EFFECT OF BIOLOGIC DISEASE MODIFIERS ON CARDIOVASCULAR RISK OF PATIENTS WITH RHEUMATOID ARTHRITIS (RA) – 2 YEARS PROSPECTIVE COHORT STUDY

M. Khraishi[1,2]; R. Aslanov[2]; K. Doyle[1]

[1]NEXUS Clinical Research; [2]Memorial University of Newfoundland (MUN).

ABSTRACT

People with RA have a higher risk for developing heart disease such as silent ischemia, early myocardial infection (MI), stroke and sudden death than the general population. This study aimed to assess the effect of Biologic Disease Modifier Anti-Rheumatic Drugs (BDMARDs) on a 10-year CV event risk in patients with RA after 24 months of follow-up and to evaluate the impact of BDMARDs on the incidence of CV events in patients with RA during the 2 years of observation. The Framingham Risk Score (FRS) was used for the assessment of 10-year CVD risk. The presence of CV risk factors was ascertained at the baseline and at every six months of observation up to 24 months. TC did not change significantly after 1 year but was significantly reduced after 2 years of observation (3.0±2.8 vs. 2.0±2.5, p<0.001). HDL increased significantly at 12-month and then significantly reduced at 24-month period (0.7±0.7 vs. 0.8±0.7, p=0.042 and 0.7±0.7 vs. 0.6±0.7, p=0.025, respectively). Comparison of LDL measurements at 12 and 24-month periods showed significant improvement from 1.8±1.6 to 1.3±1.5 with p<0.001. The AI was significantly reduced during the two follow-up periods. CRP, ESR and DAS28 were also significantly reduced from the baseline levels. The overall risk of cardiovascular event significantly reduced in 12 months from 12.5±9.3 to 12.1±9.0 (p=0.019; 95%CI 0.1-0.7) and in 24 months of the study from 12.5±9.3 to 11.9±8.9 (p<0.001; 95%CI 0.3-0.9).

CONTACT

Dr. Majed Khraishi
NEXUS Clinical Research/NL Research Technologies
Email: mkhraishi@gmail.com
Phone: 709-726-3386
Website: www.nlrt.ca

NLRT Website QR code

INTRODUCTION

People with RA have a higher risk for developing cardiovascular diseases such as silent ischemia, early myocardial infection (MI), stroke and sudden death than the general population. The pathogenic mechanisms involved in increased cardiovascular complications in RA appear to be complex and multifactorial due to RA-related inflammation as well as the risk factors which affect the general population. We hypothesized, that treatment of RA patients with BDMARDs will significantly reduce the 10-year risk for CV event.

OBJECTIVES

To assess the effect of Biologic Disease Modifier Anti-Rheumatic Drugs (BDMARDs) on a 10-year CV event risk in patients with RA after 24 months of follow-up

To evaluate the impact of BDMARDs on the incidence of CV events in patients with RA during the 2 years of observation

METHODS and PATIENTS

A total of 228 patients with RA receiving biologic therapy were prospectively followed-up in this study. The Framingham Risk Score (FRS) was used for the assessment of 10-year CVD risk. The presence of CV risk factors (fasting serum TC, HDL and LDL levels, history of HTN, DM, previously and currently recorded CV events) was ascertained at the baseline and at every six months of observation up to 24 months.
Analyses of the relationships between lipids and inflammatory indices (CRP and DAS28) before and after treatment with biologics, as well as of biologic modifiers were performed. Treatment changes including introduction of lipid-lowering medication and correlation between BDMARDs and CV events were also analyzed.
Ten-year CVD event risk was assessed by gender and age. Paired t-test and Multivariate Regression analyses were performed using SPSS (IBM version 20.0) software.

