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Original article

TNFα antagonist continuation rates in 442 patients with inflammatory joint disease

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Abstract

Objective: To evaluate TNFα antagonist continuation rates in patients with rheumatoid arthritis (RA), ankylosing spondylitis (AS), or psoriatic arthritis (PsA).
Methods: We retrospectively reviewed the charts of patients treated with etanercept, infliximab, or adalimumab at our teaching hospital. Drug continuation was evaluated using Kaplan–Meier survival curves. The logrank test was used to compare continuation rates.
Results: We identified 442 patients who were prescribed 571 TNFα antagonist treatments between August 1999 and June 2005. Among them, 304 had RA, 92 AS, and 46 PsA. In the RA group, continuation rates were high with etanercept ($n = 157$; 87% after 12 months and 68% after 24 months) and adalimumab ($n = 43$, 83% and 66%) but significantly lower with infliximab ($n = 104$, 68% and 46%; $P = 0.0001$ vs. etanercept and $P = 0.01$ vs. adalimumab). In the AS group, in contrast, infliximab ($n = 53$) showed significantly higher continuation rates (89% and 83%) than did etanercept ($n = 39$; 76% after 12 months: $P = 0.03$). Overall continuation rates were higher in AS than in RA ($P = 0.01$).
Conclusion: Continuation was better with etanercept than with infliximab in patients with RA, whereas the opposite was noted in patients with AS.

Keywords: Rheumatic disease; Chronic inflammatory joint disease; TNFα antagonist; Treatment continuation rate

1. Introduction

The advent of biotherapies has profoundly changed the management of rheumatoid arthritis (RA), ankylosing spondylitis (AS), and psoriatic arthritis (PsA) [1–11]. In France, the first TNFα antagonist was introduced in 1999, and three agents are now available (etanercept, infliximab, and adalimumab). TNFα antagonist therapy is indicated in patients with persistently active disease despite conventional treatment (methotrexate, leflunomide, or sulfasalazine for RA and PsA; and non-steroidal antiinflammatory drugs [NSAIDs] for AS). In this situation, TNFα antagonist therapy may prove dramatically effective in controlling symptoms and laboratory test abnormalities, slowing radiological damage [7], and improving quality of life [8]. Nevertheless, some patients fail to respond to TNFα antagonist therapy, and others experience treatment-limiting adverse effects [9]. Switching to another TNFα antagonist is beneficial in 60–70% of these patients [12–14].

Although the benefits of TNFα antagonist therapy are well established, treatment continuation rates are unclear. We retrospectively evaluated the continuation rates of etanercept, infliximab, and adalimumab in patients with RA, AS, or PsA.

2. Methods

The medical charts of patients with RA, AS, or PsA who were prescribed TNFα antagonist therapy at our teaching

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hospital between August 1999 and June 2005 were reviewed. RA was defined using American College of Rheumatology criteria [15], AS using modified New York criteria [16], and PsA using Moll and Wright criteria [17]. Etanercept, infliximab, and/or adalimumab were used.

These drugs were prescribed in accordance with international recommendations and French marketing license requirements regarding indications, contraindications, modalities of administration, and modalities of discontinuation. Thus, eligibility criteria for TNFα antagonist therapy in patients with RA were failure of methotrexate therapy and a disease activity score (DAS) greater than 5.1. Eligibility criteria in patients with AS were failure of several NSAIDs (axial disease) or of sulfasalazine with local glucocorticoid injections (peripheral disease) and a Bath Ankylosing Spondylitis Disease Activity Score (BASDAI) greater than 40. Patients with PsA were eligible if they had failed at least one disease-modifying antirheumatic drug (DMARD) and had three or more swollen tender joints. Etanercept was given in a dosage of 25 mg twice a week subcutaneously with or without concomitant DMARD therapy. In patients with RA, infliximab was consistently combined with a DMARD. The infliximab schedule was 3 mg/kg at weeks 0, 2, and 6 then at 8-week intervals; if needed, the dosing interval was reduced to no less than 4 weeks or the dosage was increased to 5 mg/kg every 8 weeks. In patients with AS or PsA, infliximab dosing intervals were the same as for RA but the dosage was 5 mg/kg and concomitant DMARD treatment was not given consistently. Adalimumab was used in a dosage of 40 mg twice a month subcutaneously, with or without concomitant DMARD therapy. TNFα antagonist therapy was discontinued if any of the following occurred: unacceptable adverse effects; primary failure to respond after 3 months, as assessed using EULAR criteria for RA [18], ASAS criteria for SA [19], and PsARC criteria for PsA [20]; or escape phenomenon, defined as an initial response followed by with failure to respond (compared to baseline) according to the above-described criteria.

The date of drug discontinuation was recorded and used to compute survival times for each TNFα antagonist and each disease. Survival curves were constructed using the Kaplan–Meier method. Survival was compared across drugs and diseases using the log-rank test. The reason for treatment discontinuation and the effect of TNFα antagonist use on glucocorticoid requirements were recorded.

3. Results

3.1. Patients

We identified 442 patients given TNFα antagonist therapy between August 1999 and July 2005, and we reviewed their medical charts. The diagnosis was RA in 304 patients (247 women and 57 men), AS in 92 patients (30 women and 62 men), and PsA in 46 patients (17 women and 29 men). Etanercept was introduced on the French market in August 1999, infliximab in January 2000, and adalimumab in June 2002. Of the 304 patients with RA, 157 received etanercept, 104 infliximab, and 43 adalimumab, as the first-line TNFα antagonist. Of the 92 patients with AS, 39 took etanercept and 53 infliximab initially. Of the 46 patients with PsA, 32 were started on etanercept, 9 on infliximab, and 5 on adalimumab.

Table 1 reports the baseline characteristics of the study patients. In the RA group, the time from diagnosis to TNFα antagonist initiation was significantly shorter with adalimumab than with the other two agents; there was no difference in this parameter between etanercept and infliximab. In this group, no differences were found between the three initial TNFα antagonists regarding patient age, number of prior DMARDs, and DAS. In the AS group, no differences were found between the etanercept and infliximab subgroups regarding patient age, time from diagnosis to TNFα antagonist initiation, number of prior DMARDs, and the BASDAI. In the PsA group, the numbers of patients in the subgroups

Table 1
Baseline patient characteristics (only the first-line TNFα antagonists are shown)

	Total	Etanercept	Infliximab	Adalimumab	*P* value
Rheumatoid arthritis (RA): 304 patients (247 women and 57 men)					
Number of patients	304	157	104	43	NS
Age (years)	58	57.8	59.9	58.4	NS
Time from RA diagnosis to treatment (years)	10	10.3	10	8.32	<0.05*
Number of prior DMARDs	2.7	2.72	2.74	2.55	NS
DAS	6.4	6.4	6.58	6.10	NS
Ankylosing spondylitis (AS): 92 patients (30 women and 62 men)					
Number of patients	92	39	53	0	
Age (years)	46	46.3	45.5		NS
Time from AS diagnosis to treatment (years)	11.3	11.4	11.3		NS
Number of prior DMARDs	1.64	1.61	1.67		NS
BASDAI	66	65 .2	66.7		NS
Psoriatic arthritis (PsA): 46 patients (17 women and 29 men)					
Number of patients	46	32	9	5	
Age (years)	52	49.5	48.8	58.5	
Time from PsA diagnosis to treatment (years)	9	9.8	11.4	7.1	
Number of prior DMARDs	2,3	2.25	2.55	2.20	

The number of patients was too small for statistical evaluation.