REVIEW

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Literature review of non-pharmacological treatment for patients with axial spondyloarthritis

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Axial spondyloarthritis (axSpA) is a chronic inflammatory disorder affecting the sacroiliac joints and axial spine. Along with pharmacotherapy, non-pharmacological interventions for axSpA are crucial and constitute the cornerstone of treatment. Here, we review the evidence for non-pharmacological treatment of axSpA as a basis for the 2023 Korean treatment recommendations for patients with axSpA. The effectiveness of the core non-pharmacological approaches, such as education, smoking cessation, and exercise, has been reaffirmed. High-quality research on surgical treatment is limited. However, total hip replacement is advised in patients with ongoing pain or disability and visible structural damage to the hip on imaging. Urgent spinal intervention should be considered in cases of acute spinal pain with neurological deficiency or concurrent unstable fractures. Evidence for complementary therapies, including spas and acupuncture, remains insufficient.

Keywords: Axial spondyloarthritis; Ankylosing spondylitis; Non-pharmacological treatment

INTRODUCTION

Axial spondyloarthritis (axSpA) is a chronic inflammatory disorder affecting the sacroiliac joint and axial spine [1]. Chronic back pain and spinal stiffness are its most common symptoms; however, axSpA can involve other organs or tissues, including the peripheral joints, entheses, skin, eyes, and gastrointestinal tract. AxSpA is a progressive disease that can lead to a fully ankylosed spine and has a considerable impact on the patient's overall life; therefore, it is crucial to provide appropriate timely treatment.

Both pharmacological and non-pharmacological treatments are essential in the management of patients with axSpA. Pharmacological treatments have been emphasized over the past decade based on abundant clinical trial results. However, non-pharmacological treatments, which were relatively underemphasized due to scanty evidence, are being increasingly supported by a growing body of evidence [2]. The Development Committee for the Korean Axial Spondyloarthritis Treatment Recommendations categorized items related to non-pharmacological therapy into education, smoking, exercise, surgery, and complementary medicine based on clinical questions in a Korean context. This was reflected in the evidence review and formulation of treatment recommendations. The purpose of this paper was to review the evidence for the non-pharmacological therapies included in the axSpA treatment recommendations [3].

NON-PHARMACOLOGICAL TREATMENT FOR AXIAL SPONDYLOARTHRITIS

Education

Appropriate education plays a pivotal role in the management of axSpA. The goal of education is not limited to conveying knowledge about the nature, treatment, and prognosis of the disease but also enables patients to align their preferences with treatment options by facilitating collabora-

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tive work between clinicians and patients. Self-management and shared decision-making are important for empowering patients to improve their quality of life [4]. However, the assessment of educational effects can be challenging because distinguishing their impacts from concurrent treatments requires much effort, and there are many types of treatment and methods of delivery. Nonetheless, evidence indicates that patient education enhances physical activity. One randomized controlled trial (RCT) demonstrated that a 2-hour information session about the disease resulted in a better Bath Ankylosing Spondylitis Disease Activity Index (BASDAI; -0.65, 95% confidence interval [CI]: -0.82 to -0.47 in the education group vs. -0.37, 95% CI: -0.55 to -0.19 in the control), Bath Ankylosing Spondylitis Functional Index (BASFI) (-0.54, 95% CI: -0.68 to -0.40 in the education group vs. -0.21, 95% CI: -0.36 to -0.0007 in the control), and ankylosing spondylitis quality of life (ASQoL) (-0.98, 95% CI: -1.29 to -0.68 in the education group vs. -0.23, 95% CI: -0.54 to 0.07 in the control) at 6 months [5]. Another RCT showed that a 3-month behavioral program improved moderate/vigorous-intensity physical activity measured by accelerometry (+58 minutes, in the education group vs. -65 minutes in the control group, $p < 0.001$), which was sustained for over 3 months [6]. Therefore, education is an essential complement to pharmacological treatment, to achieve therapeutic goals in patients with axSpA. In addition, providers must update their skills regularly to deliver high-quality education effectively.

