45 (P<0.001) at 3 years. Thirty-seven patients reported recurrence of pain, and most chose CAM treatment for management of relapse symptoms.

Conclusions: Although absence of a control group prevents validation of effectiveness, many patients showed favorable long term outcomes.

TRIAL REGISTRATION

ClinicalTrials.gov Identifier: NCT01989403.

Article summary: Strengths and limitations of this study

*The first strength of this study is that it is a rigorous cohort observation on CAM treatment over a period of three years.

*The second strength of the study is the high compliance with treatment and low adverse reaction rate (1 case of mild allergic reaction to bee venom).

*The most important limitation of this study is that our findings provide no insight into which intervention(s) have the greatest impact on improvement. The comparative effectiveness of overall treatment and individual treatment modalities cannot be verified due to the integrative treatment modality and observational design.

*The second limitation is the low long term compliance rate (57%) due to strict follow-up inclusion criteria.

INTRODUCTION

Sciatica associated with lumbar herniated disc (LHD) is the most common cause of sciatica in working populations.[1] Based on several RCTs on LHD patients with sciatica that report no significant difference in long-term clinical outcomes between surgery versus non-surgery,[2, 3] guidelines generally agree that in the absence of symptoms requiring emergency surgery the first line of treatment should be conservative treatment, yet there is lack of consensus regarding the type of treatment.[4] Recently, conservative approaches for low back pain (LBP) are being evaluated multidimensionally, and options are not limited to conventional treatment but also include complementary and alternative medicine (CAM).[5] A 2004 survey by Brunelli and Gorson reported that 43% of patients with peripheral neuropathy used CAM to manage their symptoms, and the main reason for seeking CAM was due to unsatisfactory management of symptoms with standard care.[6]

Korea has a dual medical system where western and Korean traditional medical doctors have equal individual treatment rights, and the patient usually decides the means of primary health care. We recruited participants from consecutive outpatients visiting for treatment purposes and administered CAM treatment, excluding conventional treatment (e.g. analgesics, physical therapy, injections), and published the 6 month results.[7] The participants had severe leg pain, and 60% had previously been diagnosed as needing surgery for LHD at other hospitals or clinics.

The purpose of this study is to evaluate the feasibility of this model of integrative treatment as a valid alternative option for LHD patients with sciatica and to investigate pain relapse, use of medical care and surgery rates in patients who actively chose non-surgical CAM treatment for LDH. In an attempt to answer this question, we report the 3 year follow-up results of a prospective cohort observational study on CAM treatment.

METHODS

Design & Ethics Statement

LHD patients with a main complaint of sciatica were recruited at Jaseng Hospital of Korean Medicine, Seoul, Korea, an integrative hospital that offers both western and Korean traditional medical services, from November

2006 to April 2007. A prospective cohort study was conducted, and this study is a report of the 3 year follow-up analysis of a previous trial.[7] The protocol has been registered at ClinicalTrials.gov under the registration number NCT01989403.[8]

Participants

The participants were recruited from outpatients who had not previously been treated for LBP at this hospital. The inclusion criteria were: (1) LBP with sciatica, with a numeral rating scale (NRS) leg pain intensity of 5 or higher and onset within 1 year; (2) sciatica due to LDH as confirmed by MRI and neurological examinations; (3) age 18 to 60 years; (4) written consent to attend 6 months of integrative CAM treatment and following assessment visits.

The exclusion criteria were: (1) other treatment regarding current LBP and/or sciatica (e.g. surgery, nerve blocks, analgesic medication); (2) non-spinal or soft tissue problems potentially related to back pain or sciatica (e.g. pregnancy, spinal tumor, rheumatoid arthritis); (3) history of spinal surgery, vertebral dislocation, or fracture; (4) severe neurological symptoms (e.g. cauda equina syndrome).

Follow-up sessions were conducted annually through hospital visits on participants who had completed the 6 months of treatment and previous assessments, including MRI scans, physical examinations and surveys. The interviewer was not given any prior information about a participant before the interview, and all participants provided written consent to participate in the study.

Interventions

Participants received integrative CAM treatment for back pain and sciatica. The contents of the treatment package were decided from LHD treatment frequently used in current clinical practice.[9] The treatment package included herbal medicine, acupuncture, bee-venom pharmacopuncture and Chuna therapy (Korean spinal manipulation). Treatment was conducted once a week for 24 weeks, except herbal medication which was taken twice daily for 24 weeks; (1) Acupuncture: frequently used acupoints (BL23, BL24, BL25, BL31, BL32, BL33, BL34, BL40, BL60, GB30, GV3, and GV4)[10, 11] and the site of pain were selected, and the needles were left in situ for 20 minutes. Sterilized disposable needles (stainless steel, 0.30x40mm, Dong Bang Acupuncture Co., Korea) were used; (2) Chuna therapy:[12, 13] Chuna is a Korean spinal manipulation that includes high-velocity,

low amplitude thrusts to spinal joints slightly beyond the passive range of motion for spinal mobilization, and manual force to joints within the passive range; (3) Bee-venom pharmacopuncture:[14] 0.5-1cc of diluted bee-venom solution (saline:bee-venom ratio, 1,000:1) was injected into 4-5 acupoints around the lumbar spine area to a total amount of 1cc using disposable injection needles (CPL, 1cc, 26Gx1.5 syringe, Shinchang medical Co., Korea); (4) Herbal medicine was taken twice a day in dry powder (2g) and water extracted decoction form (120ml) (Ostericum koreanum, Eucommia ulmoides, Acanthopanax sessiliflorus, Achyranthes bidentata, Psoralea corylifolia, Peucedanum japonicum, Cibotium barometz, Lycium chinense, Boschniakia rossica, Cuscuta chinensis, and Atractylodes japonica). These herbs were selected from herbs frequently prescribed for LBP (or nerve root pain) treatment in Korean medicine and traditional Chinese medicine[15] and the prescription was further developed through clinical practice at Jaseng Hospital of Korean Medicine.[9] In addition, recent investigations report that compounds of Cibotium barometz inhibit osteoclast formation in vitro,[16] and Atractylodes japonica extracts protect osteoblast cells from oxidative stress.[17] Eucommia ulmoides has been reported to have osteoclast inhibitive,[18] osteoblast-like cell proliferative, and bone mineral density enhancing effects.[19]

Patients were given instructions by their physician at treatment sessions to remain active and continue with daily activities while not aggravating pre-existing symptoms. Also, ample information about the favorable prognosis and encouragement for non-surgical treatment was given.

Outcome measures

All assessments were conducted by trained physicians during visits to the hospital for follow-up purposes. Assessing doctors did not participate in any part of the treatment. The 1st follow-up period consisted of assessments performed at baseline, 4, 12, 16, 20 and 24 weeks for the duration of treatment. Further results were obtained through the 2nd follow-up period with annual follow-up visits at 1, 2 and 3 years.

Outcome measures of back pain and referred pain were assessed using the Visual Analogue Scale (VAS, 0-10),[20] Oswestry Disability Index (ODI)[21] and SF-36 Health Related Quality of Life Questionnaire.[22, 23] Levels of neurological damage were evaluated through assessments of muscular weakness and sensory loss. A Straight Leg Raise test (SLRT) of 60 degrees or lower in the leg with radiating pain was considered a positive test result. Lumbar Range of Motion (ROM) was also checked to assess pain occurring within normal range of motion.

MRI scans were conducted at baseline, 24 weeks, and 1, 2 and 3 years. Changes in size and severity of the main herniated disc causing radiating pain were evaluated by radiology specialists and KMDs and categorized into 3 groups (improved, worse or no discernible change) in comparison with the immediate previous MRI image to track yearly changes and assess for correlations in subjective clinical symptoms and objective physical evaluation and MRI results. Recurrence of pain and use of medical care (type, frequency) were also investigated.

