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Original article

First update of the current evidence for the management of ankylosing spondylitis with non-pharmacological treatment and non-biologic drugs: a systematic literature review for the ASAS/EULAR management recommendations in ankylosing spondylitis

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Abstract

Objective. To perform a systematic literature review as a basis for the update of the Assessment in SpondyloArthritis International Society and European League Against Reumatism (ASAS/EULAR) recommendations for the management of AS with non-pharmacological interventions and non-biologic drugs.

Methods. The search was performed in PubMed, EMBASE, PEDro and Cochrane between 1 January 2005 and 1 December 2009, and in abstracts of EULAR and ACR meetings (2007–09). Effect sizes for outcomes on pain, disease activity, spinal mobility and physical function and level of evidence were presented.

Results. Of 2383 papers, 35 with complete data were included. Physical therapy exercises in various modalities have positive effects on BASFI, BASDAI, pain and mobility function. Various NSAIDs including coxibs improve BASDAI, disease activity and BASFI. No effect of SSZ and MTX on any variable was found. Surgical interventions of the spine and the hip can give excellent results by restoring function.

Conclusion. This concise summary of current evidence for non-pharmacological interventions and non-biologic drugs formed the basis for the update of the ASAS/EULAR recommendations for the management of AS.

Key words: ankylosing spondylitis, management, recommendations, systematic literature review.

CLINICAL SCIENCE

Introduction

AS is a chronic, inflammatory rheumatic disease, generally starting early in life [1–4]. Inflammatory back pain due to sacroiliitis and spondylitis, and formation of syndesmophytes leading to ankylosis of the spine, characterize AS [4, 5]. Although AS is difficult to treat, the treatment armamentarium of AS has been broadened since the discovery of anti-TNF-α agents as effective treatments [6–8]. Clinicians need to be aware of the relative benefits and risks of the available treatments, and need to have evidence-based information about the most efficacious strategies in particular patient settings [4].

In 2005 Zochling *et al.* [4] performed a systematic literature search for evidence-based recommendations by the Assessment in SpondyloArthritis International Society and European League Against Reumatism (ASAS/EULAR) for the management of AS. In 2010 an update of this systematic literature search was performed to serve as a base for the development of an update of the ASAS/EULAR

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recommendations [9]. The details and results of the performed systematic review on non-pharmacological interventions and non-biologic drugs are presented in this article. The results on biologics are presented in the article by Baraliakos elsewhere in this journal.

Methods

Participants and outcome measures

Participants were defined as patients with a diagnosis of AS or axial spondyloarthritis. The required treatments were non-pharmacological interventions and non-biologic drugs. There were no restrictions with regard to type of non-pharmacological intervention, or to dose, duration or route of administration of non-biologic drugs.

The primary outcomes of interest include pain, disease activity (including BASDAI), spinal mobility (including BASMI) and physical function (including BASFI).

Inclusion/exclusion criteria

Randomized controlled trials (RCTs) and controlled trials are the ideal study designs for inclusion in this review. However, the aim of this review is to provide evidence of all types of non-pharmacological interventions and non-biologic drugs. Since not all types of treatment can be studied within RCTs alone, the main focus of interest was also on systematic reviews, uncontrolled trials/cohort studies, case–control studies and cross-sectional studies. Studies about non-axial spondyloarthritides and other inflammatory joint conditions, animal studies, non-clinical outcome studies and non-treatment studies, narrative review articles, commentaries, guidelines, case reports, letters and editorials and studies in other languages than English, Dutch and German were excluded. Studies about biologic drugs were also excluded because those studies will be included in a search performed by Baraliakos.

Systematic literature search

A search strategy was built in collaboration with an experienced librarian, based on the previous search of Zochling *et al*. [4]. The systematic literature search for published papers was performed in the electronic databases PubMed, EMBASE, PEDro and Cochrane between 1 January 2005, which is the end date of the literature search by Zochling *et al.* [4], and 1 December 2009. The complete search strategies for the databases are provided in supplementary Appendix S1, available as supplementary data at *Rheumatology* Online. Abstracts of rheumatology scientific meetings (EULAR, ACR) from the years 2007, 2008 and 2009 were searched by hand to ensure that all potential studies were identified for this review. Furthermore, references of relevant reviews and included papers were hand searched for information on any other relevant studies.

