The Community Use of Biologic Response Modifiers in Rheumatoid Arthritis

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Abstract

Objective:
To review the profile of biologic therapies utilization, response and adverse events in RA in a rheumatology clinic in Newfoundland and Labrador.
Methods:
A retrospective descriptive study was performed by auditing charts of patients in a rheumatology practice in St. John's, Newfoundland seen between 2002-2006. Criteria for inclusion were a diagnosis of rheumatoid arthritis and current treatment with a biologic response modifier. One researcher audited the selected charts and recorded the following information: basic patient data (age, gender, comorbidities); disease data (duration of disease, RF factor status); past use of DMARDs and side effects; current and past use of Biologics (dosage, duration of use, side effects); serology before and after treatment (RF, ANA, CRP, ESR, Hb); disease status measures before and after treatment (joint counts and HAQ scores); PPD Tuberculin Test results. Basic statistical analyses were calculated on the collected data, including means, medians, modes, ranges, and standard deviations.
Results:
Seventy-five patients, 48 female and 27 male, were included in the study, of whom the majority (73.3%) were RF positive and the mean duration of disease among them was 9.6 years. The mean number of previous DMARDs used was 3.9 and the most commonly used were Methotrexate and Prednisone. Etanercept was the biologic used by the highest number of subjects, followed by Adalimumab; 29.3% of subjects experienced side effects from a biologic, of which the most common was flu-like illness. Twenty-four percent of subjects had low hemoglobin (> 5% less than normal) before treatment with a biologic and their levels increased by a mean of 16.4g/L following treatment. The mean ESR was 43.9 before treatment and 26.4 after treatment. The mean joint count was 10.5 before treatment and 5.0 after treatment. The mean HAQ score was 1.47 before treatment and 0.98 after treatment. Of the patients who had PPD tests, 34% were positive (>5mm) and were treated with Isoniazid.
Conclusions:
The inherent limitations of a retrospective study limit the direct causality that can be assumed from the results. There are, nonetheless, several important findings. Subjects experienced considerable improvements in swollen joint counts and HAQ scores following treatment with biologic therapies. The mean joint count at initiation of therapy was 10.5, considerably lower than the norm for many clinical trials, and subsequent improvement in disease measures were greater than that being found in these same trials. There was a decrease in ESR following treatment. There was also a considerable improvement in hemoglobin following treatment and it is uncertain whether this is due to an improvement in chronic disease status or to an inherent property of the biologics. Finally, there were a large percentage of subjects with a positive PPD test, consistent with the trend found in Newfoundland and Labrador.

Introduction

The use of biologic response modifiers has become the mainstay of treatment for moderate to severe rheumatoid arthritis that is not adequately treated by traditional DMARDs. Six biologics are currently approved for use in Canada: Etenercept (Enbrel), Infliximab (Remicaide), Adalimumab (Humira), Anakinra (Kineret), and most recently Abatacept (Orencia) and Rituximab (Rituxin). The choice of medications is tailored to the patient and depends on many factors including general health and medical history, severity of their RA, disease progression, and previous medications.

This study reviewed the profile of biologic therapies utilization for the treatment of rheumatoid arthritis in Newfoundland and Labrador. The purpose was to examine the characteristics of patients being selected for treatment, which biologics were prescribed and at what dosage, the adverse effects, and the disease status of patients before and after treatment.

Methods

A retrospective descriptive study was performed by auditing charts of patients in a rheumatology practice in St. John's, Newfoundland seen between 2002-2006. The patients were followed by one rheumatologist in a mixed community and academic setting.

Criteria for inclusion were a diagnosis of rheumatoid arthritis and current treatment with a biologic response modifier. One researcher audited the selected charts and recorded the following information: basic patient data (age, gender, co-morbidities); disease data (duration of disease, RF factor status); past use of DMARDs and side effects; current and past use of Biologics (dosage, duration of use, side effects); serology before and after treatment (RF, ANA, CRP, ESR, Hb); disease status measures before and after treatment (joint counts and HAQ scores); PPD Tuberculin Test results. Basic statistical analyses were calculated on the collected data, including means, medians, modes, ranges, and standard deviations.