Statistical analysis

Descriptive analyses were performed using SPSS software for Windows (Version 18.0, SPSS Corp., Chicago, IL, USA) for all data. Confirmatory analyses of single primary outcomes were not included in this study. Instead, changes from baseline for primary outcome measures were presented as mean differences with a 95% confidence interval. The paired t-test was conducted to assess whether the 24 week outcome results were sustained after completion of treatment.

RESULTS

A total of 4,184 LBP and leg pain patients were screened and 150 eligible patients were enrolled in the study and started treatment. A hundred and twenty-eight patients completed the 6 months of treatment and 1st follow-up. Twenty-two patients discontinued treatment and participation due to surgery or personal reasons.

The mean duration of treatment for the 22 patients who prematurely terminated treatment was 6.91±4.59 weeks. Of these patients, 8 underwent lumbar operations at an average of 6.75±4.30 weeks after participating in the study. The remaining 128 patients who completed treatment did not receive any treatment other than that assigned in the protocol and were followed up annually and 73 patients completed the 2nd follow-up period to 3 years post-baseline. The participants' demographic characteristics and medical history were assessed at baseline <**Table 1**>.

Table 1. Patient characteristics at baseline

Characteristics[a]	**Follow-up** (n=73) **% (n)**	**Drop-out** (n=55) **% (n)**	**p-value**

Age (yr), mean (SD)	35.38 (8.09)	33.25 (8.60)	0.154
Gender, male	58% (42)	58% (32)	0.941
Smoking status			0.076
Yes	37% (27)	53% (29)	
No	63% (46)	47% (26)	
Drinking[b]			0.756
Yes	85% (62)	88% (21)	
No	15% (11)	12% (3)	
Body Mass Index, mean (SD)	23.88 (2.91)	23.94 (2.97)	0.905
Length of current episode (month), mean (SD)	2.71 (3.13)	2.49 (2.98)	0.686
Positive history of prescription medication intake regarding current episode	67% (49)	78% (43)	0.168
Recommendation of surgery[c]	62% (45)	62% (34)	0.984
Previous back pain			0.347
None	93% (68)	98% (54)	
Disc herniation	4 % (3)	2% (1)	
Others	3% (2)		
Comorbid illnesses[d], yes	5% (4)	4% (2)	0.625
Positive physical examination findings[e]			
Muscular weakness	47% (34)	49% (27)	0.778
Sensory loss	25% (18)	29% (16)	0.574
Abnormal Deep Tendon Reflex (DTR)	37% (27)	42% (23)	0.579
Straight Leg Raise test < 60°	63% (46)	69% (38)	0.474
Limited range of lumbar motion with pain[f]	80% (59)	87% (48)	0.329
Low back pain VAS score, mean (SD)	4.37 (2.70)	4.35 (2.65)	0.968
Radiating leg pain VAS score, mean (SD)	7.57 (1.39)	7.09 (1.21)	0.043
Oswestry disability index (0–100), mean (SD)	40.74 (16.15)	41.75 (12.84)	0.705
SF-36 score (0–100), mean (SD)	34.95 (13.30)	33.12 (12.38)	0.428
Magnetic Resonance Imaging (MRI) reading[g]			0.587
Protrusion	59% (43)	64% (35)	
Extrusion	41% (30)	36% (20)	
Number of degenerative discs, mean (SD)[h]	1.92 (0.92)	1.84 (0.98)	0.631

VAS; Visual analogue scale (1-10).
[a]Characteristics of the 73 participants who were available for 3 year follow-up evaluation of the total 128 participants who completed 6 months of integrative CAM treatment. In the mean difference of characteristics between follow-up patients (n=73) and drop-out patients (n=55), there is no statistically significant difference for all characteristics (p-value≥0.05) except radiating leg pain VAS score; [b]Twenty-four missing values in drop-out cases; [c]Surgery recommended by surgeons consulted prior to participation in study; [d]Any self-reported gastritis, tuberculosis poliomyelitis, cardiovascular disease, uterine myoma, or hepatitis B carrier; [e]Number of patients with positive physical examination findings including muscle strength, sensation, and reflex abnormality; [f]Number of patients with restricted physical examination findings including lumbar flexion, extension, right lateral bending, left lateral bending; [g]MRI reading of sciatica as diagnosed by physicians; [h]Based on the classification by *Pfirrmann et al.*,[24] the number of lumbar intervertebral discs with a degeneration level of Grade 4 or higher of 5 grades in each patient. The grade is classified according to the average number of degenerated discs of the 5 lumbar spinal discs from L1/2 to L5/S1.

The authors lost contact with most of the 55 patients who failed to attend the 3 year follow-up. The main reason for failure to attend the 3 year follow-up was loss of contact (n=36), and other personal reasons <**Fig. 1**>.

We compared the outcomes (VAS, ODI, SF-36 scores) of each follow-up with the immediate previous evaluation over the 2nd follow-up period. The pain intensity of LBP in the 73 patients showed a steady and significant decrease up to 1 year, which slightly increased at the 3 year follow-up. Pain intensity for sciatica showed a stable and significant decrease up to 24 weeks, but no significant change was observed from 1 to 3 years. ODI and SF-36 scores decreased significantly up to 1 year and showed no significant change at 3 years. Difference in VAS for LBP, leg pain and ODI scores from baseline were maintained above minimal clinically important change (MCIC) at 1, 2 and 3 years <**Table 2**>.

Table 2. **Change in pain, functional status and quality of life at 3 years from baseline**

	Baseline	12 wks	24 wks	1 yr	3 yrs
Low back pain VAS					
Mean (SD)	4.37 (2.70)	2.14 (1.72)	0.90 (1.01)	0.59 (0.74)	1.12 (1.64)
Mean change[a] (95% CI)		2.23 (1.56 to 2.91)	3.47 (2.81 to 4.14)	3.78 (3.15 to 4.42)	3.26 (2.58 to 3.93)
Radiating leg pain VAS					
Mean (SD)	7.57 (1.40)	2.19 (1.82)	0.82 (1.18)	0.62 (2.12)*	0.99 (1.58)*
Mean change[a] (95% CI)		5.38 (4.86 to 5.90)	6.75 (6.33 to 7.17)	6.95 (6.50 to7.39)	6.58 (6.10 to 7.07)
Oswestry disability index					
Mean (SD)	40.74 (16.15)	18.99 (14.56)	9.84 (9.67)	6.47 (6.94)	6.30 (7.19)*
Mean change[a] (95% CI)		21.75 (17.03 to 26.48)	30.90 (26.58 to 35.23)	34.27 (30.19 to 38.36)	34.44 (30.24 to 38.64)
SF-36 total					
Mean (SD)	34.96 (13.30))	57.78 (18.56)	69.20 (14.96)	75.45 (12.64)	76.19(14.45)*
Mean change[a] (95% CI)		-23.09 (-27.31 to -18.33)	-34.37 (-38.55 to -29.96)	-39.58 (-44.70 to -36.28)	-40.38 (-45.72 to -36.75)

VAS, Visual analog scale (1-10); CI, Confidence interval.
[a]Mean difference from baseline.
*Indicates a P value of over 0.05 after the paired t-test on the difference with the immediate previous follow-up.