Selection of studies

One reviewer (R.vdB.) assessed each title and abstract on suitability for inclusion in the review, according to the inclusion and exclusion criteria described above. Papers not addressing the topic of interest were excluded and reasons recorded. The full-text paper was assessed when further information was required to determine if the inclusion criteria were met.

Data extraction and categorizing evidence

The included papers were assessed using the full-text paper by one reviewer (R.vdB.) to extract relevant data, including patient characteristics and details of treatment. If necessary, authors were contacted to provide any required additional information. The results were reported to the ASAS/EULAR expert committee at the beginning of the recommendation development process. All included papers were categorized according to their level of evidence (see legend in Table 1) [3]. The assigned levels are shown in Table 1.

Data analysis

Since different types of studies are included about various types of treatments, the results are very heterogeneous and therefore the results cannot be pooled. Yet, the results are analysed and presented per type of treatment.

Estimation of effectiveness

Per treatment group, the Cohen's effect size (Cohen's ES; mean change in score divided by the baseline SD) was calculated, and the standardized response mean (SRM; mean change divided by the SD of the change) was calculated where possible [36]. To compare the effect between treatment groups, treatment ES was calculated (mean change in the index group minus the mean change in the comparator group divided by a pooled baseline SD). For each ES, the corresponding 95% CI was constructed. An ES of 0.2 or 0.3 is considered a small change, $\sim$0.5 as moderate and $>$0.8 as a large change, and a negative ES indicates worse.

Results

Treatment modalities and types of research evidence

The general search revealed 3179 papers; 1638 in PubMed, 1486 in EMBASE, 14 in PEdro, 34 in Cochrane and 7 abstracts. After eliminating duplicates, 2383 papers remained. Of those, 2347 papers were excluded (supplementary Appendix S2, available as supplementary data at *Rheumatology* Online) and 35 papers were included, of which 3 are Cochrane reviews and 1 abstract (supplementary Appendix S3, available as supplementary data at *Rheumatology* Online). An overview of the included papers is shown in the supplementary Appendix S4, available as supplementary data at *Rheumatology* Online.

Non-pharmacological treatment

No studies on treatments about diet, education, self-help groups or lifestyle modification were present within this search.

Table 1 Cohen's ES with 95% CI for various outcome measures and different management modalities

