



Editorial

Clinical Repercussions of Introducing Biological Therapies: The Well-controlled Patient[☆]



Repercusiones clínicas de la introducción de las terapias biológicas: el paciente bien controlado

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The landscape in the treatment of chronic inflammatory arthropathies has radically changed when the first biological agents appeared at the end of the 1990s.^{1–4} Uhlig et al.⁵ have conducted a study in the Oslo Rheumatoid Arthritis Register (ORAR), on the evolution over time of clinical management of rheumatoid arthritis (RA), between 1994 and 2004. These authors demonstrate, after an analysis adjusted by age, gender, comorbidities, duration of the disease and treatments received, how the clinical impact of RA has become milder in the new millennium. They observe statistically significant improvements in the health of the studied population, especially in the physical dimensions, the pain and the global health, probably due to a better access to health care systems and to the availability of new and better treatments.

Kievitt et al.⁶ have also studied the evolution over time (1989–2008) of the clinical control of the activity of the disease in the cohort of Nijmegen, which includes patients with RA. The analysis showed (after adjustment by age, gender, serum rheumatoid factor and duration of the disease) a clear improvement in DAS28 and HAQ scores, a less need for orthopaedic surgery and an increase (during this period) of the methotrexate and biological drugs use and dose. At the end of the studied period, 20% of the patients included in the cohort were receiving treatment with biological therapies.

It was described that up to a third part of the patients with ankylosing spondylitis (AS) showed signs of depression. This phenomenon has been related to the impact of physical disability and pain suffering, but it has also been related to the potential psychopathological effects of proinflammatory cytokines (interleukin-1, TNF-alpha) released during the disease. In patients with AS, the administration of anti-TNF biological therapies can quickly improve, from the 2nd week of initiated the therapy, the scores obtained for anxiety and depression in the Hamilton rating

scale, and simultaneously improve the clinical activity assessed by the BASDAI.⁷

The biological therapies have also demonstrated to have a very important impact on the prevention and/or the attenuation of the organic joint injury triggered by the inflammatory arthropathy. Ørnbjerg et al.⁸ have demonstrated, in patients with RA treated with biological drugs after an inadequate response to DMARD therapy coming from DANBIO registry, a reduction in the advance of the mean for total Sharp score (TSS) from the 1.8 units/year (during DMARD period) to 0.7 units/year during the biological therapy period. A multivariate regression analysis, adjusted by baseline predictors, the use of steroids and DMARD therapy,⁹ performed in the cohort of Wichita (USA) of patients with RA, clearly demonstrates that the fact the RA is currently less severe (regarding the smaller progression of the damage and the functional disability) is due to the more effective treatments of the disease and not to a change in the natural evolution of the process.

The effect of biological therapies on the structural component in AS is more controversial. However, a recent investigation¹⁰ studied the progression of the radiological damage measured by the modified Stokes Ankylosing Spondylitis Spine Score (mSASSS). According to this study, the treatment with anti-TNF reduces the risk of progression of the disease by 50% (OR=0.52; 95% CI, 0.30–0.88; $P=0.02$). In addition, a delay of 10 years in the beginning of the biological treatment significantly increases the risk of developing structural injuries in opposition to early beginning of treatment (OR=2.4; 95% CI, 1.09–5.3; $P=0.03$). A systematic review of the evidence and a meta-analysis analysed the effect of anti-TNF drugs on the radiological progression of the structural damage in psoriatic arthritis,¹¹ concluding that 84.5% of the patients treated with anti-TNF therapy did not show progression of the damage, in opposition to the 68.6% of those who received placebo (OR=2.68; 95% CI, 1.99–3.60; $p<0.001$).

Krishnan et al.¹² have recently observed how biological therapies reduce the disability in patients with RA, studied prospectively between 1983 and 2006. The biological treatments are also reducing the need of orthopaedic surgeries in patients with chronic inflammatory arthropathies. Louie and Wards¹³ have analysed

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the need of orthopaedic surgery in patients with RA, residents of California (USA), of 40 years of age or older, between 1983 and 2007. During this period, the rate of total knee replacement was reduced by 19% and hip replacement was reduced by 40% in patients between 40 and 50 years of age. It has been observed greater reduction rates in ankle and wrist surgery. In contrast to this reduction, the evolution of the rate in general surgery for the global population, between 1998 and 2007, goes from 260/100 000 to 360/100 000 interventions.

In Japan, the observational cohort IORRA^{14,15} of patients with RA shows a constant reduction in the number of interventions, globally, and specially in prosthesis replacement interventions, since the years 2002–2003. In contrast to this, the total rate of joint replacement has increased, for the same period, from 2 to 10 times in the general population. In the same way, the need for performing knee synovectomies in patients with RA has been reduced. Leon et al.,¹⁶ in Spain, have also detected a reduction in the orthopaedic surgery procedures in patients with RA in the biological treatments era, which they relate to the better control of the disease.

Biological therapies are expensive, but the intensive control of the articular inflammation obtained through them has a positive effect on the cardiovascular events¹⁷ reducing the mortality caused by such cause.¹⁸ In addition, biological therapies drastically diminish work disabilities, reducing them by 50%¹⁹ and increasing in almost 9 h the weekly capacity to work²⁰ (which would compensate 40% of the annual payments of anti-TNF drugs).

In conclusion, biological therapies have significantly improved the clinical control of rheumatic diseases and have reduced the progression of structural damage and of disability, triggered by the disease itself. At the same time, they have provided the adequate approach and clinical management of the chronic articular inflammatory processes by the early diagnosis, the measurement of the disease activity, the definition of control objectives and the assessments of guidelines for treatment. All of the above together with a favourable cost-benefit relation. All these evidences allow us to affirm that our patients are nowadays better controlled in the inflammatory activity of the disease.

Conflict of Interest

Jesus Tornero-Molina has received funds from Abvie, Pfizer, Roche and UCB for research.

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