For LBP at 3 years, 65 patients (89%) reported almost no or mild pain (VAS<3), 6 (8%) moderate (3≤VAS<6) and 2 (3%) severe pain (6≤VAS≤10). For sciatica, 66 patients (90%) had almost no or mild pain (VAS<3), 5

(7%) moderate (3≤VAS<6) and 2 (3%) severe pain. In ODI scores, 58 patients (79%) could be considered as having almost no difficulty with daily life (ODI<10), 15 (21%) mild functional disability (10≤ODI<30) and none had severe functional disability (ODI≥30). In SF-36 scores, 35 patients (48%) reported scores of 80-100, 26 (36%) reported scores of 60-80 and 12 (16%) reported scores of 30-60 <**Fig. 2**>.

Observations of change in size of the main herniated disc by MRI at baseline, 24 weeks, and 1, 2 and 3 years revealed temperamental changes with many cases showing fluctuation in volume. Of the patients who displayed abnormality in neurological and physical exams, most recovered to normal range in muscular weakness, sensory loss, SLRT and lumbar ROM by week 24 <**Table 3**>.

Table 3. Changes in physical examination findings and herniated disc as assessed by MRI up to 3 years

	Evaluation			
Number of patients (n)	Baseline	24 wks	1 yr	3 yrs
Outcome assessed by MRI[a]				
Similar		36	27	23
Improved		21	37	42
Aggravated		16	9	8
Limited range of motion (ROM)	59	10	7	9
Muscle weakness	34	6	2	2
Sensory loss	18	4	2	3
Straight leg raise test < 60°, mean (SD)	51	11	3	5

[a]Changes in size of the main herniated disc most likely to produce sciatic symptoms were compared by MRI with results from the previous follow-up and classified into three categories as evaluated by a radiologist and Korean medicine doctor: improved, similar and worse.

Twenty-seven (37%) out of 73 patients reported having sought medical care for recurrence of LBP and/or sciatica at 3 years, of which 23 patients (85%) continued with CAM, and the rest opted for conservative treatment such as medication, physical therapy, exercise or nerve block injection <**Table 4**>.

Table 4. Use of health care service by 27 patients with low back pain and/or sciatica recurrence (after the pre-defined 6 months of treatment) at 3 years

Type of treatment	Number of patients[b]	Number of sessions (SD)
CAM therapy[a]	23	21.54 (17.97)
Conventional medication	2	3.00 (1.41)
Korean medicine Physical therapy	8	28.50 (35.74)
Exercise therapy	1	10.00
Nerve block injection	3	4.00 (3.61)

[a]Refers to integrative treatment including acupuncture, Chuna manipulation, bee venom pharmacopuncture and herbal medicine.
[b]Number of patients was tallied allowing for multiple choices.

Ninety-two out of 128 patients answered whether they had undergone surgery at 3 years, and 4 patients reported having received surgical operations.

DISCUSSION

Patients with sciatica due to LHD reported improvement in leg pain and ODI scores above MCIC from week 8 during the 24 weeks of CAM treatment. Clinically significant improvements in LBP also became apparent, and most patients no longer presented neurological disorders from week 24. We found moderate time by group interaction difference in VAS for LBP and ODI scores in subgrouping by duration of LBP, and significant time by group interactions in VAS for LBP when subgrouped by operation recommendation.[7] In additional investigations over 3 years, patients showed further improvement or maintained their improved state. Cases with continuous neurological disability were few.

In cases of recurrent pain, most patients (23 out of 27 patients, 85%) reselected CAM therapy and only a few cases sought conventional treatments. Thirty-six of 73 patients reported minimal levels of pain intensity and functional disability that did not require further treatment at the 3 year follow-up. The fact that a high percentage returned to CAM suggests a high satisfaction rate and these results imply that CAM could be considered an effective treatment option for LHD patients with neurological symptoms.

One of the major strengths of our study is that it is a rigorous cohort observation on CAM treatment over a period of three years. All participants underwent multidimensional pain and functional ability assessments including MRI scans and physical examinations.

The combined approach of integrative treatment is similar to real-world settings and the collected data can be highly informative to clinicians as examinations and treatment were performed under circumstances comparable to typical Korean medicine clinics. During the 24 weeks of treatment, patients were subjected to an intense

regimen of integrative treatment, but the high compliance rate of 85.3% (128 out of 150) indicates that patients were highly satisfied with treatment. Additionally, the fact that no side effects other than a mild allergic reaction to bee venom occurred is noteworthy.

Previous long term follow-ups of studies focusing on neurological injury due to intervertebral disc displacement are mainly comparisons of the effects of surgical versus non-surgical treatment. Leiden-The Hague Spine Intervention Prognostic Study Group compared early surgery versus prolonged conservative care given by family practitioners, with conservative care consisting mainly of counseling, guidance from a physiotherapist, and prescription of painkillers.[2] The long-term follow-up results at 1 and 2 years showed no significant difference between the two groups in leg pain and lumbar function. However, 46% of the patients allocated to the non-surgical group received surgery, and the results were intention-to-treat analyzed. As-treated analysis was performed in the Spine Patient Outcomes Research Trial (SPORT) study, and the long-term follow-up results at 1 and 2 years all showed superior results in SF-36 bodily pain and physical function scales in the surgery group compared to nonoperative care (active physical therapy, counseling and education with home exercise instructions, and presciption of nonsteroidal anti-inflammatory drugs).[25]

In studies comparing conventional non-surgical treatment (e.g. education, rest, pain medication, physical therapy, etc.) and CAM non-surgical treatment (e.g. hot compress using Chinese medicine, electroacupuncture, Chinese herbal injection, Chinese Tuina, etc.), CAM treatment showed better results in lumbar functional scores at 6 months' short-term follow-up.

A systematic review on the effectiveness of conservative treatments for lumbosacral radicular syndrome evaluated injections, traction, physical therapy, bed rest, manipulation, medication, and acupuncture, deducing that corticosteroid injections and traction did not have sufficient evidence to be recommended as treatment options, and that it was difficult to reach a conclusion whether the other treatments should be prescribed by clinicians or whether a certain type of treatment is superior to others.[26]

A recent review of eight studies on the efficacy of Chinese herbal medicine for lumbar disc herniation compared with conventional treatment analyzed the results of 5 studies reporting that Chinese herbal medicine was better than conventional medicine, and 2 studies stating that clinical outcomes were better in Chinese herbal medicine

groups than in physiotherapy and placebo groups.[27] However, all trials were of poor methodological quality.

There are also weaknesses and limitations of our study. One particular limitation is due to the innate nature of a prospective cohort study where we cannot draw any definite conclusions regarding treatment efficacy. Due to lack of a control group, we are unable to conclusively comment on the effectiveness of individual treatments or on the comparative effectiveness of this integrative package to conventional treatment modalities.

Perhaps the most significant limitation is the low long term compliance rate. The 3 year follow-up was conducted only on patients who had completed the 24 weeks of treatment and 1 and 2 year follow-up sessions, leaving 73 of the original 128 participants (57%) who initially completed treatment. The study design was conceived to the aim of comparing the patient's state each year with the previous year to track changes multidimensionally, and the reason for the increasing loss of follow-up may be partly explained by the strict follow-up inclusion criteria. MRI scans and assessments of neurological and physical function required regular visits to the hospital as they could not be replaced with phone interviews or online assessments. A large proportion of the study population refused further participation in the study due to personal reasons; some no longer required treatment, others refused to travel long distances after moving.

We lost track of many patients in the course of this study, and this may be due in part to the rapidly changing communications industry in Korea. Many Koreans are replacing home phones with internet or personal mobile phones and frequently changing personal contact information. Also, while there was an increasing loss of follow-up patients, it cannot be decisively said that the patients that did not attend the 3 year follow-up were necessarily in worse medical states. As seen in Table 1, the baseline characteristics of drop-out patients did not differ greatly from follow-up patients, and as we had made it known to the participants prior to follow-up that all MRIs and tests were free of charge, it is possible that patients in worse medical conditions were more committed to the yearly check-ups.

