Tapering tumour necrosis factor inhibitors in rheumatoid arthritis: a retrospective study

Sirs,

Tumour necrosis factor (TNF) inhibitors have been shown to improve all measures of rheumatoid arthritis (RA) activity. The high cost of these drugs along with their important adverse events constitute major concerns for their long-term use. On the other hand, several randomised controlled studies as well as uncontrolled studies have shown the feasibility of dose reduction strategies for a substantial proportion of RA patients (1). In the light of these findings, current guidelines on RA treatment recommend tapering of biologic disease-modifying anti-rheumatic drugs for patients in persistent remission (2, 3) but data on the practicality and consequences of this recommendation in real-life settings are limited.

In this retrospective study we used the hospital database to identify all RA patients with a first time prescription of one of the 3 TNF inhibitors (etanercept, adalimumab, infliximab) between January 2012 and the end of December 2013. We retrieved all data on patient demographics and information on treatment and outcome from the medical charts. Data were censored at the end of May 2016.

The database search identified 125 RA patients. Of these, 104 were registered in our clinic and had available follow-up data until the end of May 2016 (Table I). Tapering was attempted in 44 (42%) patients after a mean duration of 14±7.6 SD months during follow-up**.** This was in the form of spacing in 39 patients (etanercept=16, adalimumab=9, infliximab=14) and dose reduction in 5 (all etanercept). Tapering strategy was left solely to the discretion of the treating physician without using a pre-specified protocol. The indication for tapering was good clinical response that was defined as the absence of any articular symptoms in the presence of normal acute phase reactions without using a composite outcome measure reflecting the 'real-life' setting of the survey. This setting was used for all patients except one who requested tapering because of fear from possible adverse effects. There was no difference regarding baseline characteristics between patients who tapered TNF inhibitors and who did not (Table I).

Table I. Demographic and disease characteristics of the patients.

	All patients (n=104)	Tapered anti-TNF (n=44)	Did not taper anti-TNF (n=60)
Mean (SD) age, years	47.7 ± 13.1	47.2 ± 12.2	48.1 ± 13.7
Female, n (%)	79 (76)	31 (70.5)	48 (80)
Median (IQR) disease duration, years	6 (2-10.25)	5.5 (1.6-7.75)	6 (2-13)
Seropositivity, n (%)			
RF	47 (46)	18 (49)	29 (62)
CCP	37 (60)	15 (54)	22 (65)
RF or CCP	55 (66.5)	22 (63)	33 (67)
Anti-TNF agent, n (%)			
IFX	18 (17)	14 (32)	4 (7)
ADA	24 (23)	9 (20)	15 (25)
ETA	62 (60)	21 (48)	41 (68)
Mean (SD) number of concomitant csDMARD	1.35 ± 0.7	1.37 ± 0.8	1.34 ± 0.7
Median (IQR) daily dose of prednisolone, mg/day	5 (2.5-5)	5 (2.5-5)	5 (2.5-5)
Number of patients using prednisolone, n (%)	82 (80)	34 (79)	48 (81)
Median (IQR) follow-up, months	44 (39-50)	47 (40-51)	42.5 (36-48.75)

RF: rheumatoid factor; CCP: cyclic citrullinated peptide; TNF: tumor necrosis factor; IFX: infliximab; ADA: adalimumab; ETA: etanercept; csDMARD: conventional synthetic disease-modifying antirheumatic drugs.

Among the 44 patients who tapered TNF inhibitors, disease flare was seen in 16 (36%) requiring a dose increase to the original schedule for a mean of 8.8±9.7 SD months after tapering. All patients responded to restoration of the original schedule. The remaining 28 patients (64%) preserved their good clinical response for a mean follow-up of 46.1±6.3 SD months allowing further tapering in 20 of them.

At the end of the follow-up, among the whole group of 104 patients, 73 (70%) were on biologics (TNF inhibitors = 49, non-TNF biologics = 24). The reasons for stopping biologics in the remaining 31 patients were persistent remission (16 patients; 15%), pregnancy (1 patient), non-compliance (4 patients), injection site reactions (3 patients), fear from adverse events (1 patient), request of the patient for trying complementary medicine (1 patient) and other issues such as losing insurance and family issues (5 patients).

The missing information on composite measures of disease activity and radiological data comprise the main limitation of our study.

In conclusion, tapering of TNF inhibitors was possible in 40% of our RA patients during follow-up. One third of them flared after tapering whereas the remaining two thirds maintained their good outcome allowing cessation in 15%.

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