Impact of different Biologic Agents on the Improvement of Fatigue

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Background and objectives

Fatigue is a factor significantly affecting the physical health of patients with rheumatoid arthritis (RA) and limiting their social life. It was reported recently that TNFα leads to prolonged brain activity upon nociceptive stimulation, which is rapidly reversed with TNF-blockade. Considering this effect in the central nervous system our aim was to examine whether the improvement of fatigue is different for the various biologic agents.

Methods

We used data from our German biologics register RABBIT, which observes patients with RA from start of treatment with any approved biologic agent or with start of a new DMARD. The regular assessments performed at least every six months after inclusion include clinical status with disease activity measured by the DAS28 as well as detailed treatment information. Besides information of the treating rheumatologist, patients report their disease activity, health care use, limitations in work and social life. The level of fatigue is reported on a 0 (no) to 10 (very high) numerical rating scale.

In the current analysis only patients with a follow-up of at least 6 months and a minimum of two DMARD failures were included.

Multiple logistic regression analysis was used to compare treatment with various biologic agents to non-biologic DMARDs. Adjustment was made for the following baseline variables: fatigue, DAS28, functional capacity, co-morbid conditions (4 subgroups), previous treatment with biologics (yes/no), treatment with glucocorticoids (no,<10 mg/d, ≥10 mg/d), pain and morning stiffness ≥30 minutes.

Conclusion

Treatment with a biologic agent improved fatigue significantly more frequently than with a conventional DMARD. The higher chance for improvement of fatigue under treatment with biologics was already seen after three months and independent of disease activity.

This finding is supported by experimental research[1] reporting that blocking TNFα does not only have anti-inflammatory effects but also an impact on processes in the CNS.

1) Hess A, Axmann R, Rech J et al. Blockade of TNFa rapidly inhibits pain response in the central nervous system. Proc Natl Acad Sci USA 2011; 108:3731-6.

Results

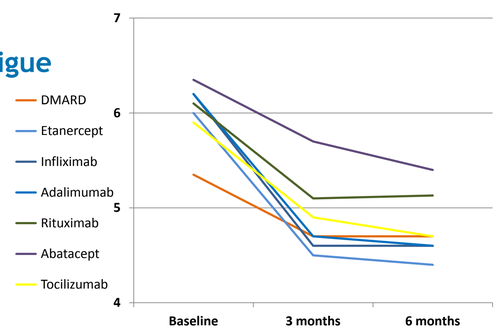
Fatigue was reported from 89% of all patients in the register. A high level of fatigue (≥ 7) was reported by 39% of patients (30% of patients in the DMARD treated group, 43% of patients treated with biologics).

In the current analysis 5,430 patients were included.

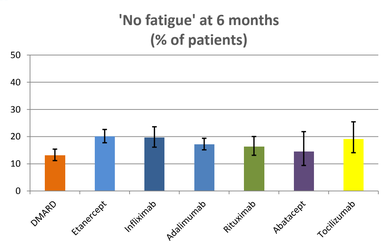
Baseline characteristics

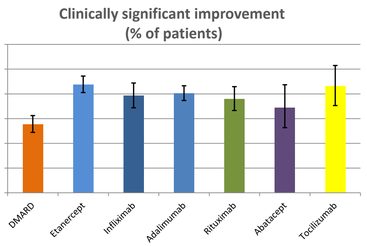
	DMARD	Anti-TNF	RTX	TOC	ABA
N	1059	3186	783	222	180
Female (%)	82	78	79	85	77
Rheumatoid factor positive (%)	72	80	84	77	75
Age (SD)	57.1 (11.4)	54.0 (12.5)	57.2 (11.8)	56.1 (13.1)	55.1 (12.8)
DAS28 (SD)	5.0 (1.3)	5.6 (1.3)	5.5 (1.3)	5.4 (1.4)	5.5 (1.3)
Disease duration (years, SD)	10.8 (9.0)	11.4 (9.1)	14.0 (9.9)	11.4 (8.7)	13.3 (9.0)
No. of previous therapy failures (SD)	2.6 (0.9)	3.4 (1.5)	4.8 (1.8)	3.9 (1.6)	5.6 (1.9)

Mean level of fatigue at baseline and after 3 and 6 months of treatment



Adjusted# frequency of patients achieving ‚no fatigue' or a significant improvement ≥ 3 points after 6 months of treatment





Patients without comorbidities had in all treatment groups a 40% higher chance of reaching a state of 'no fatigue' than patients with comorbidities (OR 1.4).

Adjusted# odds ratios (OR) of patients achieving 'no fatigue' or a clinically significant improvement of ≥ 3 points

Treatment	No. of patients	‚No fatigue' at 6 months		Significant improvement	
		Adj.# OR	95% CI	Adj. # OR	95% CI
DMARD	1,059	Referent	-	Referent	-
Etanercept	1,272	1.7 *	1.3-2.1	2.0 *	1.7-2.5
Infliximab	507	1.6 *	1.2-2.2	1.7 *	1.3-2.2
Adalimumab	1,407	1.4 *	1.1-1.7	1.8 *	1.4-2.2
Rituximab	783	1.3	0.9-1.8	1.6 *	1.2-2.1
Abatacept	180	1.1	0.7-1.9	1.4	0.9-2.1
Tocilizumab	222	1.6 *	1.0-2.4	2.0 *	1.4-2.9

Adjustments see Methods, * significant difference compared to DMARD control group

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