Rethinking the discordance between guidelines and practice in rheumatoid arthritis treatment

A failure of practice, or a failure of evidence?

Drug treatment of rheumatoid arthritis (RA) has evolved significantly in recent decades, owing to increasing evidence supporting early intervention with disease-modifying therapies and the advent of novel biological therapies that specifically target the immunological and cellular mediators of disease. In the past 10 years, there have been over 60 systematic reviews and meta-analyses of pharmacotherapy in RA, reflecting the growth in development of new drugs and the shifting landscape of treatment regimens. Although these reviews vary in scope and focus, there is considerable overlap of the studies that are included. The findings of these reviews are mostly consistent and support early use of disease-modifying antirheumatic drugs (DMARDs) titrated appropriately for control of the disease process; the safety and efficacy of methotrexate as a first-line agent; and the clinical utility of corticosteroids in managing RA refractory to synthetic DMARDs, but also for identification of some areas of lacking on the long-term safety and efficacy of biological agents may confer different benefits and harms in different patients; and economically, because it compromises comparative cost-effectiveness analysis. Data are also}

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Efficacy and its safety at varying doses, particularly among certain ethnic groups and during pregnancy and breastfeeding. And despite the fact that numerous trials of individual biological agents have demonstrated their short-term efficacy and safety, it is difficult to compare them as there have been few head-to-head trials of these drugs. This is problematic clinically, because different agents may confer different benefits and harms in different patients; and economically, because it compromises comparative cost-effectiveness analysis. Data are also lacking on the long-term safety and efficacy of biological agents, and the relative and absolute benefits of these agents when they are used at different time points in the clinical course of patients with RA, although some long-term safety data are beginning to emerge. Finally, there is considerable uncertainty about the various ways in which the synthetic DMARDs and the newer biological agents should be combined.

Against the background of these limitations and the consistent support for early use of DMARDs, what are rheumatologists’ prescribing habits? A French study found little conformity between rheumatologists’ prescribing practices and clinical practice guidelines — 34% of patients with early RA did not receive any DMARD. A Canadian study also found an inappropriately low rate of prescribing: 84% of patients who regularly saw a rheumatologist were prescribed a DMARD, as were 73% of patients who consulted a rheumatologist intermittently. One common explanation for these findings is that clinicians are slow to translate research into practice, even where the evidence appears to be clear, as is the case for early use of DMARDs. An alternative explanation is that clinicians are cognisant of deficiencies in the evidence base, sceptical of the content of guidelines, sensitive to “non-clinical” concerns such as the cost of medicines, and wary of generalising data from systematic reviews and meta-analyses to the care of individual patients. It might not be that clinicians are resistant to change — apparent “failures” in translation might equally be attributable to problems in the evidence base (and the potentially confusing proliferation of clinical practice guidelines by diverse stakeholders and for various target audiences) as they are to habit, lack of motivation, and external barriers such as lack of time, resources and organisational support.

This has a number of practical implications. First, concordance among systematic reviews and agreement among clinical practice guidelines should not obscure important deficiencies in the evidence regarding RA. But neither is it enough for commentators and expert bodies to simply identify gaps in the literature. Health care and research communities both have a responsibility to question the evidence upon which guidelines are based. The absence of head-to-head studies and long-term data from postmarketing surveillance studies should raise
questions about possible biases arising from industry sponsorship of clinical trials and from trials designed according to the requirements of regulatory agencies. The relative absence of data on non-pharmacological therapies in RA should also raise questions about the dataset and the emphasis in clinical research on pharmaotherapies. While Australia’s National Medicines Policy provides a framework for improving prescribing practices through advocating the quality use of medicines, this relies upon a comprehensive and clinically relevant evidence base, and all stakeholders have a responsibility to ensure that the right research questions are asked and the right methods are used to answer them.

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