Results

Table 1: Patient Data

Total Patients	75	
Gender Distribution		
Females	48	0.64
Males	27	0.36
F:M	1.78:1	
Age (years)	53.5	(Range 27-87)
Disease Duration	12.77 years	(Range 2-35)
RF Status	79.6% positive	
# Comorbidities	2.09	(Range 0 – 6)

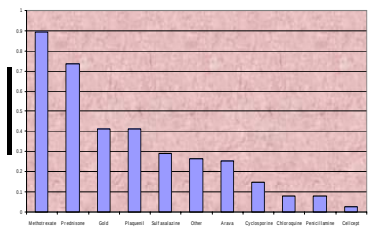

Figure 1: Number of patients having previously utilized each DMARD

Adverse Effects:
26.7% of patients experienced an adverse reaction to a DMARD.

PPD Test
24.2% of patients tested had a positive PPD skin test (5mm+) and were treated with Isoniazid.

Table 2: Biologic therapy utilized, dosage, duration of use, adverse effects

	# patients	Median dosage
Humira	28	40mg sc q2w
Enbrel	21	25mg sc TIW
Remicaide	20	300mg IV q8w
Kineret	6	100mg sc od

Mean duration of use was 1.82 years (range 0.1-55)

Adverse effects: 16 patients experienced a total of 27 events including flu-like/viral illness (6), rash (5), injection site reaction (4), sinusitis (2), swelling/abscess (2), pneumonia (2)

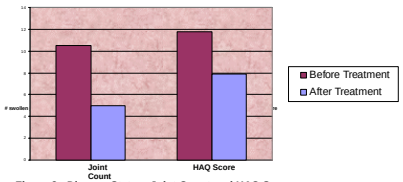

Figure 2: Disease Status: Joint Count and HAQ Score Pre- and Post- Biologic Therapy

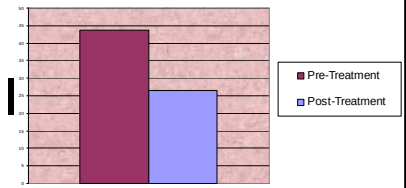

Figure 3: Erythrocyte Sedimentation Rate Pre- and Post-Biologic Therapy

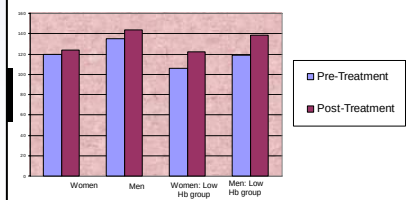

Figure 4: Hemoglobin Pre- and Post- Biologic Therapy
Note: Patients with low Hb (greater than 5% below normal range) were considered separately and this group experienced the greatest increase in Hb post-treatment.

Conclusions

The inherent limitations of a retrospective study limit the direct causality that can be assumed from the results. There are, nonetheless, several important findings in our study. our patients experienced considerable improvements in swollen joint counts and HAQ scores following treatment with biologic therapies. The mean joint count at initiation of therapy was 10.5, was considerably lower than the norm for many pivotal clinical trials of TNF antagonists, and subsequent improvement in disease measures were greater than that being reported in these same trials. There was a decrease in ESR following treatment. There was also a significant improvement in hemoglobin following treatment and it is uncertain whether this is due to an improvement in chronic disease status or to an inherent property of the TNF antagonists. Finally, we found that there were a large percentage of subjects with a positive PPD test, consistent with the trend found in Newfoundland and Labrador but probably higher than expected in other parts of Canada.

Future Research

We anticipate further studies to look at the utilization of the new biologics in RA after TNF antagonists failure and the exact role of TNF antagonists (and possibly other biologics) in controlling anemia in RA patients. We also believe that studying the economic impact of these therapies in a community setting would add to the understanding of the role of biologics use in the patient population and the community at large.

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