Smoking cessation

Smoking is a substantial public health burden and is associated with various chronic illnesses, including respiratory and cardiovascular diseases and malignancies. There is accumulating evidence of a relationship between smoking and rheumatic disorders. Smoking has been identified as a risk factor for axSpA [7]. The exact mechanisms by which smoking influences the development and progression of axSpA are not fully understood; smoking may trigger and perpetuate inflammatory processes, contributing to disease progression and treatment non-responsiveness [8]. In addition, the complex interplay between smoking and genetic factors, such as variants of the *endoplasmic reticulum aminopeptidase-1* gene may modulate the risk of axSpA [9]. Studies have demonstrated that smoking negatively affects bony progression based on the unit increase in the Ankylosing Spondylitis Disease Activity Score (ASDAS; odds ratio [OR] 2.15, 95% CI: 1.01 to 3.30) in axSpA patients [10]. One systematic literature review demonstrated the dose-dependent impact of smoking on structural damage progression (OR 3.57, 95% CI: 1.33 to 9.60 in heavy smokers) [7]. Furthermore, smoking patients with axSpA had worse physical mobility and quality of life than non-smoking patients with axSpA. Considering the detrimental effects of smoking on axSpA, it is imperative to encourage and provide support for smoking cessation in all patients with this condition. Several studies have demonstrated that physicians' advice to quit smoking serves as a strong motivator to pursue smoking cessation (smoking cessation rate: 3% vs. 6%) [11].

Exercise

Since axSpA can affect the flexibility of the spine, muscle strength, and cardiopulmonary function, exercise is an integral nonpharmacological treatment of axSpA. Biomechanical stress and aberrant loads are key factors in the pathophysiology of axSpA [12]. From an immunological perspective, however, it is still unclear whether physical activity can exacerbate this disease. Based on the low likelihood of exercise-related harm and the accumulated evidence of its positive effects, including improved joint flexibility and range of motion and enhanced muscle power and aerobic capacity, various guidelines emphasize the importance of exercise therapy [13-15]. Several RCTs have evaluated the benefits of exercise on disease activity, physical function, pain, and quality of life in patients with axSpA [16-29].

Active physical exercise vs. passive physical therapy

Therapeutic exercises can be categorized as active or passive physical therapy. Active physical therapy involves the patient's active participation in the intervention, such as through advice, home exercises, or supervised exercises. Passive physical therapy refers to intervention where the patient has a more passive role, such as massage, ultrasound, and hot packs [30]. Passive stretching exercises with low-level laser therapy (ΔBASDAI -0.5, $p < 0.05$; ΔBASFI -1.3, $p < 0.01$) or whole-body cryotherapy (ΔBASDAI -2.1 vs. -0.7, $p < 0.01$; ΔBASFI -1.4 vs. -0.7, $p < 0.01$) have short-term effects, while long-term effects are lacking [26,27] (Table 1). Although the effects of active and passive physical therapy have not been compared directly, active physical therapy has received greater emphasis, while passive physical therapy plays a supportive role.

