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〔Original Paper〕

Safety and efficacy of repetitive hyperbaric oxygen therapy in patients with lumber spinal stenosis － a prospective, open-label case control study

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SUMMARY

Background: Hyperbaric oxygen therapy（HBOT）has an established role in the palliation of several conditions. However, few reports of HBOT in patients with lumbar spinal stenosis（LSS）have been published. The purpose of this study was to clarify the efficacy and safety of HBOT in patients with LSS.

Methods: This prospective, open-label case control study included 24 LSS patients（19 who received HBOT, 5 who did not）diagnosed by clinical symptoms and imaging findings. HBOT was conducted 10 times over 4 weeks. Each treatment was conducted for 90 minutes total in a room-sized hyperbaric chamber: 15 minutes of pressure with compressed air from 1.0 atmosphere absolute（ATA）to 2.0 ATA, 60 minutes of maintenance in which patients breathed 100% oxygen to 2.0 ATA, and 15 minutes of decompression from 2.0 ATA to 1.0 ATA. The follow-up period was 3 months.

Results: Patients who underwent HBOT showed significant improvement in walking ability, pain scale scores and quality of life. In contrast, patients who did not receive HBOT did not experience significant changes. One adverse event occurred in 1 patient（5%）in the HBOT group.

Conclusions: We suggest that HBOT can be a safe and an effective conservative treatment for LSS patients.

Key words: **hyperbaric oxygen therapy, lumber spinal stenosis**

Ⅰ. Introduction

Lumbar spinal stenosis（LSS）is one of the most common diagnoses for low back pain and leg pain symptoms for which conservative treatment or surgery is performed[1]. LSS is defined as a narrowing of the spinal canal, lateral recesses, and/or neural foramina, resulting in compression of the neurogenic and vascular structures at one or more levels. Compression and ischemia of spinal nerves are widely accepted as causative symptoms of LSS.

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Hyperbaric oxygen therapy (HBOT) has an established role in the palliation of mandibular osteoradionecrosis[2]. The utility of HBOT has also been reported for several other conditions, including radiation-induced brachial plexopathy[3], refractory hemorrhagic cystitis following pelvic radiotherapy [4], radiation myelopathy[2], radiation-induced optic neuropathy[5], and radiation-induced sacral plexopathy [6]. However, to the best of our knowledge, no reports of HBOT in patients with LSS have been published. The purpose of this study was first to clarify a safety of HBOT in patients with LSS and second to demonstrate the efficacy.

Ⅱ. Materials and Methods

This prospective, open-label, case-control study, which was conducted at a local hospital, evaluated a safety and an efficacy of HBOT for the treatment of LSS. This study was approved by the hospital's institutional review board, and all participants provided informed consent.

Inclusion criteria were: age ＞20 years and LSS diagnosed by clinical symptoms (low back and leg pain) and imaging (x-ray and magnetic resonance imaging [MRI]) findings. After receiving an explanation about HBOT, patients either elected to undergo HBOT (HBOT group) or to not receive HBOT but to undergo follow-up observation (natural course group). As this was a preliminary study to confirm the safety rather than the efficacy, all the patients were allowed to keep their medication except epidural injection. Of 24 patients, the HBOT group consisted of 19 patients (8 males, 11 females) and the natural course group consisted of 5 patients (3 males, 2 females). Mean age at baseline was 78.2 years in the HBOT group and 73.6 years in the natural course group without statistical difference (P＞ 0.05).

Patients in the HBOT group underwent 10 repetitive treatments over 4 weeks. Each treatment was conducted for 90 minutes total in a room-sized hyperbaric chamber: 15 minutes of pressure with compressed air from 1.0 atmosphere absolute (ATA) to 2.0 ATA, 60 minutes of maintenance, during which patients breathed 100% oxygen to 2.0 ATA, and 15 minutes of decompression from 2.0 ATA to 1.0 ATA.

At baseline, all patients were evaluated for walking distance, step, visual analogue scale (VAS) score for low back pain, leg pain and numbness, Japanese Orthopaedic Association lumbar score (JOA score) [7], and JOA Back Pain Evaluation Questionnaire (JOABPEQ) score[8-9]. Three months after study initiation, all patients were reevaluated for the same outcome measures. Any adverse events were reported during the study period.