The results of a meta-analysis on the effectiveness of integrative Chinese medical therapies including Tuina on low back pain patients showed that groups receiving Tuina with Chinese herbal medicine and Tuina with acupuncture showed better pain and functional status than groups receiving Tuina alone.[28] Our results also reflect the discussions of CAM clinicians on selecting effective treatment methods for disc herniation patients,

and the outcome of those consultations was an integrative treatment package consisting of herbal medicine, acupuncture, bee-venom pharmacopuncture and Chuna manipulation. The reason for this multi-modality approach is that each approach has different targets, effects, mechanisms and time-windows, and no single therapy is clearly superior to others or unequivocally successful.

Although integrative treatment may be considered pragmatic, this leads to another limitation. A combined approach makes it difficult to discern the level of contribution of individual factors. Current clinical guidelines[29, 30] suggest composition of integrative treatment should be based on a coherent theoretical basis and evidence-based effectiveness. However, the present study treatment was pre-decided through clinical experience and preferential consensus of KMDs. Therefore, this study requires further consideration of such factors as evidence-based effectiveness and cost-effectiveness in treatment construction for a more organized gradient intervention.

These limitations notwithstanding, the study results show that the herniated disc patients included in the present study were able to control their symptoms using only CAM without the help of conventional treatments[31, 32] during the treatment period. Only a few people reported need of conventional treatment at the 2nd follow-up also.

This study is one of the few studies and only study conducted in Korea to evaluate the effects of CAM treatment in LHD patients with sciatica multidimensionally using standardized imaging and examinations. In the current study, integrative treatments were proven safe and brought about improvement in pain, functional disability, quality of life and neurological disorders. Further investigations and RCTs are required to assess the comparative benefits of integrative CAM treatment to contemporary conventional medicine.

Contributors

IHH drafted the study, and MRK and IHH wrote the final manuscript. JSS, JHL, BCS and MSL contributed to the study design and made critical revisions. All of the authors have read and approved the final manuscript.

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Competing interests

None declared.

Ethics approval

The study protocol was approved by the Institutional Review Board of Jaseng Hospital of Korean Medicine.

Data sharing statement

No additional data are available.

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Fig. 1. Flow diagram of study

Fig. 2. Distribution of pain classified by pain severity over time

Objectives: This study aimed to (1) assess the efficacy and safety of an integrative complementary and alternative medicine (CAM) approach in management of lumbar disc herniation (LDH) with sciatic pain and (2) investigate pain relapse, ~~and~~ use of medical care and surgery rates in patients who actively chose non-surgical CAM treatment for LDH.

Study design/Setting: This prospective observational study was undertaken at a Korean medicine hospital outpatient setting in Korea.

Participants: A total of 128 consecutive LDH patients with a numeral rating scale for leg pain of ≥5 completed 6 months of CAM treatment after recruitment from November 2006, and 73/128 participants (57%) attended follow-up 3 years later.

Interventions: Six months of CAM treatment (herbal medicine, acupuncture, bee-venom pharmacopuncture, and Chuna manipulation).

Primary outcome measures: Visual analogue scale (VAS) for low back and leg pain, Oswestry Disability Index (ODI), and SF-36 Health Survey.

Secondary outcome measures: Neurological impairment (muscular weakness, sensory loss, straight leg raise test), MRIs, recurrence of low back pain and/or radiating pain, and use of medical care.

Results: Ninety-~~one~~ two patients could be assessed for surgical state, of which 4 replied they had received surgery. Seventy-three patients attended the 3 year follow-up. The baseline VAS of back pain (4.37±2.70) decreased after treatment (0.90±1.01; P<0.001) and was maintained at 3 years (1.12±1.64; P=0.19). Baseline VAS of leg pain (7.57±1.40) also decreased upon treatment (0.82±1.18; P<0.001) and was sustained at 3 years (0.99±1.58; P=0.34). ODI scores declined from 40.74±16.15 to 9.84±9.67 (P<0.001), then decreased further to 6.30±7.19 (P<0.01). SF-36 scores increased from 34.96±13.30 to 69.20±14.96 (P<0.001), reaching 76.19±14.45 (P<0.001) at 3 years. Thirty-seven patients reported recurrence of pain, and most chose CAM treatment for management of relapse symptoms.

Conclusions: Although absence of a control group prevents validation of effectiveness, many patients showed favorable long term outcomes.

TRIAL REGISTRATION

ClinicalTrials.gov Identifier: NCT01989403.

KEYWORDS

Lumbar herniated disc; Sciatica; Complementary and alternative medicine; Integrative treatment

Article summary: Strengths and limitations of this study

*The first strength of this study is that it is a rigorous cohort observation on CAM treatment over a period of three years.

*The second strength of the study is the high compliance ~~of~~ with treatment and low adverse reaction rate (1 case of mild allergic reaction to bee venom).

*The most important limitation of this study is that our findings provide no insight into which intervention(s) have the greatest impact on improvement. The comparative effectiveness of overall treatment and individual treatment modalities cannot be verified due to the integrative treatment modality and observational design.

*The second limitation is the low long term compliance rate (57%) due to strict follow-up inclusion criteria.

INTRODUCTION

Sciatica associated with lumbar herniated disc (LHD) is the most common cause of sciatica in working populations.[1] Based on several RCTs on LHD patients with sciatica that report no significant difference in long-term clinical outcomes between surgery ~~vs.~~versus non-surgery,[2, 3] guidelines generally agree that in the absence of symptoms requiring emergency surgery the first line of treatment should be conservative treatment, yet there is lack of consensus regarding the type of treatment.[4] Recently, conservative approaches for low back pain (LBP) are being evaluated ~~multidimensionality~~multidimensionally, and options are not limited to conventional treatment but also include complementary and alternative medicine (CAM).[5] A 2004 survey by Brunelli and Gorson reported that 43% of patients with peripheral neuropathy used CAM to manage their symptoms, and the main reason for seeking CAM was due to unsatisfactory management of symptoms with standard care.[6]

Korea has a dual medical system where western and Korean traditional medical doctors have equal individual treatment rights, and the patient usually decides the means of primary health care. We recruited participants from consecutive outpatients visiting for treatment purposes and administered CAM treatment, excluding conventional treatment (e.g. analgesics, physical therapy, injections), and published the 6 month results ~~have been published~~.[7] The participants had severe leg pain, and 60% had previously been diagnosed as needing surgery for LHD at other hospitals or clinics.

The purpose of this study is to evaluate the feasibility of this model of integrative treatment as a valid alternative option for LHD patients with sciatica and to investigate pain relapse, use of medical care and surgery rates in patients who actively chose non-surgical CAM treatment for LDH. In an attempt to answer this question, we report the 3 year follow-up results of a prospective cohort observational study on CAM treatment.

METHODS

Design & Ethics Statement

LHD patients with a main complaint of sciatica were recruited at Jaseng Hospital of Korean Medicine, Seoul,

Korea, an integrative hospital that offers both western and Korean traditional medical services, from November 2006 to April 2007. A prospective cohort study ~~with a follow-up period of 3 years~~ was conducted~~.~~ and ~~This~~ this study is a report of the 3 year follow-up analysis of a previous trial.[77] ~~and the~~ The protocol has been registered at ClinicalTrials.gov under the registration number NCT01989403.[88] ~~The interviewer was not given any prior information about a participant before the interview, and all participants provided written consent to participate in the study.~~

Participants

The participants were recruited from outpatients who had not previously been treated for LBP at this hospital. The inclusion criteria were: (1) LBP with sciatica, with a numeral rating scale (NRS) leg pain intensity of 5 or higher and onset within 1 year; (2) sciatica due to LDH as confirmed by MRI and neurological examinations; (3) age 18 to 60 years; (4) written consent to attend 6 months of integrative CAM treatment and following assessment visits.