Table 1. Characteristics and outcomes of the included studies of exercise

Study ID	Study design	Interventions (intervention/control)	Sample size	Frequency of intervention	Duration (wk)	Evaluation (wk)	Outcome (mean difference ± SD or mean difference [95% CI])			
							BASDAI	BASFI	BASMI	BAS-G
Active physical therapy										
Altan et al., 2012 [17]	RCT	1-hour pilates exercise program	55 (30:25)	3 times a week	12	24	-0.4 ± 2.1	-0.7 ± 1.2*	-0.4 ± 0.8*	N/A
		Standard care		Supervised			0.4 ± 0.9	0.1 ± 1.1	0.2 ± 1.1	
Sweeney et al., 2002 [19]	RCT	Home-based exercise video	155 (75:80)	-	24	24	-0.3 ± 1.9	-0.4 ± 1.8	N/A	-0.2 ± 2.9*
		Standard care					-0.6 ± 0.6	-0.2 ± 1.9		1.6 ± 3.5
Kjeken et al., 2013 [20]	RCT	In-patient rehabilitation program	95 (46:49)	Once a week	3	12	-1.4 (-2.3, -0.6)**	-0.6 (-1.3, 0.1)	N/A	-0.6 (-1.5, 0.2)
		Standard care								
Aydın et al., 2016 [21]	RCT	Hospital-based calisthenic exercise	37 (18:19)	5 days a week (mean 45 min)	8	8	-0.5 ± 1.0	-0.5 ± 1.2	-0.6 ± 0.8**	-0.3 ± 1.4
		Home-based calisthenic exercise					-0.4 ± 1.1	0.1 ± 1.5	0.1 ± 0.6	-0.1 ± 1.5
Viitanen and Heikkilä, 2001 [22]	RCT	Intensive physiotherapy and exercise	43 (25:18)	3 week Supervised	3	3	-1.3 (-1.9, -0.6)**	-0.5 (-1.1, 0.1)	N/A	-1.3 (-2.0, -0.6)**
		Standard care								
Dundar et al., 2014 [25]	RCT	Aquatic exercise	69 (35:34)	5 times a week	4	12	-0.3 ± 0.1	-0.3 ± 0.1	-0.2 ± 0.1-	-0.5 ± 0.2**
		Home-based exercise					-0.3 ± 0.1	-0.3 ± 0.1	0.2 ± 0.1	-0.3 ± 0.2
Passive physical therapy										
Widberg et al., 2009 [23]	RCT	Self- and manual mobilization	32 (16:16)	1-hour twice a week	8	8	-0.4 ± 1.4	-0.6 ± 0.8	-0.9 ± 0.7**	-1.2 ± 1.5
		Standard care					N/A	N/A	N/A	N/A
Stasinopoulos et al., 2016 [26]	RCT	LLLT with passive stretching	48 (24:24)	12 sessions	8	8	-0.5 (-0.9, 0.2)*	-1.3 (-2.2, -0.4)**	N/A	-3.3 (-3.9, -2.6)**
		Passive stretching exercises								
Stanek et al., 2018 [27]	RCT	Whole-body cryotherapy with subsequent kinesiotherapy	32 (16:16)	3 min a day	1.5	1.5	-2.1 ± 1.2**	-1.4 ± 1.0**	N/A	N/A
		Kinesiotherapy only					-0.7 ± 0.4	-0.7 ± 0.4		

SD, standard deviation; CI, confidence interval; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; BAS-MI, Bath Ankylosing Spondylitis Metrology Index; BAS-G, Bath Ankylosing Spondylitis Patient Global Score; RCT, randomized controlled trial; N/A, not applicable; LLLT, low-level laser therapy.

*$p < 0.05$ between the intervention group and control group; **$p < 0.01$ between the intervention group and control group.

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Supervised vs. non-supervised exercises

There are significant differences in the type, intensity, frequency, and duration of the exercises, including rehabilitation programs, Pilates, aquatic exercise, and high-intensity exercise (Table 1). Therefore, it is difficult to define a standardized exercise program for patients with axSpA. Despite this heterogeneity, supervised exercise resulted in better improvements in BASDAI, BASFI, and the Bath Ankylosing Spondylitis Metrology Index (BASMI), while no significant differences were observed in pain, chest expansion, or the Bath ankylosing spondylitis patient global score when compared with unsupervised or home-based exercise [20-24]. One RCT showed that a 1-hour supervised Pilates exercise program (3 times a week) improved function (ΔBASFI -0.7 in exercise group vs. 0.1 in standard care group, $p < 0.05$) and mobility (ΔBASMI -0.4 in exercise group vs. 0.2 in standard care group, $p < 0.05$ compared to standard care) [17]; another RCT showed that a supervised in-patient rehabilitation program (once a week) significantly reduced disease activity (ΔBASDAI -1.4 95% CI: -2.3 to -0.6) compared to standard care [20]. While both the American College of Rheumatology (ACR) and the European League Against Rheumatism (EULAR) advocate for supervised physical therapy as the preferred option [13,14], it remains challenging for patients with axSpA to locate and access such services.

Aquatic vs. land-based exercises

Although the difference was not substantial, aquatic exercises had better outcomes for short-term pain (ΔVAS -0.50 in aquatic exercise group vs. -0.30 in land-based exercise group, $p < 0.001$) and quality of life (Δshort form 36 health survey score 0.24 in aquatic exercise group vs. 0.13 in land-based exercise group, $p < 0.001$) than land-based exercises (Table 1) [25]. Owing to the lack of strong evidence supporting aquatic therapy and the high accessibility of land-based physical therapy, the ACR recommended a conditional preference for land-based therapy over aquatic therapy.

Manual therapy

Manual therapy is popular, but its potential adverse effects such as myelopathy, radiculopathy, and cerebral vascular accidents in patients with axSpA remain unverified. The fused cervical spine is prone to injury, and fracture-dislocation of the cervical spine has been reported, albeit rarely [28]. These fractures often lead to significant neurological impairment and increased mortality. Therefore, spinal manipulation is not recommended for patients with axSpA. Given the specific circumstances of an individual's health, exercise programs require precise clarification of maintenance and supervision strategies in routine practice.