Statistical Analysis

Baseline categorical variables and those at 3 months were compared using the Wilcoxon signed ranks test. Progress in the HBOT and natural course groups were compared using the Mann-Whitney U test. Data analysis was performed using SPSS Statistics version 16.0 software (IBM statistics, Chicago, IL). A p-value＜0.05 was considered statistically significant.

Ⅲ. Results

In the HBOT group, walking distance significantly improved after 3 months from 297 m to 344 m (P = 0.0437, Table 1). VAS scores for low back pain, leg

Table 1 Clinical data − HBOT group

	Baseline	After 3 months	p-value
Walking distance (m)	297 (304)	344 (314)	0.0437
Step (cm)	49.7 (12.4)	50.7 (11.2)	N.S.
VAS (back pain, mm)	46.9 (27.8)	33.3 (21.2)	0.0003
VAS (leg pain, mm)	54.2 (29.1)	33.9 (19.4)	0.0006
VAS (numbness, mm)	56.2 (29.7)	34.4 (21.3)	0.0005
JOA score (points)	14.5 (4.9)	15.6 (5.6)	0.0399
JOABPEQ			
Low back pain	42.9 (37.2)	68.5 (29.0)	0.0014
Lumbar function	53.0 (29.0)	64.5 (26.4)	N.S.
Walking ability	25.8 (25.5)	42.9 (28.2)	0.0089
Social life function	37.4 (17.0)	46.6 (20.5)	0.0276
Mental health	45.0 (16.5)	47.1 (19.8)	N.S.

HBOT: hyperbaric oxygen therapy, VAS: visual analogue scale, JOABPEQ: Japanese Orthopaedic Association Back Pain Evaluation Questionnaire. Mean (standard deviation), Wilcoxon signed rank test, N.S.: not significant.

pain, and numbness were significantly better after 3 months ($P = 0.0003$, 0.0006, and 0.0005, respectively). JOA scores also improved significantly from 14.5 points to 15.6 points ($P = 0.0399$). Finally, scores for JOABPEQ, a parameter of low back pain, walking ability, and social life function, significantly improved ($P = 0.0014$, 0.0089, and 0.0276, respectively). Lumbar function and mental health also improved, but not to a statistically significant degree. In contrast, in the natural course group, walking distance, VAS, JOA score, and JOABPEQ did not change significantly (Table 2).

Table 2 Clinical data − natural course group

	Baseline	After 3 months	p-value
Walking distance (m)	390 (368)	322 (314)	N.S
Step (cm)	50.8 (6.1)	51.6 (7.6)	N.S.
VAS (back pain, mm)	44.8 (34.0)	45.0 (28.5)	N.S.
VAS (leg pain, mm)	66.8 (26.8)	65.4 (22.3)	N.S.
VAS (numbness, mm)	55.8 (41.1)	54.2 (37.5)	N.S.
JOA score (points)	12.8 (5.0)	13.0 (3.7)	N.S.
JOABPEQ			
Low back pain	40.0 (38.4)	42.8 (39.2)	N.S.
Lumbar function	56.6 (34.5)	51.6 (23.9)	N.S.
Walking ability	48.4 (35.6)	49.8 (23.0)	N.S.
Social life function	53.8 (20.4)	42.2 (20.1)	N.S.
Mental health	42.6 (20.8)	46.0 (21.9)	N.S.

VAS: visual analogue scale, JOABPEQ: Japanese Orthopaedic Association Back Pain Evaluation Questionnaire. Mean (standard deviation), Wilcoxon signed rank test, N.S.: not significant.

Table 3 Progress of patients in the HBOT and natural course groups from baseline to final evaluation

	HBOT	Natural course	p-value
Walking distance (m)	47 (137)	-68 (152)	0.0225
Step (cm)	0.9 (4.5)	0.8 (1.8)	N.S.
VAS (back pain, mm)	-13.7 (15.6)	0.2 (6.1)	0.0497
VAS (leg pain, mm)	-20.3 (24.2)	-1.4 (12.2)	0.0454
VAS (numbness, mm)	-21.8 (41.1)	-1.6 (12.2)	0.0275
JOA score (points)	1.1 (2.4)	0.2 (1.5)	N.S.
JOABPEQ			
Low back pain	25.6 (22.1)	2.8 (32.6)	N.S.
Lumbar function	12.6 (25.6)	-5.0 (16.0)	N.S.
Walking ability	14.7 (22.7)	1.4 (15.7)	N.S.
Social life function	8.8 (18.9)	-11.6 (8.7)	0.0154
Mental health	6.3 (11.2)	3.4 (9.4)	N.S.