Intervention	Assessment point	No. of patients	Level of evidence	Cohen's ES BASFI (95% CI)	Cohen's ES BASDAI (95% CI)	Cohen's ES pain (95% CI)	Cohen's ES disease activity (95% CI)	Cohen's ES BASMI (95% CI)
Exercise therapy								
Group exercise [10]	6 weeks	22	2b	0.27 (−0.33, 0.86)	–	0.50 (−0.10, 1.10)	–	0.26 (−0.34, 0.86)
Home exercise		16		0 (−0.69, 0.69)	–	0.20 (−0.50, 0.89)	–	0.05 (−0.64, 0.69)
Exercise group [11]	6 weeks	22	3	0.10 (−0.49, 0.69)	–	–	–	–
Exercise Group [12]	8 weeks	16	1b	0.41 (−0.29, 1.11)	0.38 (−0.31, 1.08)	–	–	**1.11 (0.37, 1.86)**
Control group		16		0.22 (−0.47, 0.92)	0.24 (-0.46, 0.93)	–	–	0.10 (−0.60, 0.79)
Hospital exercise [13]	12 weeks	23	1b	**0.94 (0.34, 1.55)**	**1.00 (0.39, 1.61)**	**0.76 (0.16, 1.36)**	–	–
Home exercise		23		0.22 (−0.36, 0.80)	**0.88 (0.28, 1.49)**	0.11 (−0.47, 0.69)	–	–
Hospital exercise	6 months	23		**0.78 (0.18, 1.38)**	**0.84 (0.24, 1.45)**	0.48 (−0.10, 1.07)	–	–
Home exercise		23		0.48 (−0.11, 1.06)	**1.12 (0.50, 1.74)**	0.48 (−0.10, 1.07)	–	–
Home exercise [14]	12 weeks	25	2b	**0.63 (0.07, 1.20)**	**0.94 (0.35, 1.52)**	–	–	–
Control group		18		0.18 (−0.48, 0.83)	0.19 (-0.48, 0.84)	–	–	–
Exercise GPR method [15]	12 weeks	20	2b	0.57 (−0.06, 1.21)	**1.07 (0.41, 1.73)**	**1.28 (0.60, 1.96)**	–	–
Conventional exercise		21		**0.66 (0.04, 1.28)**	**1.20 (0.54, 1.86)**	**1.03 (0.38, 1.67)**	–	–
Control group		15		0.13 (−0.59, 0.85)	0.32 (-0.40, 1.04)	0.19 (−0.53, 0.91)	–	–
Balneotherapy								
Exercise + stangerbath [16]	3 weeks	29	1b	1.05 (−0.08, 2.17)	**1.71 (0.33, 3.09)**	–	–	0.30 (−0.44, 1.05)
Exercise		28		0.20 (−0.48, 0.88)	0.36 (−0.43, 1.15)	–	–	0.06 (−0.52, 0.63)
Balneotherapy [17]	3 weeks	20	1b	–	–	0.81 (−0.26, 1.88)	–	–
Balneotherapy + NSAIDs		21		–	–	0.83 (−0.26, 1.92)	–	–
NSAID		20		–	–	0.58 (−0.38, 1.54)	–	–
Balneotherapy	6 months	20		–	–	0.97 (−0.17, 2.11)	–	–
Balneotherapy + NSAIDs		21		–	–	1.10 (−0.10, 2.10)	–	–
NSAID		20		–	–	0.96 (−0.18, 2.09)	–	–
Rehabilitation [18]	3 weeks	52	3	**2.23 (1.74, 2.72)**	–	**5.10 (4.31, 5.89)**	–	–
	6 weeks			**1.70 (1.25, 2.14)**	–	**3.62 (3.00, 4.24)**	–	–
	12 weeks			**1.16 (0.75, 1.58)**	–	**2.06 (1.58, 2.54)**	–	–
NSAIDs								
Celecoxib (200 mg) [19]	12 weeks	153	1b	**0.35 (0.12, 0.57)**	**0.60 (0.37, 0.83)**	**1.96 (1.69, 2.23)**	**1.11 (0.87, 1.35)**	**0.52 (0.29, 0.75)**
Celecoxib (400 mg)		150		**0.41 (0.18, 0.64)**	**0.80 (0.56, 1.03)**	**1.79 (1.52, 2.06)**	**1.29 (1.05, 1.54)**	0.13 (−0.10, 0.36)
Diclofenac (150 mg)		155		**0.35 (0.12, 0.57)**	**0.83 (0.60, 1.06)**	**1.84 (1.57, 2.10)**	**1.28 (1.03, 1.52)**	0.18 (−0.04, 0.40)
Etoricoxib (90 mg) [20]	6 weeks	22	3	**1.08 (0.45, 1.71)**	**1.08 (0.45, 1.71)**	**1.44 (0.77, 2.10)**	**0.93 (0.31, 1.56)**	–
DMARDs								
SSZ (2 g) [21]	24 weeks	120	1b	0.19 (−0.06, 0.44)	**1.11 (0.84, 1.38)**	–	–	–
SSZ (3 g) [22]	16 weeks	187	1b	**0.29 (0.08, 0.49)**	**1.24 (1.02, 1.46)**	**0.95 (0.74, 1.17)**	–	0.08 (−0.13, 0.28)
Etanercept (50 mg)		379		**0.48 (0.33, 0.62)**	**1.96 (1.79, 2.14)**	**1.68 (1.51, 1.84)**	–	**0.34 (0.20, 0.48)**
SSZ (2 g) [23]	52 weeks	16	3	–	0.43 (−0.28, 1.13)	–	–	–
MTX (15 mg up to 20 mg) [24]	16 weeks	20	3	0.01 (−0.61, 0.63)	0.00 (−0.62, 0.62)	0.00 (−0.62, 0.62)	–	0.23 (−0.12, 1.14)
Other								
Radium-224 [25]	6 months	278	3	**0.68 (0.39, 0.97)**	**0.86 (0.57, 1.15)**	**1.14 (0.85, 1.44)**	**1.22 (0.92, 1.52)**	–