Surgical treatment

AxSpA typically emerges at a younger age, with varying degrees of spinal involvement, and significantly affects quality of life due to pain and gait disturbances [31]. Although studies of surgical treatments are limited to retrospective studies, physicians should recommend surgical intervention for patients with axSpA at an appropriate time.

Hip surgery

Hip joint involvement occurs in 25–40% of the patients with axSpA and is associated with notable functional deterioration, occasionally necessitating hip arthroplasty [32]. In Korea, although hip joint involvement is less prevalent in patients with AS than in Western countries, the number of hip arthroplasties performed in patients with hip involvement is comparable to that in other countries [33]. Given the crucial role of the hip, limitations in hip function are associated with restricted body function in patients with axSpA. While no RCTs have assessed the effectiveness of total hip arthroplasty in axSpA, several observational studies have suggested that this intervention leads to reduced pain, improved range of motion, and enhanced joint function [31,34-37]. Notably, the average age of the participants involved in these studies was predominantly within the range 30 to 40 years, affirming the indication of surgical interventions for younger patients [14]. In younger individuals, cementless prostheses are the preferred option [31]. Meanwhile, one retrospective study demonstrated that the 20-year cumulative occurrence of revisions after primary total hip arthroplasty was 17.5%, with a cumulative occurrence of dislocation of only 2.9% [38]. Hence, total hip arthroplasty is advisable for patients experiencing persistent pain or disability and evidence of structural damage in the hip joint on radiographs, regardless of age; such patients should be informed about the likelihood of revision before they undergo surgery.

Spinal surgery

Evidence regarding spinal surgery is limited to retrospective studies that have demonstrated the effectiveness of surgical treatment for spinal kyphosis in patients with advanced axSpA. Several case reviews have shown that spinal

osteotomies using different surgical techniques have good outcomes [39-41]. However, other studies have reported perioperative complications with 2.4–4.0% mortality and 4.9% permanent neurological sequelae [42-44]. Although evidence regarding surgical treatment is limited, the EULAR recommends osteotomy for advanced spinal kyphosis in axSpA, emphasizing its potential benefits [14]. However, the ACR does not suggest spinal surgery because of its associated high mortality, despite acknowledging the possibility of limited elective surgery for severe kyphosis impairing horizontal vision [13]. In Korea, it would be advisable to approach spinal surgery with caution and strict limitations, considering insufficient specialized surgical centers and the inherent risks of the operation, based on a shared decision with the patient.

Spinal fractures and spinal cord injury after spinal fracture are major complications, especially after spinal trauma, and the reported prevalence in patients with axSpA is 10–17% and 29–91%, respectively [45], which largely leads to worse clinical outcomes [46]. The diagnosis is often delayed because the unusual vertebral structure makes radiographic evaluation challenging in patients, and pain from spinal fractures can be overlooked as the disease activity of axSpA [37,47]. Unless the surgical risks are substantial, surgical intervention is essential for the treatment of spinal fractures in patients with axSpA. Observational studies have demonstrated that surgery often leads to neurological improvement and a reduction in complications compared with conservative management [37]. Therefore, immediate surgical treatment should be considered, especially in patients with axSpA presenting with acute spinal pain with neurological symptoms or accompanying unstable fractures [48-50].

Complementary medicine

Non-pharmacological approaches encompass a diverse range of treatments, including thermal water treatment and acupuncture. Complementary therapies have been used to manage musculoskeletal diseases since ancient times.

Spa therapy

Spa therapy includes hydrotherapy and balneotherapy, plus the experience of treatment in a resort-like atmosphere. Hydrotherapy involves the use of regular water, whereas balneotherapy uses warm natural mineral water. These terms are used interchangeably in various studies [51,52]. Standardized spa therapy has not yet been established, and there is limited evidence of its effects in inflammatory arthritis, including axSpA. Thermal water offers several benefits, including buoyancy, high heat capacity, and an enhanced pain threshold. Several small trials demonstrated that spa therapy helped relieve pain and improved the quality of life in patients with axSpA [16,29,53]. One RCT demonstrated that daily 20-minute spa therapy significantly improved disease activity (ΔBASDAI -1.61, 95% CI: -2.20 to -1.02), functional capacity (ΔBASFI -1.36, 95% CI: -1.84 to -0.87), spinal mobility (ΔBASMI -0.56, 95% CI: -0.96 to -0.17), and quality of life (ΔASQoL -2.06, 95% CI: -3.02 to -1.10), although these effects were evaluated immediately after a 3-week intervention [53] (Table 2).