The exclusion criteria were: (1) other treatment regarding current LBP and/or sciatica (e.g. surgery, nerve blocks, analgesic medication); (2) non-spinal or soft tissue problems potentially related to back pain or sciatica (e.g. pregnancy, spinal tumor, rheumatoid arthritis); (3) history of spinal surgery, vertebral dislocation, or fracture; (4) severe neurological symptoms (e.g. cauda equina syndrome).

Follow-up sessions were conducted annually through hospital visits on participants who had completed the 6 months of treatment and previous assessments, including MRI scans, physical examinations and surveys. The interviewer was not given any prior information about a participant before the interview, and all participants provided written consent to participate in the study.

Interventions

Participants received integrative CAM treatment for back pain and sciatica. The contents of the treatment package were decided from LHD treatment frequently used in current clinical practice.[99] The treatment package included herbal medicine, acupuncture, bee-venom pharmacopuncture and Chuna therapy (Korean spinal manipulation). Treatment was conducted once a week for 24 weeks, except herbal medication which was taken twice daily for 24 weeks; (1) Acupuncture: frequently used acupoints (BL23, BL24, BL25, BL31, BL32, BL33,

BL34, BL40, BL60, GB30, GV3, and GV4)[10, 11] and the site of pain were selected, and the needles were left in situ for 20 minutes. Sterilized disposable needles (stainless steel, 0.30x40mm, Dong Bang Acupuncture Co., Korea) were used; (2) Chuna therapy[12, 13]: Chuna is a Korean spinal manipulation that includes high-velocity, low amplitude thrusts to spinal joints slightly beyond the passive range of motion for spinal mobilization, and manual force to joints within the passive range; (3) Bee-venom pharmacopuncture[14]: 0.5-1cc of diluted bee-venom solution (saline:bee-venom ratio, 1,000:1) was injected into 4-5 acupoints around the lumbar spine area to a total amount of 1cc using disposable injection needles (CPL, 1cc, 26Gx1.5 syringe, Shinchang medical coCo., Korea); (4) Herbal medicine was taken twice a day in dry powder (2g) and water extracted decoction form (120ml) (Ostericum koreanum, Eucommia ulmoides, Acanthopanax sessiliflorus, Achyranthes bidentata, Psoralea corylifolia, Peucedanum japonicum, Cibotium barometz, Lycium chinense, Boschniakia rossica, Cuscuta chinensis, and Atractylodes japonica). These herbs were selected from herbs frequently prescribed for LBP (or nerve root pain) treatment in Korean medicine and traditional Chinese medicine[15] and the prescription was further developed through clinical practice at Jaseng Hospital of Korean Medicine.[9] In addition, recent investigations report that compounds of Cibotium barometz inhibit osteoclast formation in vitro,[16] and Atractylodes japonica extracts protect osteoblast cells from oxidative stress.[17] Eucommia ulmoides has been reported to have osteoclast inhibitive,[18] osteoblast-like cell proliferative, and bone mineral density enhancing effects.[19]

Patients were given instructions by their physician at treatment sessions to remain active and continue with daily activities while not aggravating pre-existing symptoms. Also, ample information about the favorable prognosis and encouragement for non-surgical treatment was given.

Outcome measures

All assessments were conducted by trained physicians at during visits to the hospital for follow-up purposes. Assessing doctors did not participate in any part of the treatment. The 1st follow-up period consisted of assessments performed at baseline, 4, 12, 16, 20 and 24 weeks for the duration of treatment. Further results were obtained through the 2nd follow-up period with annual follow-up visits at 1, 2 and 3 years.

Outcome measures of back pain and referred pain were assessed using the Visual Analogue Scale (VAS, 0-10),[20] Oswestry Disability Index (ODI)[21] and SF-36 Health Related Quality of Life Questionnaire.[22, 23]

Levels of neurological damage were evaluated through assessments of muscular weakness and sensory loss. A Straight Leg Raise test (SLRT) of 60 degrees or lower in the leg with radiating pain was considered a positive test result. Lumbar Range of Motion (ROM) was also checked to assess pain occurring within normal range of motion. MRI scans were conducted at baseline, 24 weeks, and 1, 2 and 3 years. Changes in size and severity of the main herniated disc causing radiating pain were evaluated by radiology specialists and KMDs and categorized into 3 groups (improved, worse or no discernible change) in comparison with the immediate previous MRI image to track yearly changes and assess for correlations in subjective clinical symptoms and objective physical evaluation and MRI results. Recurrence of pain and use of medical care (type, frequency) were also investigated.

Statistical analysis

Descriptive analyses were performed using SPSS software for Windows (Version 18.0, SPSS Corp., Chicago, IL, USA) for all data. Confirmatory analyses of single primary outcomes were not included in this study. Instead, changes from baseline for primary outcome measures were presented as mean differences with a 95% confidence interval. The paired t-test was conducted to assess whether the 24 week outcome results were sustained after completion of treatment.

RESULTS

A total of 4,184 LBP and leg pain patients were screened and 150 eligible patients were enrolled in the study and started treatment. A hundred and twenty-eight patients completed the 6 months of treatment and 1st follow-up. ~~22~~ Twenty-two patients discontinued treatment and participation due to surgery or personal reasons.

The mean duration of treatment for the 22 patients who prematurely terminated treatment was 6.91±4.59 weeks. Of these patients, 8 underwent lumbar operations at an average of 6.75±4.30 weeks after participating in the study. The remaining 128 patients who completed treatment did not receive any treatment other than that assigned in the protocol and were followed up annually and 73 patients completed the 2nd follow-up period to 3 years post-baseline. The participants' demographic characteristics and medical history were assessed at baseline <**Table 1**>.

Table 1. Patient characteristics at baseline

Characteristics[a]	Follow-up (n=73) % (n)	Drop-out (n=55) % (n)	p-value
Age (yr), mean (SD)	35.38 (8.09)	33.25 (8.60)	0.154
Gender, male	58% (42)	58% (32)	0.941
Smoking status			0.076
Yes	37% (27)	53% (29)	
No	63% (46)	47% (26)	
Drinking[b]			0.756
Yes	85% (62)	88% (21)	
No	15% (11)	12% (3)	
Body Mass Index, mean (SD)	23.88 (2.91)	23.94 (2.97)	0.905
Length of current episode (month), mean (SD)	2.71 (3.13)	2.49 (2.98)	0.686
Positive history of prescription medication intake regarding current episode	67% (49)	78% (43)	0.168
Recommendation of surgery[c]	62% (45)	62% (34)	0.984
Previous back pain			0.347
None	93% (68)	98% (54)	
Disc herniation	4 % (3)	2% (1)	
Others	3% (2)		
Comorbid illnesses[d], yes	5% (4)	4% (2)	0.625
Positive physical examination findings[e]			
Muscular weakness	47% (34)	49% (27)	0.778
Sensory loss	25% (18)	29% (16)	0.574
Abnormal Deep Tendon Reflex (DTR)	37% (27)	42% (23)	0.579
Straight Leg Raise test < 60°	63% (46)	69% (38)	0.474
Limited range of lumbar motion with pain[f]	80% (59)	87% (48)	0.329
Low back pain VAS score, mean (SD)	4.37 (2.70)	4.35 (2.65)	0.968
Radiating leg pain VAS score, mean (SD)	7.57 (1.39)	7.09 (1.21)	0.043
Oswestry disability index (0–100), mean (SD)	40.74 (16.15)	41.75 (12.84)	0.705
SF-36 score (0–100), mean (SD)	34.95 (13.30)	33.12 (12.38)	0.428
Magnetic Resonance Imaging (MRI) reading[g]			0.587
Protrusion	59% (43)	64% (35)	
Extrusion	41% (30)	36% (20)	
Number of degenerative discs, mean (SD)[h]	1.92 (0.92)	1.84 (0.98)	0.631