(continued)

TABLE 1 Continued

Surgery	No. of patients	Results
Hip resurfacing [26]	23 (38 hips)	Both groups ROM ↑: resurfacing group significantly better than THR group
THR	25 (41 hips)	
Posterior correction and fixation without anterior fusion (posterior OWO) [27]	30	Neurologic deficit ↑: good correction of kyphosis
OWO [28]	51	Both techniques have good clinical outcome, patient quality of life ↑, high patient satisfaction: no difference between the two techniques
CWO	66	
Cervicothoracic extension osteotomy [29]	26	Neck pain and swallowing problems ↑: both groups restored horizontal gaze
Cervical extension osteotomy: conventional technique [30]	114	High patient satisfaction, function ↑, psycho-social body image ↑: no difference in outcome between the two groups
Cervical extension osteotomy: current technique	17	
Smith-Peterson osteotomy [31]	12	Pain and neurologic deficits ↑, high patient satisfaction
Lumbar closing wedge osteotomy [32]	11	Horizontal gaze restored in all patients
Cervical osteotomy: sitting position [33]	11	Good correction of kyphosis, no loss of correction
Cervical osteotomy: prone position	5	
Cervical decancellation closing wedge osteotomy [34]	8	Horizontal gaze ↑, good subjective outcome
Closing wedge osteotomy [35]	21	Quality of life ↑, good functional outcome

Significant ES in bold. Category of evidence: Ia: meta-analysis RCTs; Ib: RCT; IIa: controlled study without randomization; IIb: quasi-experimental study; III: non-experimental descriptive studies (comparative, correlation and case–control studies); IV: expert committee reports or opinion or clinical experience of respected authorities, or both.

Exercise therapy

The effect of physiotherapy has been reviewed in a Cochrane review in 2008 [37]. The results of this review show that individual home-based or supervised exercise programmes are better than no intervention at all on pain, physical function, spinal mobility and patient global assessment, and that supervised group physiotherapy is better than home exercise [37].

Besides the Cochrane review, nine papers were identified [10–15, 38–40] of which three were already included in the Cochrane review [38–40]. In the six additional papers, the effects of various exercises in AS patients are compared (supplementary Appendix S4, available as supplementary data at *Rheumatology* Online). The results of these six studies confirm the results of the Cochrane review. Various types of exercise [supervised group, home and Global Posture Reeducation (GPR) method exercise] have moderate to good effects on BASFI, BASDAI, pain and mobility, as shown by the calculated Cohen's ES and SRM (Table 1 and Fig. 1). The calculated treatment ES showed that supervised group physiotherapy is better than home exercise on BASFI, pain and mobility, and slightly better on BASDAI. Home exercise is better than no exercise at all on BASFI and BASDAI (Table 2). Although most papers had level 1b evidence, the studies investigated various exercises with variable durations and had small patient samples. Therefore, many ES are not statistically significant, showing only a trend (Table 1).