RESULTS

From 228 patients enrolled at the baseline, 2 patients deceased and 6 patients dropped out of the study. Total 220 patients (73% females) with the mean (SD) age of 56.2 (11.6) years were prospectively followed up to 24 months. The mean (SD) age at RA diagnosis was 41.6 (12.9) years with the mean (SD) duration of RA symptoms 14.5 (8.5) years. Nine patients with documented MI and 5 patients with TIA/Stroke had their CV events prior to the study. Two patients had MI during the observation period. One was a 66 y.o. male with the history of DM and another was a 56 y.o. male with long history of smoking and Angina. Forty-two (19.1%) patients (62% females) smoked at the baseline (one quitted during the period of observation). Sixty-five patients were on Lipid-lowering treatment, of them 31 (48%) started it after the initiation of the treatment with biologics (Table1).
Tender joint (TJC) and Swollen joint counts (SJC) were significantly reduced after 12 and 24 months of treatment. TC did not change significantly after 1 year but was significantly reduced after 2 years of observation (3.0±2.8 vs. 2.0±2.5, p<0.001). HDL increased significantly at 12-month and then significantly reduced at 24-month period (0.7±0.7 vs. 0.8±0.7, p=0.042 and 0.7±0.7 vs. 0.6±0.7, p=0.025, respectively).

RESULTS

Patients were grouped by their 10-year CVD risk level: Low Risk (<10%), Moderate Risk (10% to 19%) and High Risk (20% and more). The trend analysis of 10-year CVD risk by gender showed that 1.4% of men in an 24-month period moved from the high to moderate risk category (40.7% vs. 39.0%) and 3.7% of females lowered their risk from the high/moderate to low (55.9% vs. 59.6%).
There was not significant association between lipids and inflammation indices. The correlation between Adalimumab and TC/LDL lipids was significant (r=0.161, p=0.017 and r=0.150, p=0.026, respectively) as well as between Golimumab and HDL/LDL levels (r=0.143, p=0.034 and r=0.145, p=0.032, respectively).
The overall risk of cardiovascular event significantly reduced in 12 months from 12.5±9.3 to 12.1±9.0 (p=0.019; 95%CI 0.1-0.7) and in 24 months of the study from 12.5±9.3 to 11.9±8.9 (p<0.001; 95%CI 0.3-0.9) (Table 2).
Thirty seven patients switched biologics during their treatment course. The analysis of the impact of individual biologic DMARD on 10-year CV event risk showed significant improvement at 24-month period in Tocilizumab (14.3±9.1 vs. 12.9±8.5) with p=0.002 and Abatacept (14.0±10.0 vs. 13.4±10.0) with p=0.042 treatment groups (Table 3).

TABLE 1: Demographics and other Characteristics of Patients with RA

Age, years, mean (SD)	56.2±11.6
Female, n (%)	161 (73.2%)
Age at RA diagnosis in years, mean (SD)	41.6 ± 12.9
RA duration years, mean (SD)	14.5 ± 8.5
Smoking Status, n (%)	42 (19.1%)
Hypertension (HTN), n (%)	68 (30.9%)
Diabetes Mellitus (DM), n (%)	32 (14.5%)
Dyslipidemia, n (%)	69 (32.1%)
Atrial Fibrillation (AF), n (%)	9 (4.1%)
Coronary Artery Disease, n (%):	24 (10.9%)
1. Angina, n (%)	13 (5.9%)
2. Myocardial Infraction (MI), n (%)	11 (5.0%)
TIA/Stroke, n (%)	5 (2.3%)
Hypertension Treatment, n (%)	63 (28.6%)
Diabetes Treatment, n (%)	30 (13.6%)
Lipid-lowering Treatment, n (%)	65 (29.5%)

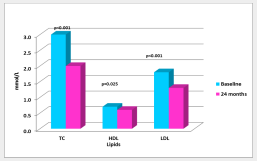
TABLE 2: Comparison of RA Characteristics and Lipid Levels at Baseline, 12 and 24 months of Follow-up

