Does an RA target make sense?

Treating-to-target or treating the patient in rheumatoid arthritis?

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The outlook for people presenting with rheumatoid arthritis (RA) has changed dramatically within a generation. Rheumatology outpatient clinics are no longer full of wheelchair bound patients, and most rheumatologists no longer have access to inpatient beds for the dedicated use of people with rheumatoid arthritis. Writing in the “Principles and Practice of Medicine” published in 1892, [1]

Sir William Osler (of eponymous note fame) observed that “arthritis deformans is an incurable disease.... Too often it invades successively all the articulations and in ten, fifteen or twenty years the crippling becomes general and permanent.” In the same textbook, he recommended that with regard to treatment, “It is useless to saturate the patient with iodide of potassium, salicylates or quinine...[but]... arsenic seems to do good as a general tonic.” Thankfully, times have changed.

Of the many potential drivers of the improved outlook for patients with rheumatoid arthritis, three in particular are noteworthy. Firstly, the recognition of the importance of early intervention with any disease modifying anti-rheumatic drug (DMARD); second, advances in understanding of the pathobiology of disease and the identification of many potential therapeutic targets, several of which have subsequently been validated in clinic trials; and finally, the recognised importance and implementation of a so-called tight control approach to inflammatory responses, with a view to limiting or even abrogating the many consequences of inflammation [2]. Given the devastating impacts of joint tissue destruction for patients with rheumatoid arthritis, as described by Osler and others, the principle aim of the tight control approach has been to limit or prevent structural damage and preserve functional status. That this aim can be achieved has been abundantly confirmed in the many clinical studies adopting a treat-to-target paradigm. [3] This approach requires regular assessment of people living with rheumatoid arthritis based on composite scores of disease activity, and subsequent titration of pharmacotherapeutic interventions, with a view to attaining the ideal target of remission, or low disease activity if remission is not possible. However, progressive structural damage to joints in patients with rheumatoid arthritis has become a less marked problem in contemporary times than it has been in the past [4]. Many reasons might explain the decreased focus on joint damage, including expansion of the therapeutic armamentarium, the development of new tools to establish classification criteria for rheumatoid arthritis for early-stage disease, [5] and environmental changes (perhaps including change in smoking behaviour, improved oral hygiene, decreased serious infections, and improved overall nutritional status). Consequently, although prevention of deformity and functional loss remains an imperative of rheumatoid arthritis management, the unmet need of patients has shifted away from a focus on inexorably progressive joint destruction. By contrast, many areas of contemporary unmet need are subjective in nature, and their true effects known only to the patient themselves [6]. Examples include pain, fatigue and mental

health effects, all of which can adversely affect social interaction, the ability to work, sexual activity, and overall wellbeing [7]. In addition to clinical symptoms being improved, patient reported outcomes can also benefit from a continuous goal-oriented approach to the management of rheumatoid arthritis, with a view to minimising cumulative inflammation exposure [8]. But in the contemporary era of protocol-driven medical practices, in which drug reimbursement is often dependent on a restricted set of outcome metrics, the treating physician needs to recognise the aspects of life that most trouble the patient and, when possible, address them with pharmacological and non-pharmacological interventions as appropriate. Such an approach might be particularly important for the patient who attains a treatment target for objective disease activity (such as the absence of swollen joints and elevated inflammatory markers) and yet has ongoing symptoms. In the context of a busy clinic, for example, in which the physician must struggle with completion of an electronic patient record, ongoing symptoms can be easily overlooked in a patient who meets composite criteria for remission or low disease activity. Conversely, even in the absence of swollen joints, patients often do not meet remission criteria because of the patient's global assessment of disease activity.

Having begun by quoting the recommendations of Sir William Osler for the treatment of rheumatoid arthritis, we would all do well to recall his wise remark that “the good physician treats the disease but the great physician treats the patient who has the disease.” Treating to target is an approach to pharmacological management that enhances achievable outcomes for patients with rheumatoid arthritis at a group level, and therefore, we have a responsibility to implement it in the individual, as far as feasibility permits while avoiding overtreatment and the potential for harm. But clinicians should implement treat-to-target as a means to benefit people living with rheumatoid arthritis, and should also consider treatment options that might improve the quality of life for patients rather than robotically treating a disease activity metric alone. Patient-centred treatment should involve shared goals with respect to what matters most to individuals living with rheumatoid arthritis.

Only a minority of patients in the established phase of rheumatoid arthritis in real-world practice both attain and maintain a robust remission over the long term [9,10]. For those patients who consistently do not achieve the desirable treatment target despite changes in pharmacotherapy up to every 3 months, the current treat-to-target recommendations are of limited use. In such individuals, who are refractory to many DMARDs and in whom the greatest achievable reduction in inflammatory burden has been reached, the question arises as to whether clinicians can use patient reported outcome measures to identify aspects of life that matter most to the individual, and then make use of this information to inform additional management choices [11].

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Many of the symptoms associated with active rheumatoid arthritis are known to represent generic features of inflammation. But some symptoms have multifactorial causes and might be the result of inflammatory or non-inflammatory processes (or both). Furthermore, with respect to inflammatory causes, distinct inflammatory pathways might contribute differentially to specific symptoms. In an era of targeted therapies, this possibility merits further research and could potentially refine future thinking regarding the treat-to-target paradigm.

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