Balneotherapy, spa therapy and rehabilitation

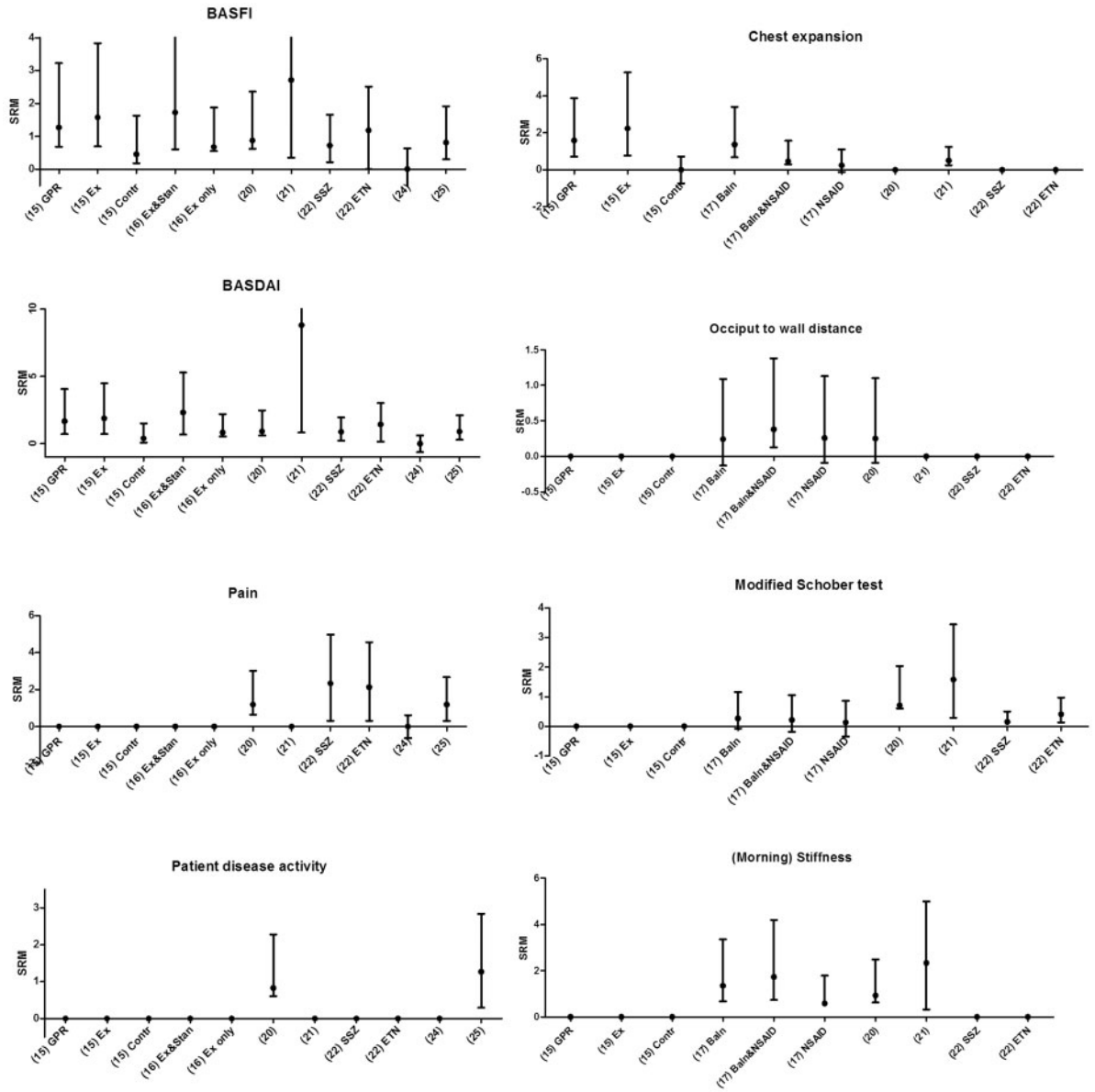
The same Cochrane review also revealed that combined inpatient spa exercise therapy followed by group physiotherapy is better than group physiotherapy alone [37]. In addition to the Cochrane review, four RCTs [16, 17, 42, 43] about various types of balneotherapy and spa therapy in AS patients were identified (level 1b evidence), of which two were already presented in the Cochrane review [42, 43].

