Participants

The inclusion criteria were: (1) back pain with sciatica, leg pain intensity of 5 or higher as assessed with numeric rating scale (NRS) and onset within 1 year; (2) sciatica from lumbar intervertebral disc herniation as confirmed on magnetic resonance imaging (MRI) and neurologic examinations; (3) age between 18 to 60 years; (4) written informed consent to participate in study, and attend 6 months of integrative CAM treatment and follow-up assessments.

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

Interventions

Participants received a standardized and consistent integrative complementary and alternative medicine (CAM) treatment package for back pain and sciatica for 24 weeks. Contents of the treatment package were predetermined from lumbar intervertebral disc herniation treatments frequently used in Korean medicine clinical practice. The treatment consisted of herbal medicine, acupuncture, bee venom pharmacopuncture and Chuna manual therapy (a Korean version of spinal manipulation). Treatment sessions were conducted once a week for duration of treatment (24 weeks), and herbal medication was taken twice a day for 24 weeks.

1. In acupuncture, frequently used acupoints (BL23, BL24, BL25, BL31, BL32, BL33, BL34, BL40, BL60, GB30, GV3 and GV4) and points at the site of pain were selected by the physician and the needle retention time was 20 min. Sterilized disposable needles (0.30×40 mm, stainless steel, Dong Bang Acupuncture Co., Korea) were used.

2. Chuna manual therapy is a Korean spinal manipulation that applies high-velocity, low amplitude thrusts to joints slightly beyond the passive range of movement for spinal mobilization and gentle force to joints within the passive range.

3. Bee venom pharmacopuncture injects 0.5-1 cc of diluted bee venom solution (saline:bee venom ratio=1000:1) at 4-5 acupoints around the lumbar spine to a maximum total 1 cc using disposable injection needles (1 cc, 26G×1.5 syringe, Shinchang medical Co., Korea).

4. Herbal medicine was administered twice daily in powder (2 g) and water-based decoction form (120 mL) (Ostericum koreanum, Eucommia ulmoides, Acanthopanax sessiliflorus, Achyranthes bidentata, Pсорalea corylifolia, Saposhnikovia divaricata, Cibotium barometz, Lycium chinense, Boschniakia rossica, Cuscuta chinensis, Glycine max, and Atractylodes japonica). These herbal contents were selected from medicinal herbs frequently prescribed for back pain (or nerve root pain) treatment in traditional Korean and Chinese medicine, and through clinical practice at Jaseng Hospital of Korean Medicine the initial herbal prescription was further developed to its current form. In addition, recent in vitro studies report on how Cibotium barometz inhibits osteoclast formation and Atractylodes japonica extracts protect osteoblast cells from oxidative stress. Eucommia ulmoides has also been reported to have in vitro osteoclast inhibitive effects, and osteoblast-like cell proliferative and in vivo bone mineral density increase effects.

Participants received educational instructions at treatment sessions to stay active and maintain daily activities and self-management within the range of non-aggravation of symptoms. Also, patients were informed of the favorable prognosis and encouraged to continue with non-surgical treatment.
Adverse events\textsuperscript{13}

Participants were monitored closely for possible adverse events. In consideration of potential herbal medicine associated drug-induced liver injury (DILI), liver function tests were conducted at baseline, and 12 and 24 weeks post-baseline. Liver function tests included serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), and total bilirubin (TBR) levels. For participants with baseline AST and ALT levels within normal range (AST $\leq$ 35 U/L; ALT $\leq$ 31 U/L; TBL $\leq$ 1.4 U/L), this study used the Council for International Organizations of Medical Science criteria, which requires at least two of the following criteria be met to be regarded as DILI: (a) criterion I: plasma ALT concentrations above 2 ULN (upper limit of normal range); (b) criterion II: conjugated bilirubin above 2 ULN; or (c) criterion III: combined increase of AST, alkaline phosphatase (AP) and TBR provided one value is above 2 ULN.\textsuperscript{14}

Following the method reported by Sulkowski et al.\textsuperscript{15} patients with elevated serum AST and ALT levels (higher than ULN) at baseline were classified according to changes relative to baseline as opposed to ULN: grade 0 ($<1.25 \times$ baseline); grade 1 (1.25-2.5$\times$baseline); grade 2 (2.6-3.5$\times$baseline); grade 3 (3.6-5$\times$baseline); and grade 4 ($>5 \times$baseline). Change in serum TBR was categorized according to changes relative to ULN: grade 0 ($>1.1 \times$ULN); grade 1 (1.1—1.5$\times$ULN); grade 2 (1.6—2.9$\times$ULN); grade 3 (3—5$\times$ULN); and grade 4 ($>5 \times$ULN).
References of supplement file