VAS; Visual analogue scale (1-10).
[a]Characteristics of the 73 participants who were available for 3 year follow-up evaluation of the total 128 participants who completed 6 months of integrative CAM treatment. In the mean difference of characteristics between follow-up patients (n=73) and drop-out patients (n=55), there is no statistically significant difference for all characteristics (p-value≥0.05) except radiating leg pain VAS score; [b]Twenty-four missing values in drop-out cases; [c]Surgery recommended by surgeons consulted prior to participation in study; [d]Any self-reported gastritis, tuberculosis poliomyelitis, cardiovascular disease, uterine myoma, or hepatitis B carrier; [e]Number of patients with positive physical examination findings including muscle strength, sensation, and reflex abnormality; [f]Number of patients with restricted physical examination findings including lumbar flexion, extension, right lateral bending, left lateral bending; [g]MRI reading of sciatica as diagnosed by physicians; [h]Based on the classification by *Pfirrmann et al.*,[2424] the number of lumbar intervertebral discs with a degeneration level of Grade 4 or higher of 5 grades in each patient. The grade is classified according to the average number of degenerated discs of the 5 lumbar spinal discs from L1/2 to L5/S1.

The authors lost contact with most of the 55 patients who failed to attend the 3 year follow-up. The main reason for failure to attend the 3 year follow-up was loss of contact (n=~~37~~36), and other personal reasons <**Fig. 1**>.

~~**Fig. 1. Flow diagram of study**~~

We compared the outcomes (VAS, ODI, SF-36 scores) of each follow-up with the immediate previous evaluation over the 2nd follow-up period. The pain intensity of LBP in the 73 patients showed a steady and significant decrease up to 1 year, which slightly increased at the 3 year follow-up. Pain intensity for sciatica showed a stable and significant decrease up to 24 weeks, but no significant change was observed from 1 to 3 years. ODI and SF-36 scores decreased significantly up to 1 year and showed no significant change at 3 years. Difference in VAS for LBP, leg pain and ODI scores from baseline were maintained above minimal clinically important change (MCIC) at 1, 2 and 3 years <**Table 2**>.

Table 2. **Change in pain, functional status and quality of life at 3 years from baseline**

	Baseline	12 wks	24 wks	1 yr	3 yrs
Low back pain VAS					
Mean (SD)	4.37 (2.70)	2.14 (1.72)	0.90 (1.01)	0.59 (0.74)	1.12 (1.64)
Mean change[a] (95% CI)		2.23 (1.56 to 2.91)	3.47 (2.81 to 4.14)	3.78 (3.15 to 4.42)	3.26 (2.58 to 3.93)
Radiating leg pain VAS					
Mean (SD)	7.57 (1.40)	2.19 (1.82)	0.82 (1.18)	0.62 (2.12)*	0.99 (1.58)*
Mean change[a] (95% CI)		5.38 (4.86 to 5.90)	6.75 (6.33 to 7.17)	6.95 (6.50 to7.39)	6.58 (6.10 to 7.07)
Oswestry disability index					
Mean (SD)	40.74 (16.15)	18.99 (14.56)	9.84 (9.67)	6.47 (6.94)	6.30 (7.19)*
Mean change[a] (95% CI)		21.75 (17.03 to 26.48)	30.90 (26.58 to 35.23)	34.27 (30.19 to 38.36)	34.44 (30.24 to 38.64)
SF-36 total					
Mean (SD)	34.96 (13.30))	57.78 (18.56)	69.20 (14.96)	75.45 (12.64)	76.19(14.45)*
Mean change[a] (95% CI)		-23.09 (-27.31 to -18.33)	-34.37 (-38.55 to -29.96)	-39.58 (-44.70 to -36.28)	-40.38 (-45.72 to -36.75)

VAS, Visual analog scale (1-10); CI, Confidence interval.
[a]Mean difference from baseline.
*Indicates a P value of over 0.05 after the paired t-test on the difference with the immediate previous follow-up.

For LBP at 3 years, 65 patients (89%) reported almost no or mild pain (VAS<3), 6 (8%) moderate (3≤VAS<6) and 2 (3%) severe pain (6≤VAS≤10). For sciatica, 66 patients (90%) had almost no or mild pain (VAS<3), 5 (7%) moderate (3≤VAS<6) and 2 (3%) severe pain. In ODI scores, 58 patients (79%) could be considered as having almost no difficulty with daily life (ODI<10), 15 (21%) mild functional disability (10≤ODI<30) and none had severe functional disability (ODI≥30). In SF-36 scores, 35 patients (48%) reported scores of 80-100, 26 (36%) reported scores of 60-80 and 12 (16%) reported scores of 30-60 <**Fig. 2**>.

~~**Fig. 2. Distribution of pain classified by pain severity over time**~~

Observations of change in size of the main herniated disc by MRI at baseline, 24 weeks, and 1, 2 and 3 years revealed temperamental changes with many cases showing fluctuation in volume. Of the patients who displayed abnormality in neurological and physical exams, most recovered to normal range in muscular weakness, sensory loss, SLRT and lumbar ROM by week 24 <**Table 3**>.

Table 3. Changes in physical examination findings and herniated disc as assessed by MRI up to 3 years

	Evaluation			
Number of patients (n)	Baseline	24 wks	1 yr	3 yrs
Outcome assessed by MRI[a]				
Similar		36	27	23
Improved		21	37	42
Aggravated		16	9	8
Limited range of motion (ROM)	59	10	7	9
Muscle weakness	34	6	2	2
Sensory loss	18	4	2	3
Straight leg raise test < 60°, mean (SD)	51	11	3	5

[a]Changes in size of the main herniated disc most likely to produce sciatic symptoms were compared by MRI with results from the previous follow-up and classified into three categories as evaluated by a radiologist and Korean medicine doctor: improved, similar and worse.

Twenty-seven (37%) out of 73 patients reported having sought medical care for recurrence of LBP and/or sciatica at 3 years, of which 23 patients (85%) continued with CAM, and the rest opted for conservative treatment such as medication, physical therapy, exercise or nerve block injection <**Table 4**>.

Table 4. Use of health care service by 27 patients with low back pain and/or sciatica recurrence (after the pre-defined 6 months of treatment) at 3 years

Type of treatment	Number of patients[b]	Number of sessions (SD)
CAM therapy[a]	23	21.54 (17.97)
Conventional medication	2	3.00 (1.41)
Korean medicine Physical therapy	8	28.50 (35.74)
Exercise therapy	1	10.00
Nerve block injection	3	4.00 (3.61)

[a]Refers to integrative treatment including acupuncture, Chuna manipulation, bee venom pharmacopuncture and herbal medicine.
[b]Number of patients was tallied allowing for multiple choices.

Ninety-two out of 128 patients answered whether they had undergone surgery at 3 years, and 4 patients reported having received surgical operations.

DISCUSSION

Patients with sciatica due to LHD reported improvement in leg pain and ODI scores above MCIC from week 8 during the 24 weeks of CAM treatment. Clinically significant improvements in LBP also became apparent, and most patients no longer presented neurological disorders from week 24. We found moderate time by group interaction difference in VAS for LBP and ODI scores in subgrouping by duration of LBP, and significant time by group interactions in VAS for LBP when subgrouped by operation recommendation.[7~~7~~] In additional investigations over 3 years, patients showed further improvement or maintained their improved state. Cases with continuous neurological disability were few.