As in the exercise therapy studies, the studies about balneotherapy included only small patient numbers in various therapies, resulting in not statistically significant ES. However, the trend shows that balneotherapy in all its modalities is (moderate) effective on BASFI, BASDAI and pain, as shown by the calculated Cohen's ES and treatment ES (Tables 1 and 2). The effect of balneotherapy on pain is equal to the effect of NSAIDs (either mono or combined) [17]. Stangerbath therapy combined with exercises is effective on BASFI and BASDAI, only directly after therapy [16] (Fig. 1). One level 3 evidence study about the effect of inpatient rehabilitation was identified that showed a strong effect on BASFI, pain and OWD (Table 1) [18].

NSAIDs

Three studies about the effects of different NSAIDs in AS patients were identified [19, 20, 41]. The effect of celecoxib (200 and 400 mg daily) in comparison with diclofenac (150 mg daily) (level 1b evidence) [19], the effect of etoricoxib (90 mg daily) (level 3 evidence) [20] and the

FIG. 1 SRM of different outcome parameters.



effect of NSAIDs in continuous usage in comparison with NSAID usage on demand (level 1b evidence) [41] were investigated.

The latter study is a follow-up study of a double-blind RCT about the effect of celecoxib 200 mg *vs* ketoprofen 200 mg *vs* placebo after 6 weeks [44]. This study was already included in the review of Zochling *et al*. [4], showing a significant improvement in pain and function after 6 weeks of use of both NSAIDs in comparison with placebo [44]. The follow-up study showed that measures of disease activity, including pain and BASDAI, were stable over a time period of 24 months in both the continuous and on-demand groups and not statistically significant between the groups [41]. Although the clinical effects of both treatment strategies are similar, inhibition of structural damage progression in the spine is better with continuous use than with on-demand use [41].

The calculated Cohen's ES and SRM of the other two studies showed that all NSAIDs have statistically significantly moderate to good effect on BASFI, BASDAI, disease activity and pain (Table 1 and Fig. 1). Various NSAIDs have a similar effect as assessed by treatment ES (Table 2). Furthermore, no new signs of toxicity were discovered.

DMARDs

In 2005 and 2006, two Cochrane reviews summarized the effects of MTX and SSZ, respectively [45, 46]. The MTX

