Periprosthetic joint infections in RA patients treated with biologics or conventional DMARDs

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Conclusion

In general, the rates for periprosthetic joint infections observed in our register are low and in line with reported incidence rates in RA patients.

Compared to patients treated with conventional DMARDs only, we found non-significantly increased rates of PPIs in those treated with anti-TNF agents. No PPIs were observed in patients treated with rituximab, abatacept or tocilizumab.

Background

A substantial proportion of patients with rheumatoid arthritis (RA) undergo total joint replacement (TJR). Periprosthetic infections (PPI) are serious complications with significant morbidity.

Based upon case series, it was suspected that patients with TJR are at increased risk for PPI when being treated with TNF inhibitors or other biologics.

Objectives

To analyse the frequency of PPIs in RA patients with TJR treated with biologics or conventional DMARD treatment.

Patients & Methods

Data from the German biologics register RABBIT. RA patients are eligible to be enrolled with the start of one of the approved biologic agents or when a new conventional DMARD is prescribed after at least one DMARD failure. Once enrolled, each patient is observed for at least five years. Treatment, clinical status and adverse events (including surgical procedures like joint replacement) are assessed regularly.

Only TJR of hip, knee, shoulder or ankle were included in the analysis. Exposure time was either the total follow-up time in patients with prior TJR at baseline or the time after TJR in patients undergoing TJR during the observation. All PPIs observed before May 2010 were included.

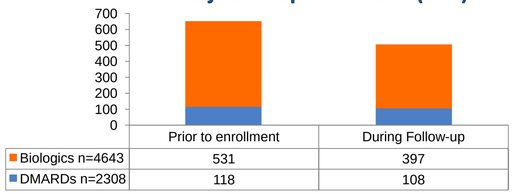
Results

Baseline characteristics of 7,536 patients enrolled until May 2010.

	DMARD	Anti-TNF	Tocilizumab	Rituximab	Abatacept
N enrolled	2,556	3,989	186	597	119
Age	57 ± 12	54 ± 12	58 ± 12	58 ± 12	55 ± 13
Female	78%	78%	83%	80%	81%
Disease duration, yrs	5 (2-11)	9 (4-16)	9 (4-18)	11 (5-20)	11 (5-17)
No. treatment failures	1 (1-2)	3 (2-4)	4 (3-5)	4 (3-5)	5 (4-6)
RF positive	67%	79%	74%	82%	69%
DAS28	4.9 ± 1.3	5.7 ± 1.3	5.6 ± 1.4	5.5 ± 1.3	5.6 ± 1.2

(Values represent mean ± standard deviation or median (IQR))

Patients with total joint replacement (TJR)



	Prior to enrollment	During Follow-up
Biologics n=4643	531	397
DMARDs n=2308	118	108

A TJR of a larger joint was reported in 928 (20%) of the patients treated with biologics and 226 (9.8%) of the patients treated with DMARDs.

The mean exposure time to biologics after implantation was 2.7 years.

15 periprosthetic joint infections in 1,495 TJR

1.0% of the prostheses got infected (15 PPIs in 1,013 patients with 1,495 TJR). In patients treated with conventional DMARDs only 1.0% and in anti-TNF treated patients 1.5% of the TJR got infected (p=0.77).

No difference was found between the single anti-TNF agents: adalimumab 5/384 = 1.5%, etanercept 5/345=1.4%, and infliximab (1/109=0.9%).

Comparison with the literature

The population based Danish Hip Arthroplasty Register[1] found an infection rate of 0.7% in 80,756 primary procedures. The Finnish Arthroplasty Register reported infection rates of 1.3% for patients with RA in 43,149 knee arthroplasties (the population based total rate was lower with 0.9%) [2].

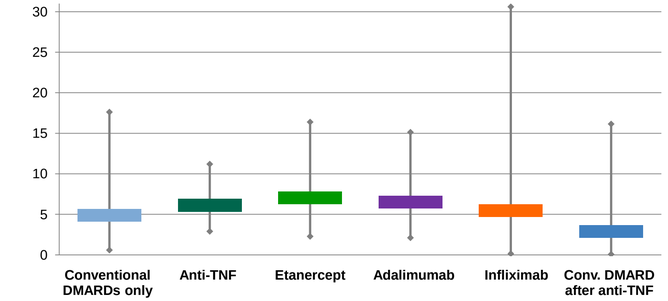
1) Pedersen A, Svendsson J, Johnssen S, Riis A, Overgaard S. Risk factors for revision due to infection after primary total hip arthroplasty. Acta Orthopaedica 2010; 81 (5): 542-547.

2) Jämsen E, Huhtala H, Puolakka T, Moilanen T. Risk factors for infection after knee arthroplasty. A register-based analysis of 43,149 cases. J Bone Joint Surg Am 2009; 91(1):38-47.

Rates of periprosthetic joint infections in patients on different treatments

Although the rate in the anti-TNF group is higher than in the group treated with conventional DMARDs it is not significantly increased.

In patients treated with rituximab (229 TJR), abatacept (59 TJR) and tocilizumab (69 TJR) no PPIs occurred within 266/58/35 PYRs of observation.



	Conventional DMARD	Anti-TNF	Conv. DMARD after anti-TNF	Anakinra
Patients with TJR	204	667	320	28
PYRs of exposure	410	1635	345	53
No. of PPI	2	10	1	2
Rate/1,000 PYR	4.9 (0.6-17.6)	6.1 (2.9-11.2)	2.9 (0.1-16.1)	37.7 (4.6-136.3)

Time after treatment start or TJR implantation until periprosthetic joint infection

One infection in an anakinra treated patient and 5 infections in the anti-TNF treated group (4 x etanercept, 1 x infliximab) occurred within 6 months after either implanting the prosthesis (n=2) or starting the biologic.

All other PPIs occurred between 10 and 37 months (mean 18.9 months) after TJR or treatment start.

In 10 of the infections the microorganism was specified. Infections with staphylococcus were most frequently reported (6 times). Enterococci (2x), candida (2x) and streptococcus agalacticae were the other infecting agents.

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