HBOT: hyperbaric oxygen therapy, VAS: visual analogue scale, JOABPEQ: Japanese Orthopaedic Association Back Pain Evaluation Questionnaire. Mean (standard deviation), Mann-Whitney U test, N.S.: not significant.

At the baseline, there were not any significant differences between the HBOT group and the natural course group at all ($P = >0.05$). However, three mouths later walking distance significantly improved in the HBOT group in comparison to the natural course group (47 m versus -68 m, $P = 0.0225$, Table 3). VAS scores for low back pain, leg pain, and numbness significantly more improved in the HBOT group, too ($P = 0.0497$, 0.0454, and 0.0275, respectively). Regarding the JOABPEQ, only the social life function parameter significantly improved in the HBOT group (8.8 points versus -11.6 points, $P = 0.0154$).

One adverse event was noted in 1 (5%) of 19 patients in the HBOT group: this patient complained of a mild buzzing in her ears after the third course of HBOT, and declined further treatment.

Ⅳ. Discussion

This is the first clinical study to demonstrate better outcomes in LSS patients who have received HBOT compared to those in patients who have not. Patients in the HBOT group showed significant improvement in walking ability, pain scale score, and quality of life. Adverse event was noted in 5%. Therefore, HBOT could be a safe and an effective conservative treatment for LSS patients.

Several possible mechanisms may explain why HBOT is beneficial in this patient population. First, HBOT promotes repair and generation of new blood vessels to the parts of the spinal nerve that have been injured and undergone apoptosis, resulting in improved metabolism after ischemia[10]. HBOT also has an established role in the palliation of mandibular osteoradionecrosis[2]. Furthermore, the efficacy of HBOT has been reported in several other conditions. Patients with vaginal vault prolapse and perineal necroses have been treated successfully with HBOT [11]. Sensory symptoms were reported to have improved in five cases with radiation myelopathy who received HBOT, although no change in motor disability was seen[2]. A small number of patients with radiation-

induced optic neuropathy have been treated with HBOT, with some experiencing a reversal of recent visual loss[5]. A single case report of a patient with radiation-induced sacral plexopathy described lasting improvement following HBOT several years after the first appearance of sensory and motor symptoms [6]. All of these effects may require time to occur. Compared to the results of several previous animal studies in myelopathy and neuropathy, human studies involve several influential factors such as age, severity of stenosis, social circumstances, prior disability, and comorbidities. Moreover, the protocol of HBOT may play a role in the prognosis of acute ischemic stroke[12].

Based on the results of previous studies, HBOT may be associated with several adverse effects, including damage to the ears and sinuses due to the pressure, seizures, and oxygen poisoning[13-15]. In this study, a mild buzzing in the ears was observed in 1 patient (5%). All of the other patients completed the treatment protocol. Thus, HBOT appears to be a safe and feasible intervention for patients with LSS.

We have previously used JOA score to evaluate low back pain and leg pain[7]. However, this score does not incorporate a comprehensive evaluation from the patient's perspective. To resolve this problem, the JOA has developed a new score to evaluate low back pain, the JOABPEQ, which incorporates several aspects from the patient's experience[8]. This score includes five categories (25 items) and has high sensitivity for assessing treatment results[9]. Patients in the HBOT group experienced significant improvements in low back pain, walking ability, and social life function for 3 months. However, the difference in social life function improvement was significantly higher in the HBOT group than in the natural course group; this difference may be partly attributable to the small number of patients in the latter group. Thus, we believe that HBOT can improve the quality of life of LSS patients, particularly in patients with poor prognoses due to serious complications or multiple back surgeries.

This study has several limitations. First, the number of patients is too small to elicit a strong conclusion. Moreover number of patients in two groups is biased, because they preferred to HBOT. We must admit that this study is preliminary, but our primary goal was to confirm the safety of HBOT rather than the efficacy. We applied a nonparametric method for statistical analysis to eliminate the distribution. Further studies are required to confirm these results. Second, patients were followed up for only 3 months. Long-term evaluation may be necessary to demonstrate the efficacy of HBOT in this patient population.

In conclusion, this study demonstrated better outcomes in LSS patients who underwent HBOT compared to those who did not. Patients in the HBOT group showed significant improvements in walking ability, pain scale scores, and quality of life. Adverse event was noted in 5%.

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