Table 2 Treatment ES with 95% CI for the different interventions

Intervention	Comparator	Assessment point	Treatment ES BASFI (95% CI)	Treatment ES BASDAI (95% CI)	Treatment ES Pain (95% CI)	Treatment ES disease activity (95% CI)	Treatment ES BASMI (95% CI)
Exercise therapy							
Group exercise [9]	Home exercise	6 weeks	0.30 (−0.35, 0.95)	−0.06 (−0.71, 0.58)	0.31 (−0.34, 0.96)	–	0.20 (−0.44, 0.85)
Exercise group [11]	Control group	8 weeks	0.17 (−0.52, 0.87)	0.00 (−0.69, 0.69)	–	–	0.53 (−0.17, 1.24)
Hospital exercise [12]	Home exercise	12 weeks	**0.59 (0.01, 1.16)**	0.22 (−0.36, 0.80)	**0.68 (0.10, 1.26)**	–	–
Hospital exercise	Home exercise	6 months	0.15 (−0.43, 0.72)	−0.17 (−0.74, 0.41)	0.04 (−0.54, 0.61)	–	–
Home exercise [13]	Control group	12 weeks	0.49 (−0.12, 1.12)	**0.84 (0.21, 1.47)**	–	–	–
Exercise (GPR method) [14]	Conventional exercise	12 weeks	0.01 (−0.60, 0.62)	−0.04 (−0.65, 0.57)	0.17 (−0.44, 0.79)	–	–
Conventional exercise	Control group		0.44 (−0.23, 1.11)	**0.82 (0.13, 1.51)**	**0.93 (0.24, 1.63)**	–	–
Exercise (GPR method)	Control group		0.41 (−0.26, 1.09)	**0.75 (0.06, 1.44)**	**1.15 (0.43, 1.87)**	–	–
Balneotherapy							
Exercise + stangerbath [15]	Exercise	3 weeks	**0.65 (0.12, 1.18)**	**1.49 (0.91, 2.08)**	–	–	0.21 (−0.31, 0.73)
Balneotherapy [16]	Balneotherapy + NSAIDs	3 weeks	–	–	0.08 (−0.53, 0.70)	–	–
Balneotherapy + NSAIDs	NSAIDs		–	–	0.36 (−0.26, 0.98)	–	–
Balneotherapy	NSAIDs		–	–	0.43 (−0.18, 1.04)	–	–
Balneotherapy	Balneotherapy + NSAIDs	6 months	–	–	0.00 (−0.61, 0.61)	–	–
Balneotherapy + NSAIDs	NSAIDs		–	–	0.31 (−0.31, 0.92)	–	–
Balneotherapy	NSAIDs		–	–	0.28 (−0.32, 0.89)	–	–
NSAIDs							
Continuous NSAID use (200–400 mg) [40]	On-demand NSAID use (200–400 mg)	104 weeks	−0.15 (−0.42, 0.12)	–	−0.053 (−0.32, 0.21)	0.1 (−0.17, 0.37)	–
Celecoxib (200 mg) [18]	Diclofenac (150 mg)	12 weeks	0 (−0.22, 0.22)	−0.30 (−0.52, 0.07)	−0.08 (−0.31, 0.14)	−0.17 (−0.39, 0.06)	–
Celecoxib (400 mg)	Diclofenac (150 mg)		0.04 (−0.18, 0.27)	−0.10 (−0.32, 0.13)	−0.07 (−0.29, 0.16)	−0.06 (−0.28, 0.17)	–
DMARDs, g							
SSZ (2 g) [20]	Placebo	24 weeks	0.08 (−0.17, 0.33)	0.15 (−0.10, 0.40)	0.05 (−0.20, 0.31)	–	–
SSZ (3 g) [21]	Etanercept (50 mg)	16 weeks	**−0.19 (−0.37, −0.01)**	**−0.76 (−0.94, −0.58)**	**−0.70 (−0.88, −0.52)**	–	**−0.23 (−0.41, −0.06)**

The interventions are grouped together. The level of evidence, duration and point of measurement are described in this table. Significant ES in bold.

review showed that there is no evidence to support any benefit of MTX in the treatment of AS. One additional open-label study about the effect of MTX was found besides the Cochrane review. The calculated Cohen's ES did not show any improvement on BASFI, BASDAI, pain or mobility (Table 1 and Fig. 1) [24].

The SSZ Cochrane review showed some benefit of SSZ in reducing ESR and easing morning stiffness, yet no benefit in physical function, pain, spinal mobility and disease activity [46]. These results are confirmed by three additional identified SSZ studies (level 1b and 3 evidences) not included in the SSZ Cochrane review [21–23] (supplementary Appendix S4, available as supplementary data at *Rheumatology* Online). Although the calculated Cohen's ES revealed moderate to good effect on BASDAI and pain (Table 1, Fig. 1), the calculated treatment ES showed that the effect of SSZ on these outcome parameters is not better than the effect of placebo, as shown in one study, and that the effect of SSZ was statistically significantly worse than the effect of etanercept (ETN) (Table 2). No new signs of toxicity for SSZ and MTX were found.

Other therapies

Two studies about other types of therapy were identified. One study investigated the effect of probiotics compared with placebo (level 1b evidence) [47] (supplementary Appendix S4, available as supplementary data at *Rheumatology* Online). The calculated ES showed that probiotics do no better on global well-being and functional index than placebo (Tables 1 and 2). The other study investigated the effect of radium chloride on BASFI, BASDAI, pain and disease activity in an uncontrolled design (level 3 evidence) (Table 1). The calculated ES demonstrated a moderate effect on BASFI and good effect on BASDAI, pain and disease activity (Table 1 and Fig. 1) [25].

