From rehabilitation to remission in ankylosing spondylitis

Dalla riabilitazione alla remissione nella spondilite anchilosante

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During the past years, exercise and non-steroidal anti-inflammatory drugs (NSAIDs) have been the mainstay of symptom control for Ankylosing Spondylitis (AS), a chronic, inflammatory rheumatic disease characterized by inflammatory back pain due to sacroiliitis and spondylitis. The ASsessment in AS (ASAS) international working group has constructed evidence based recommendations to guide the physician in the management of AS (1).

Among the major recommendations for the management of AS, the ASAS group stated that there is a level Ib evidence that NSAIDs improve spinal pain, peripheral joint pain, and function, but comparative studies (1) or population-based survey (2) of different NSAIDs/coxib have not demonstrated one preparation to be clearly better than the others. Wanders et al (3) showed that the clinical efficacy of continuous NSAIDs/coxib treatment for AS was similar to intermittent “on demand” use and they suggested that the continuous treatment with NSAIDs/coxib could slow the radiographic disease progression over 2 years. Nevertheless it is premature to conclude that continuous NSAID treatment is disease modifying in AS, because the mean difference in progression of spinal fusion scores between “continuous” and “on demand” groups was small, with a low effect size (0.07) (4).

Other anti-inflammatory options can consider the use of corticosteroid injections directed to the local site of musculoskeletal inflammation while systemic administration for axial disease is not supported by any evidence (1).

Similarly the efficacy of disease modifying antirheumatic drugs (DMARDs), including sulfasalazine (1) and methotrexate (1, 5, 6), for the treatment of axial disease is not supported by any evidence. Although the most common sites of inflammation in AS (i.e. sacroiliac joints, entheses, vertebral bodies adjacent to intervertebral discs etc.) are poorly accessible, there is a clear role for TNFalpha in the pathogenesis of AS (7).

Thus patients with persistent high disease activity despite conventional treatments should be treated with anti-TNFalpha treatment according to the ASAS recommendations, but there is no evidence to support the obligatory use of DMARDs before, or concomitant with, anti-TNFalpha treatment in AS patients with axial disease.

The review of clinical data related to adalimumab, etanercept, infliximab compared with conventional treatment plus placebo indicates that the three treatments are clinically effective in relation to assessment of ASAS response criteria, BASDAI and BASFI (8).

Whereas clinical findings demonstrate sustained, durable benefits with long-term therapy in patients with AS, x-ray evaluations suggest that progression of structural damage continued. In fact AS patients who received adalimumab (9), etanercept (10) or infliximab (11) did not show a statistically significant difference in inhibition of structural damage progression at year 2, as assessed using the mSASSS scoring system, when compared with radiographic data from the historical control OASIS
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To address the 1st point we can state that physio-
termination of non-pharmacological and pharmacological
treatments. In fact, rehabilitation is still considered
one of the main treatments showing, most of the
time, some beneficial effects and non-pharmacolo-
therapy (including education, exercise and
physiotherapy) was included in the recommenda-
tions for the AS management by the ASAS work-
group/EULAR (1).
Two important issues still to be addressed should be: what type of physical therapy/rehabilitation is
the most effective in AS patients, and what is the
duration of the positive effects of this treatment, in
other words, how long does it last for?
To address the 1st point we can state that physio-
therapy interventions for AS have shown to be an
important part of the management of the disease,
being useful with a tendency to be more effective
when done as a supervised outpatient group (12-
14). The most recent reviews on physiotherapy in-
ventions confirmed this treatment strategy, also
indicating that exercise performed by patients un-
der supervision was beneficial on spinal mobility
when compared to the home exercise regime, but
suggested that further research should be essential
to delineate which exercise protocols should be
recommended in the management of AS patients
(12). Moreover Ton Nghiem et al and Elyan et al
in their reviews on the rehabilitation of AS con-
clude, on the basis of few articles published, that
exercise should remain a mainstay of AS treatment
complementing medical therapy but there is a need
for a standardised approach to assess its real role
(15, 16).
Recently, a Korean group showed that a home-
based daily exercise program increased joint mo-
bility and functional capacity, and decreased pain
and depression in AS patients (17). They conclud-
ed that home based exercise might be an effective
intervention for the disease.
To address the 2nd point, again, there are not clear
results. In fact, on the basis of previous studies,
various other studies showed that inpatient inten-
sive rehabilitation is effective in inducing short
term improvement in spinal mobility (18), but
doubts remain about sustained improvement after
long periods of time (19-21). In fact, some data
showed that patients with AS experienced pro-
gressive loss of movement independent to the du-
ration of the disease and the reported frequency of
unsupervised exercise (22).
We showed the effectiveness of inpatient rehabili-
tation assessed by ASAS response criteria and this
was quite a novelty using a combined index to mea-
sure the real role of rehabilitation (23). Indeed and
interestingly, the effectiveness of intensive inpa-
tient rehabilitation declined over time, suggesting
that this therapeutic approach, per se, is not enough
to control the disease. However, to better measure
the effectiveness of rehabilitation, it would be ad-
visable to use the ASAS response criteria in reha-
bilitation settings.
These contradictory results may depend on
methodological differences such as patients’ se-
lection and physiotherapy regimen. However, all
these results showed, clearly, that any rehabilitation
program only plays a partial role in the treatment
of the disease and are unable to completely address
the management of AS patients. Therefore, the con-
cept of a combination treatment (biologic agents
and rehabilitation) has risen in the last few years
and, at present, just few papers showed the syner-
gistic effect of biological agents and rehabilitation:
in one study, designed by us, Etanercept and an in-
tensive inpatient rehabilitation was used for the
management of active AS, and indicating that the
combination treatment seemed to be more effective
than a simple rehabilitation program (24).
A possible explanation for the good results ob-
tained was that Etanercept, acting on inflammation
and fatigue reduction, improved the efficacy of a re-
habilitation program, resulting in a better functional
status, better quality of life and a better perception
of the benefits obtained from the rehabilitation.
Similar results were obtained by another study de-
dsigned by us in which an occupational treatment in
combination with biological agents was beneficial
with synergistic effects on pain, function and dis-
ability when compared to the control groups treat-
ed with simple occupational therapy (25). Indeed,
this manuscript also showed that an occupational
treatment could be effective when associated with
powerful biological medications and also it could
be used when the disease is stable and well con-
trolled with the drugs, representing a possible tool
to maintain and improve the health status of AS pa-
ients. Other authors showed that a combination of
TNFα agents and rehabilitation can improve the
benefit perceived by the AS patients when doing
physiotherapy (26). Therefore, there is a strong
body of evidence that anti TNFα agents, as pow-
erful treatment for AS, can improve the effects of rehabilitation. However, at present, no randomized studies on the combination treatment with any anti TNFα and rehabilitation have been carried out and our previous studies were performed as a pilot study or based on the clinical practice. Therefore, it would be advisable that to confirm these previous positive results on the combination treatment some randomized studies will be performed to better deal with this fascinating and challenging disease.

REFERENCES