Acupuncture

Acupuncture is aimed at stimulating the meridians and acupuncture points to alleviate symptoms and improve well-being [52]. Although the mechanism of action of acupuncture is not fully understood, it can induce rapid analgesic effects, likely to be via diffuse noxious inhibitory controls, which can alleviate pain by conditioning stimuli [54]. The National Institutes of Health state that acupuncture can serve as an alternative treatment option when conventional therapy fails or as a supplement for patients experiencing the side effects of medication. The World Health Organization published an official report listing 31 symptoms, including lower back pain, conditions, and diseases, that were treated effectively by acupuncture in controlled trials [55]. However, there is little evidence to support the use of acupuncture for the treatment of axSpA. A small RCT showed that acupuncture failed to demonstrate superiority in low back pain improvement compared to placebo (low back pain variation median 2 [range 0.8–5.8] acupuncture group *vs.* 1.25 [-0.2 to 5.8] in the placebo group $p > 0.05$); similarly, there were no significant differences in disease activity and function (Table 2) [56]. Furthermore, acupuncture faces challenges when controlling methodological aspects, such as double-blinding and defining control groups. Therefore, further studies of acupuncture as an adjunctive therapy for axSpA are needed.

CONCLUSIONS

This review compiled insights into current axSpA treatment choices, focusing on non-pharmacological interventions. The effectiveness of the core non-pharmacological ap-

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Table 2. Characteristics and outcomes of the included studies of complementary medicine

Study ID	Study design	Interventions (intervention/control)	Sample size (M:F)	Frequency of intervention	Duration (wk)	Evaluation (wk)	Outcome (mean difference ± SD or mean difference [95% CI])			
							BASDAI	BASFI	BASMI	BAS-G
Spa therapy										
Ciprian et al., 2013 [16]	RCT	Spa therapy and rehabilitation	30 (15:15)	10 sessions	2	2	-0.5 (-1.7, 0.6)*	N/A	-0.4 (-2.0, 1.1)*	N/A
		Standard care								
Gurcay et al., 2008 [53]	RCT	Bath therapy and exercise program	58 (30:28)	20 min daily for 15 sessions	3	3	-1.6 (-2.2, -1.0)**	-1.4 (-1.8, -0.9)**	-0.56 (-1.00, -0.2)**	N/A
		Exercise program								
van Tubergen et al., 2001 [29]	RCT	Spa-exercise therapy	120 (80:40)	5 days a week	3	28	-1.5 ± 1.6*	-0.7 ± 1.5*	N/A	-1.0 ± 2.9
		Group physical therapy (control)					0.7 ± 1.8	-0.1 ± 1.2		0.2 ± 3.0
		An exercise program (control)					0.8 ± 1.7	0.1 ± 1.7		0.0 ± 2.7
Acupuncture										
Jo et al., 2012 [56][a)]	RCT	Active acupuncture	10 (6:4)	8 sessions	4	4	1.1 (-0.6, 2.8)	0.5 (-0.5, 1.6)	N/A	2.0 (0.5, 2.9)
		Sham control					-0.1 (-1.2, 0.5)	-0.2 (-0.6, 0.3)		1.3 (0.4, 2.4)

M, male; F, female; SD, standard deviation; CI, confidence interval; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; BASMI, Bath Ankylosing Spondylitis Metrology Index; BAS-G, Bath Ankylosing Spondylitis Patient Global Score; RCT, randomized controlled trial; N/A, not applicable.

[a)]The results are presented as variation median values (minimum, maximum).

*$p < 0.05$ between the intervention group and control group; **$p < 0.01$ between the intervention group and control group.

proaches, such as education, smoking cessation, and exercise has been reaffirmed. Studies of surgical treatment have been limited to retrospective studies. However, total hip replacement is recommended for patients with persistent pain or disability and radiographic evidence of structural hip damage. Prompt spinal intervention should be considered for patients with acute spinal pain and neurological deficits or accompanying unstable fractures. Evidence for complementary therapies, including spas and acupuncture, remains insufficient.

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