Current Therapy for Seronegative Arthritides (Spondyloarthritis)

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The management of spondyloarthritis should be based on the clinical presentation (e.g., axial involvement, enthesiopathy, peripheral arthritis, extra-articular symptoms) and not on a diagnosis of a specific disease belonging to the concept of spondyloarthritis (e.g., ankylosing spondylitis, psoriatic arthritis, and arthritis related to inflammatory bowel disease). Despite the major advance in spondyloarthritis care due to the use of TNF blockade, several questions remain unresolved such as the optimal use of physiotherapy and NSAIDs as well as the management of TNF refractory patients, keeping in mind that axial involvement has been better evaluated for these different treatment modalities than the other clinical manifestations of spondyloarthritis.

From Seronegative Arthritides to Spondyloarthritis

The unifying concept initially termed seronegative spondarthritides (and currently called spondyloarthritis) was a pivotal step forward in the modern classification of rheumatic disorders. Spondyloarthritis regroups several related but phenotypically distinct disorders such as psoriatic arthritis, arthritis related to inflammatory bowel disease, reactive arthritis, a sub-group of juvenile chronic arthritis, and ankylosing spondylitis with last mentioned being the prototypic and best studied subtype. The different clinical manifestations observed in these different disorders include spinal (axial) involvement, peripheral arthritis, enthesiopathy, and extra-articular manifestations such as uveitis, psoriasis, and inflammatory bowel disease. The management (e.g., initiation of therapy) is based on the clinical presentation and not on a specific diagnosis of a disease belonging to the concept of spondyloarthritis.

The utility of this concept has been emphasized in the ASAS/EULAR recommendations of management of spondyloarthritis. Patient information and education (as for other chronic diseases) is a key component of the management strategy, in particular by informing patients presenting with a particular symptoms (e.g., inflammatory back pain and peripheral arthritis) of the risk of occurrence in his life of the other clinical manifestations (e.g., uveitis). For this purpose, several educational programs have been proposed.

Management of Axial Involvement

Physical Therapy and Exercise

A recent Cochrane systematic literature review concluded that, based on the observed results, an individual home-based exercise or supervised exercise program is better than no intervention, that supervised group physical therapy is better than home exercises, and that combined in patient spondyloarthritis-exercise therapy followed by group physical therapy is better than no group physical therapy alone.

Besides the modality of physical therapy (e.g., home exercise versus group physical therapy) the current question is related to the characteristics of the patients who should benefit most from this therapy. It is clear that patients with inactive (non-inflammatory) advanced (spinal ankylosis) disease are the best candidates. The interest of such physical therapy and its modality at an early stage or during painful inflammatory flares of the disease still remain to be investigated.

Nonsteroidal Anti-Inflammatory Drugs

Nonsteroidal anti-inflammatory drugs (NSAIDs) are regarded as the cornerstone of pharmacological interventions for axial involvement reducing pain and stiffness rapidly...
after 48 to 72 hours. Besides this dramatic, well demonstrated symptomatic effect, NSAIDs might able to reduce the level of acute phase reactants with a statistical significant difference over placebo but with a questionable clinical relevance of the observed magnitude of effect. Two studies (one randomized controlled trial and one epidemiological study) suggest that NSAIDs can retard radiological progression of the spine when given on a systematic daily intake or at a high dose. Based on these data, one could suggest that a systematic continuous daily intake of NSAIDs might be of benefit for patients. However, the argument against this stance is the potential long-term gastrointestinal and cardiovascular toxicity of this therapy, in particular these patients recognized as having more comorbidities than the general population.

**Corticosteroids**
The use of corticosteroids of axial disease is not supported by evidence. Corticosteroids injections directed to the local site of inflammation (e.g., sacroiliac, costo-vertebral, manubrio-ternal joints, and so forth) may be considered.

**Conventional Disease-Modifying Drugs**
In general, conventional disease-modifying drugs (DMARDs) have no proved efficacy for the axial manifestations of spondyloarthritis. The current debate concerns the use of sulfasalazine with, if any, a treatment effect of low magnitude.

**TNF blockade**
The major therapeutic advancement in spondyloarthritis care is the successful use of TNF blockade. Such therapy is currently recommended in case of active (e.g., BASDAI ≥ 4) refractory to at least 2 NSAIDs taken during at least 2 weeks. Such therapy seems to be more effective in patients at an early stage of the disease (e.g., before the occurrence of structural damage of the sacroiliac joints) but also at a late stage of the disease (e.g., bamboo spine).

**Other drugs**
In contradiction with previous open uncontrolled studies suggesting a beneficial effect of intra-venous injections of pamidronate, a prospective 2-year evaluation of oral bisphosphonates (alendronate 70 mg once a week) showed no benefit over placebo. Inhibition of B cells (e.g., rituximab or T cells (e.g., abatacept) does not seem to be of benefit in patients suffering from axial involvement of spondyloarthritis. Other promising drugs such as the one inhibiting IL6 or IL17 require further evaluations before they can be recommended.

**Peripheral Arthritis**
Apart from poly-articular involvement associated with psoriasis, this clinical manifestation has been poorly evaluated. It is usually admitted that:

- Low dose of corticosteroids might be of benefit as well as intra-articular injections in case of mono- or oligo-involvement; and
- DMARDs including conventional and biologics could be considered with a similar modality (e.g., indication, dose, monitoring) than in rheumatoid arthritis.

**Enthesopathy**
In case of polyenthesopathy related to spondyloarthritis, NSAIDs have to be considered as first line therapy and the use of TNF blockers only in case of definite diagnosis (with the demonstration of polyenthesopathy using MRI, bone scan of ultrasongraphy) not inadequately controlled with NSAIDs. In case of mono-enthesopathy related to spondyloarthritis (mainly heel pain), local injection of corticosteroids and non-pharmacological therapies (such as insoles) are usually considered as first line therapies keeping in mind that, in case of very disabling and refractory disease, TNF blockade might be considered.

**Extra-Srticular Manifestations**
It is not the objective of this review to detail the treatment modalities of the different extra-articular features. It is important to emphasize that extra-articular manifestations should be managed with the relevant specialists (e.g., ophthalmologists, gastro-enterologists, dermatologists, and others). Such collaboration is crucial, in particular, while discussing the initiation of a specific treatment (such as TNF blockade) with the objective to prevent extra-articular features (e.g., uveitis).

**Conclusion**
The recognition of the concept of spondyloarthritis has been an important step to facilitate the management of spondyloarthritis (in particular by making a therapeutic decision with regard to a specific clinical presentation regardless of the underlying individual disease). However, the major advance in spondyloarthritis care due to the use of TNF blockade, several questions still remain unresolved such as the optimal use of physical therapy and NSAIDs as well as the management of TNF blockade refractory patients.

**Disclosure Statement**
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**References**