RA Characteristics	Baseline, mean (SD)	12-month F-Up, mean (SD)	P	24-month F-Up, mean (SD)	P
Total Joint Count (TJC)	12.3 (8.1)	5.3 (4.7)	<0.001	5.1 (5.6)	<0.001
Swollen Joint Count (SJC)	4.3 (3.7)	2.1 (2.6)	<0.001	1.1 (1.9)	<0.001
C-Reactive Protein (CRP), mg/l	15.5 (29.0)	10.1 (15.5)	0.004	4.7 (8.3)	<0.001
ESR, mm/h	29.7 (22.8)	22.9 (20.1)	<0.001	16.4 (17.7)	<0.001
DAS28 score	4.1 (1.2)	3.6 (1.2)	<0.001	3.0 (1.1)	<0.001
CDAI score	18.2 (9.6)	14.2 (9.8)	<0.001	10.7 (7.2)	<0.001
HAQ score	1.2 (0.7)	1.1 (0.7)	0.030	0.9 (0.7)	<0.001
Total Cholesterol, mmol/l	3.0 (2.8)	3.3 (2.7)	0.038	2.0 (2.5)	<0.001
HDL Cholesterol, mmol/l	0.7 (0.7)	0.8 (0.7)	0.001	0.6 (0.7)	0.025
Atherogenic Index (TC/HDL)	4.6 (1.7)	4.1 (1.2)	<0.001	3.8 (0.8)	<0.001
Overall 10-year CV Event Risk (%)	12.5 (9.3)	12.1 (9.0)	0.019	11.9 (8.9)	<0.001

TABLE 3: Effect of Biologics on Lipids and 10-year CVD Risk after 24 months treatment (BDMARDs administered to ≥ 20 patients)

CHARACTERS	ETANERCEPT n=43	P	ADALIMUMAB n=40	P	TOCILIZUMAB n=40	P	RITUXIMAB n=29	P	ABATACEPT n=30	P
CRP	16.1(22.4) vs. 5.4(7.7)	0.004	11.7(15.3) vs. 2.9(4.6)	<0.001	8.8(11.6) vs. 1.7(4.2)	0.001	16.4(28.5) vs. 10.3(17.1)	0.221	14.9(34.5) vs. 4.3(4.6)	<0.001
DAS28	4.2(1.1) vs. 3.1(1.0)	<0.001	3.6(1.2) vs. 2.7(0.8)	<0.001	4.2(1.5) vs. 2.5(1.0)	<0.001	4.2(1.1) vs. 3.8(1.1)	0.108	4.4(1.0) vs. 3.4(1.3)	<0.001
TC	2.7(2.5) vs. 1.1(2.0)	0.001	3.0(2.7) vs. 3.1(2.5)	0.888	3.8(3.1) vs. 2.0(2.8)	<0.001	3.0(2.7) vs. 2.0(2.4)	0.059	2.8(2.5) vs. 2.1(2.3)	0.128
HDL-C	0.7(0.7) vs. 0.3(0.6)	0.002	0.8(0.8) vs. 0.9(0.7)	0.646	0.7(0.6) vs. 0.5(0.7)	0.021	0.8(0.8) vs. 0.6(0.8)	0.189	0.7(0.7) vs. 0.6(0.7)	0.550
AI	4.0(1.8) vs. 3.6(1.1)	0.316	4.6(1.9) vs. 3.8(1.0)	0.020	5.1(1.7) vs. 4.1(0.9)	0.053	3.7(1.2) vs. 3.4(0.3)	0.446	4.6(0.8) vs. 3.9(0.7)	0.017
10-YEAR CVD RISK	12.4(9.8) vs. 12.0(9.4)	0.062	9.9(7.5) vs. 9.9(7.3)	0.949	14.3(9.1) vs. 12.9(8.5)	0.002	14.5(10.4) vs. 15.0(10.5)	0.319	14.0(10.0) vs. 13.4(10.0)	0.042

Lipids Profile at baseline and 24 months



CONCLUSIONS

Two counts of CV event were observed during the study period with both patients at the higher risk for CVD. Our results showed a trend in reducing a 10-year CV event risk over 24-month period in patients with treated RA. This improvement was influenced by many factors such as lipid-lowering treatment (29.5% of patients), proper control of blood pressure and plasma glucose level (28.6% and 13.6% of patients, respectively). The study results demonstrated a favourable effect of biologic DMARDs on the serum levels of LDL-C, atheroprotective HDL-C of RA patients and their AI. Good control of the inflammation by BDMARDs effectively decreased inflammation and possibly played a pivotal role in reducing the risk for cardiovascular event in patients with chronic RA.

DISCLOSURE
Dr. Khraishi received non restricted educational grants from Hoffman-La Roche Canada, Amgen, Pfizer Canada, and Abbott Canada.