Surgical interventions

Total hip replacement

Total hip replacement (THR) is a frequently used procedure in AS patients with hip involvement. This search revealed one study about hip surgery and resurfacing of the hip (Zimmer, Wintherthur, Switzerland). The authors proposed that hip resurfacing might be an option instead of THR for young AS patients with hip involvement. They compared the effects of resurfacing with THR on pain relief, function and mobility in 38 resurfaced hips (23 AS patients) and 41 THRs (25 AS patients) over a mean follow-up time of 34.5 months. Both groups showed significant pain relief and good restoration of function and mobility [26] (Table 1).

Spine

Although spinal surgery to resolve fixed kyphotic deformity is accompanied by severe risks, it can give excellent functional results by restoring balance and horizontal vision, as shown by all nine included papers in this search [27–35]. These papers review the different available techniques. All included papers are case series, and therefore low-quality studies (level of evidence 3) (supplementary Appendices S4 and S5, available as supplementary data at *Rheumatology* Online).

One study compared open wedge osteotomy (OWO) of the cervical spine with closed wedge osteotomy (CWO). No difference in correction of kyphosis between the two techniques was found [28]. Another study compared the conventional technique of cervical extension osteotomy with a new technique in which the patients have a modified larger lateral resection area than with the conventional technique. Again, no differences between the two techniques were found concerning functional improvement, satisfaction or complications [30]. Similarly, a prone or a sitting position during the procedure demonstrated no difference in correction [33].

For thoracolumbar deformities, polysegmental wedge osteotomy might be associated with lower risks. However, the correction is often insufficient in the case of calcified intervertebral discs. Theoretically, CWO is superior to OWO in terms of efficiency and minimal loss of correction and lower accompanied risks, although technically difficult [28, 34]. For pseudoarthrosis, posterior correction is an effective treatment (posterior opening wedge osteotomy), as well as fixation without anterior fusion [27]. The data from the included papers do not show whether a specific technique gives better results for any specific indication.

Discussion

This systematic review is an update of the review by Zochling *et al.* [4] and identified available non-pharmacological and non-biologic pharmacological treatments effective for symptomatic control of AS. The results of this search confirm the 2005 findings for physiotherapy [4]; exercises in various modalities, individually at home or in a group and under supervision, land or water based, have positive effects on BASFI, BASDAI, pain and mobility function. However, the small numbers of participants, the heterogeneity of the interventions and outcome measures, and deficiency in reporting data result in wide intervals and lack of strong evidence.

Zochling *et al.* [4] revealed that different kinds of NSAIDs and coxibs improve spinal and peripheral joint pain and function. The current search confirmed these results by showing that various NSAIDs including coxibs improve BASDAI, disease activity and BASFI.

In 2005 no effect of SSZ or MTX on back pain and function was demonstrated [4], which is confirmed by new research. The current search revealed no effect of SSZ and MTX on pain, nor on BASFI and BASDAI.

THR is still the standard procedure in AS patients with hip involvement. Although a small study showed positive effects of hip resurfacing techniques [26], it must be carefully considered whether resurfacing techniques are indeed a good alternative for THR given the recent developments and accompanying problems with the resurfacing techniques from another brand. The articular surface replacement hip prosthesis from the manufacturer

DePuy (Warsaw, IN, USA) has been recalled from the market because of failing of the prosthesis. Metal debris from wear of the implant led to a reaction that destroyed the soft tissues surrounding the joint, causing long-term disability and a high revision rate of 12% over 5 years [48].

Surgical interventions of the spine give excellent results by restoring horizontal gaze and function, yet are considered with high risks. Furthermore, it is still unclear which procedure of spine surgery is the best for any specific indication.

Conclusion

This review presents a concise summary of the current evidence available for therapeutic interventions for the management of AS, both non-pharmacological and pharmacological, excluding biologics. This overview formed the basis for the update of the ASAS/EULAR recommendations for the management of AS.

Rheumatology key messages

- Physical therapy in various modalities has positive effects on pain and function in AS.
- NSAIDs including coxibs improve BASDAI, BASFI and disease activity in AS.
- DMARDs have no effects on BASDAI, BASFI and pain in AS.

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Supplementary data

Supplementary data are available at *Rheumatology* Online.

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