In cases of recurrent pain, most patients (23 out of ~~37~~ 27 patients, 85%) reselected CAM therapy and only a few cases sought conventional treatments. Thirty-six of 73 patients reported minimal levels of pain intensity and functional disability that did not require further treatment at the 3 year follow-up. The fact that a high percentage returned to CAM suggests a high satisfaction rate and these results imply that CAM could be considered an effective treatment option for LHD patients with neurological symptoms.

One of the major strengths of our study is that it is a rigorous cohort observation on CAM treatment over a period of three years. All participants underwent multidimensional pain and functional ability assessments including MRI scans and physical examinations.

The combined approach of integrative treatment is similar to real-world settings and the collected data can be highly informative to clinicians as examinations and treatment were performed under circumstances comparable to typical Korean medicine clinics. During the 24 weeks of treatment, patients were subjected to an intense regimen of integrative treatment, but the high compliance rate of 85.3% (128 out of 150) indicates that patients were highly satisfied with treatment. Additionally, the fact that no side effects other than a mild allergic reaction to bee venom occurred is noteworthy.

Previous long term follow-ups of studies focusing on neurological injury due to intervertebral disc displacement are mainly comparisons of the effects of surgical versus non-surgical treatment. Leiden-The Hague Spine Intervention Prognostic Study Group compared early surgery versus prolonged conservative care given by family practitioners, with conservative care consisting mainly of counseling, guidance from a physiotherapist, and prescription of painkillers.[2] The long-term follow-up results at 1 and 2 years showed no significant difference between the two groups in leg pain and lumbar function. However, 46% of the patients allocated to the non-surgical group received surgery, and the results were intention-to-treat analyzed. As-treated analysis was performed in the Spine Patient Outcomes Research Trial (SPORT) study, and the long-term follow-up results at 1 and 2 years all showed superior results in SF-36 bodily pain and physical function scales in the surgery group compared to nonoperative care (active physical therapy, counseling and education with home exercise instructions, and presciption of nonsteroidal anti-inflammatory drugs).[25]

In studies comparing conventional non-surgical treatment (e.g. education, rest, pain medication, physical therapy, etc.) and CAM non-surgical treatment (e.g. hot compress using Chinese medicine, electroacupuncture, Chinese herbal injection, Chinese Tuina, etc.), CAM treatment showed better results in lumbar functional scores at 6 months' short-term follow-up.

A systematic review on the effectiveness of conservative treatments for lumbosacral radicular syndrome evaluated injections, traction, physical therapy, bed rest, manipulation, medication, and acupuncture, deducing

that corticosteroid injections and traction did not have sufficient evidence to be recommended as treatment options, and that it was difficult to reach a conclusion whether the other treatments should be prescribed by clinicians or whether a certain type of treatment is superior to others.[26]

A recent review of eight studies on the efficacy of Chinese herbal medicine for lumbar disc herniation compared with conventional treatment analyzed the results of 5 studies reporting that Chinese herbal medicine was better than conventional medicine, and 2 studies stating that clinical outcomes were better in Chinese herbal medicine groups than in physiotherapy and placebo groups.[27] However, all trials were of poor methodological quality.

~~However, t~~There are also weaknesses and limitations of our study. One particular limitation is due to the innate nature of a prospective cohort study where we cannot draw any definite conclusions regarding treatment efficacy. Due to ~~the~~ lack of a control group, we are unable to conclusively comment on the effectiveness of individual treatments or on the comparative effectiveness of this integrative package to conventional treatment modalities.

Perhaps the most significant limitation is the low long term compliance rate. The 3 year follow-up was conducted only on patients who had completed the 24 weeks of treatment and ~~1~~1st-1 and 2 year follow-up ~~term~~sessions, leaving 73 of the original 128 participants (57%) who initially completed treatment. The study design was conceived to the aim of comparing the patient's state each year with the previous year to track changes multidimensionally, and t~~T~~he reason for the increasing loss of follow-up~~this poor compliance~~ may be partly explained by the strict follow-up inclusion criteria. MRI scans and assessments of~~on both~~ neurological and physical function required regular visits to the hospital as they could not be replaced with phone interviews or online assessments. A large proportion of the study population refused further participation in the study due to personal reasons; some no longer required treatment, others refused to travel long distances after moving.

We lost track of many patients in the course of this study, and this may be due~~,~~ in part~~,~~ to the rapidly changing communications industry in Korea. Many Koreans are replacing home phones with internet or personal mobile phones~~,~~ and frequently changing personal contact information. Also, while there was an increasing loss of follow-up patients, it cannot be decisively said that the patients that did not attend the 3 year follow-up were necessarily in worse medical states. As seen in Table 1, the baseline characteristics of drop-out patients did not

differ greatly from follow-up patients, and as we had made it known to the participants prior to follow-up that all~~the follow-up~~ MRIs and tests were free of charge, it is possible that patients in worse medical conditions were~~would be~~ more committed to the yearly check~~follow~~-ups.

The results of a meta-analysis on the effectiveness of integrative Chinese medical therapies including Tuina on low back pain patients showed that groups receiving Tuina with Chinese herbal medicine and Tuina with acupuncture showed better pain and functional status than groups receiving Tuina alone.[28] Our results also reflect the discussions of CAM clinicians on selecting effective treatment methods for disc herniation patients, and the outcome of those consultations was an integrative treatment package consisting of herbal medicine, acupuncture, bee-venom pharmacopuncture and Chuna manipulation. The reason for this multi-modality approach is that each approach has different targets, effects, mechanisms and time-windows, and no single therapy is clearly superior to others or unequivocally successful.

Although integrative treatment may be considered pragmatic, this leads to another limitation. A combined approach makes it difficult to discern the level of contribution of individual factors. Current clinical guidelines[29, 30~~25, 26~~] suggest composition of integrative treatment should be based on a coherent theoretical basis and evidence-based effectiveness. However, the present study treatment was pre-decided through clinical experience and preferential consensus of KMDs. Therefore, this study requires further consideration of such factors as evidence-based effectiveness and cost-effectiveness in treatment construction for a more organized gradient intervention.

These limitations notwithstanding, the study results show that the herniated disc patients included in the present study were able to control their symptoms using only CAM without the help of conventional treatments[31, 32~~27, 28~~] during the treatment period. Only a few people reported need of conventional treatment at the 2nd follow-up also.

This study is one of the few studies and only study conducted in Korea to evaluate the effects of CAM treatment in LHD patients with sciatica multi-dimensionally using standardized imaging and examinations. In the current study, integrative treatments were proven safe and brought about improvement in pain, functional disability, quality of life and neurological disorders. Further investigations and RCTs are required to assess the

comparative benefits of integrative CAM treatment to contemporary conventional medicine.

Contributors

IHH drafted the study, and MRK and IHH wrote the final manuscript. JSS, JHL, BCS and MSL contributed to the study design and made critical revisions. All of the authors have read and approved the final manuscript.

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Competing interests

None declared.

Ethics approval

The study protocol was approved by the Institutional Review Board of Jaseng Hospital of Korean Medicine.

Data sharing statement

No additional data are available.

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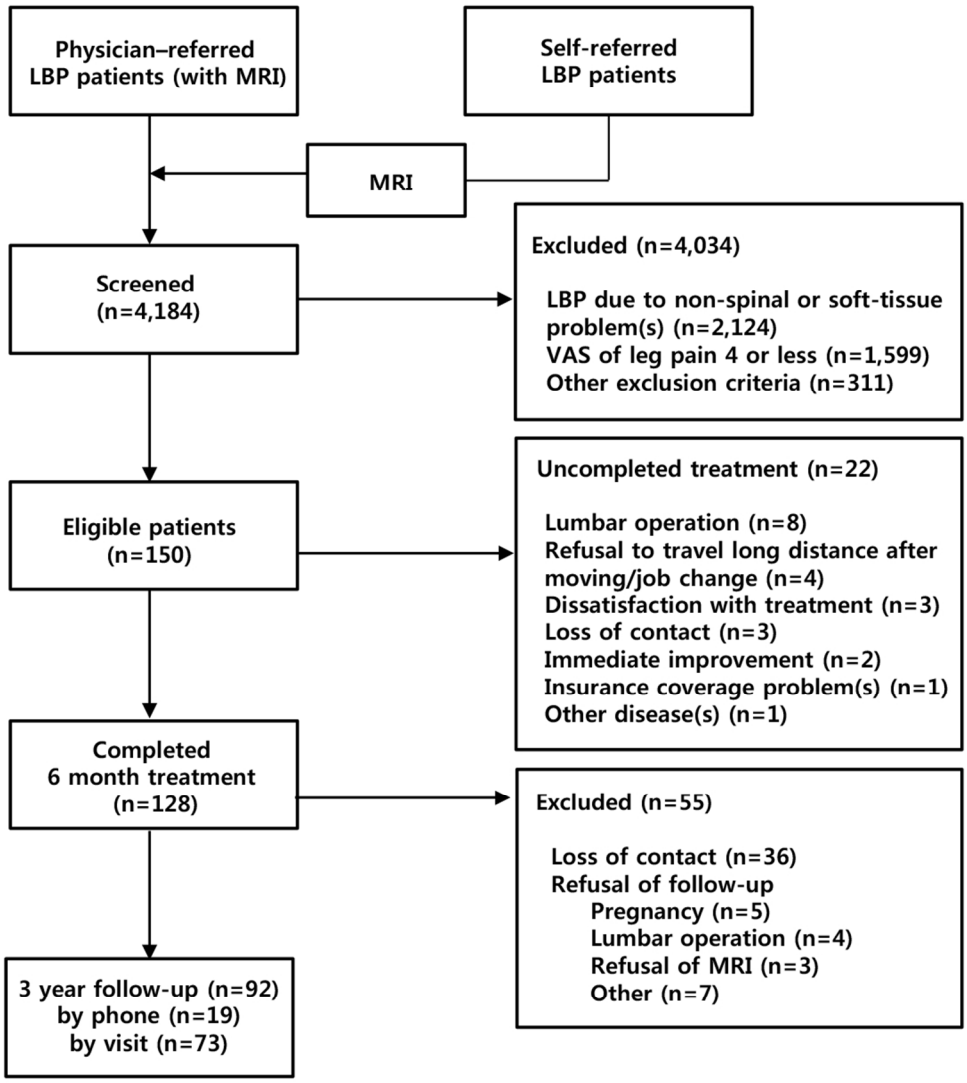
Fig. 1. Flow diagram of study

Fig. 2. Distribution of pain classified by pain severity over time



Flow diagram of study
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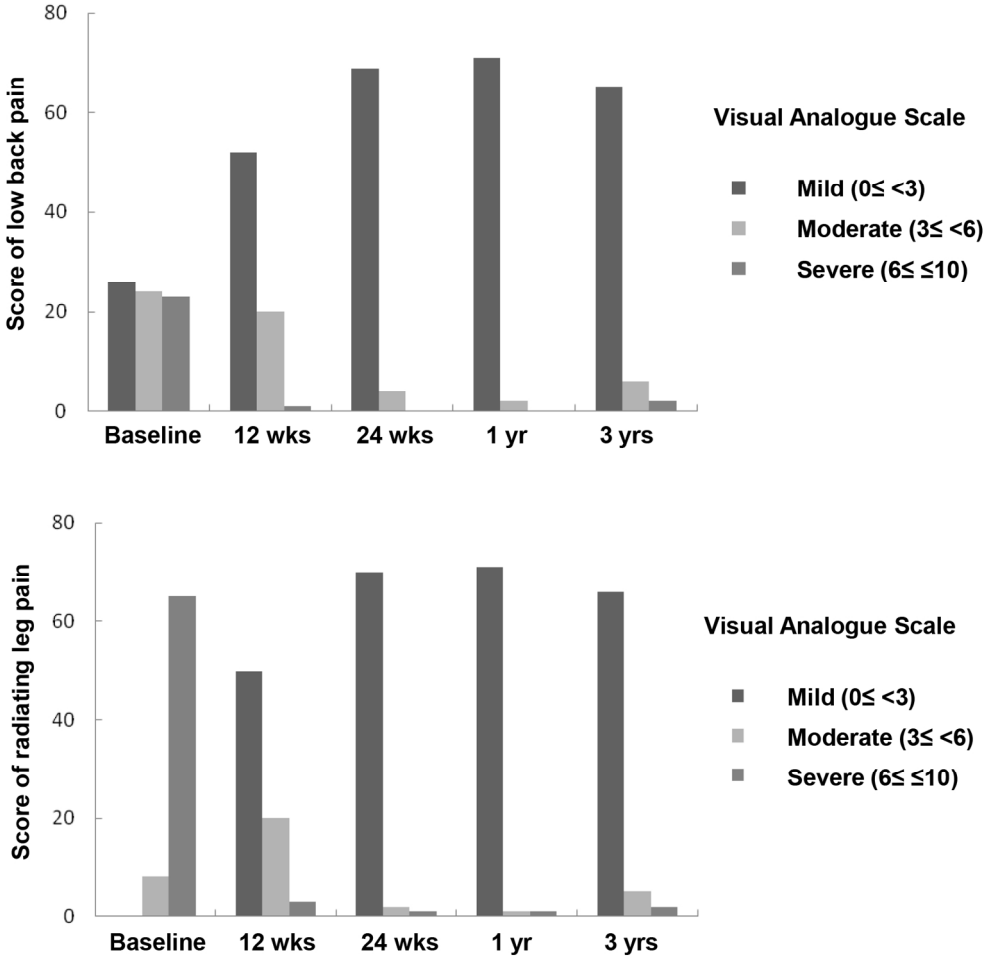

Distribution of pain classified by pain severity over time
148x145mm (300 x 300 DPI)

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cohort studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	Title page #1 Abstract #1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	Abstract #1
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	#1
Objectives	3	State specific objectives, including any prespecified hypotheses	#1
Methods			
Study design	4	Present key elements of study design early in the paper	#1-2
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	#1-2
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	#2-4
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	-
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	#3-4
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	#3-4
Bias	9	Describe any efforts to address potential sources of bias	#2-3
Study size	10	Explain how the study size was arrived at	-
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	-
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	#4
		(*b*) Describe any methods used to examine subgroups and interactions	-
		(*c*) Explain how missing data were addressed	-
		(*d*) If applicable, explain how loss to follow-up was addressed	-
		(*e*) Describe any sensitivity analyses	-

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	#4
		(b) Give reasons for non-participation at each stage	#4-5
		(c) Consider use of a flow diagram	#5
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	#4-5
		(b) Indicate number of participants with missing data for each variable of interest	-
		(c) Summarise follow-up time (eg, average and total amount)	#4
Outcome data	15*	Report numbers of outcome events or summary measures over time	#4-8
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	#6
		(*b*) Report category boundaries when continuous variables were categorized	#5-7
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	-
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	#8
Discussion			
Key results	18	Summarise key results with reference to study objectives	#8
Limitations			
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	#8-11
Generalisability	21	Discuss the generalisability (external validity) of the study results	#8-9, 11
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	#11

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.