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FRI0020

CORRELATION BETWEEN EXPRESSION LEVELS OF MIR-146A AND MIR-223 IN SYNOVIAL FLUID AND ULTRASOUND SCORES FOR ACTIVE SYNOVITIS IN RHEUMATOID ARTHRITIS PATIENTS

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Background: MicroRNAs (miRNAs) are a class of small, non-coding RNAs that negatively regulate gene expression at posttranscriptional level. In the recent years studies have shown that in rheumatoid arthritis (RA) the systemic and local expression of certain miRNAs is altered [1-2]. The correlation between their expression levels and scores for disease activity and progression in RA make them possible candidate for biomarkers in the clinical practice.

Objectives: To analyze the expression levels of miR-146a and miR-223 in synovial fluid (SF) from RA patients in regard to the ultrasound scores for disease activity.

Methods: A total number of 48 RA patients according to the 1987 ACR criteria were included in the study. Expression levels of miR-146a and miR-223 SF were determined by qPCR (SybrGreen technology) and compared to healthy controls (HCs). Relative changes of gene expression levels of the studied miRNAs were calculated by $2^{-\Delta\Delta Ct}$ method. Musculoskeletal ultrasound (MSUS) examination was performed by two independent examiners on ESAOTE, MyLab60 using both grey scale and power Doppler technic. A semi quantitative assessment of the peripheral joints was performed for detecting joint inflammation and determining the grade of synovial thickening and the degree of vascularization. Ultrasound features for active disease were correlated to the local expression of the studied miRNAs. SPSS was used for statistical analysis.

Results: RA SF showed overexpression of miR-146a (in 70.83%, $p=0.007$) and of miR-223 (in 79.17%, $p=1.64 \times 10^{-3}$) when compared to HCs. There was a statistically significant correlation between the presence of synovitis and the degree of the power Doppler signal on MSUS and the local expression of miR-146a ($p=0.030$ and $p=0.049$, respectively) and miR-223 ($p=6.19 \times 10^{-4}$ and $p=0.003$, respectively). SF levels of miR-223 correlated also with the degree of synovial hypertrophy on MSUS ($p=0.013$).

Conclusion: We found correlation between the SF expression of miR-146a and miR-223 and the ultrasound features of active joint inflammation. Further analysis with larger sets is needed to confirm if altered local miRNA expression could be used in the clinical practice as biomarker for disease activity especially in cases with subclinical synovitis.

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Rheumatoid arthritis – comorbidity and clinical aspects

FRI0021

ORAL HYGIENE STATUS IN RA PATIENTS AND PLACE OF RHEUMATOLOGIST IN THERAPEUTIC EDUCATION ON ORAL DENTAL HEALTH

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Background: The relationship between oral hygiene and rheumatoid arthritis has been demonstrated by several studies.

Objectives: To evaluate oral hygiene status in rheumatoid arthritis (RA) patients.

To inform about the therapeutic education given by the rheumatologist on the importance of adequate oral hygiene in the management of RA

Methods: This is a cross-sectional study that included 100 consecutive RA patients (89% female, mean age 46.7 years, median disease duration of 8 years, mean specialized care duration of 3 years). A questionnaire evaluating oral hygiene status was administered. It focused on following items: the daily frequency of brushing, the modalities of brushing, the use of other means of oral hygiene, the regular follow-up at a dentist's doctor and the place of the rheumatologist in therapeutic education on the oral dental hygiene status.

Results: Table I illustrates the results of oral hygiene evaluation in RA patients.

Table I : Evaluation of Oral Hygiene in RA patients

Items	N=100
Daily Brushing Frequency (%):	18
- 0 times/day	37
- once a day	34
- 2 times/day	8
- 3 times/day	3
- After each meal	
adequate brushing time (≥ 3 min) (%)	31
Correct brushing method (%)	14
Use of other means of oral hygiene (%)	36
Regular dentist visit (%)	2
Never visit a dentist (%)	27

Table II illustrates the results of the place of oral hygiene information in rheumatologic management.

Table II : Place of information on oral hygiene in rheumatologic care.

Questions	Yes (%)
1. does your rheumatologist ever examined your oral cavity?	6,0
2. have you ever been informed by your rheumatologist that poor oral hygiene has a negative impact on your rheumatoid arthritis?	11,0
3. Does your rheumatologist ever recommended regular brushing of your teeth?	8,0
4. Does your rheumatologist already recommended to you to consult a dentist?	10,0

Conclusion: This study illustrates the high prevalence of oral hygiene insufficiency in patients followed for RA. It also highlights poor therapeutic education given by the rheumatologist on the importance of adequate oral hygiene in the management of RA.

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Rheumatoid arthritis - comorbidity and clinical aspects

FRI0022

EVALUATION OF DYSFUNCTIONAL HIGH-DENSITY LIPOPROTEIN LEVELS WITH MYELOPEROXIDASE/PARAOXONASE1 RATIO IN RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is a chronic, systemic and autoimmune disease with inflammatory arthritis. Atherosclerosis and cardiovascular diseases are common in RA patients. Although chronic systemic inflammation in RA patients is considered to be the main cause of this condition, the relationship between systemic inflammation and vascular pathophysiology is not clear [1]. While high-density lipoprotein (HDL) is known to be a negative risk factor for atherosclerosis by reverse cholesterol transport, recent studies show that HDL can be pro-atherogen (dysfunctional, inflammatory) by losing this characteristic in cases of inflammation and oxidative stress. Myeloperoxidase (MPO)/paraoxonase 1 (PON1) ratio is a valuable marker that can be routinely used as an indicator of dysfunctional HDL. PON1 is a lipoprotein-derived enzyme which provides antioxidant properties of HDL. Although MPO is a bactericidal enzyme derived from granular leukocytes, it causes oxidative modification of circulating lipoproteins [2].

Objectives: The aim of this study is to evaluate the levels of dysfunctional HDL in RA patients and to explore the relationship between dysfunctional HDL and coronary artery disease (CAD) in RA patients.

Methods: Sixty seven healthy individuals and 130 RA patients without diabetes mellitus, hypertension and hyperlipidemia were included to study. Blood samples taken from patients and healthy volunteers were centrifuged to separate serum and these serum samples were stored at -80 °C until the study day. Total cholesterol (TC), triglyceride (TG), HDL, Low-density lipoprotein cholesterol (LDL), MPO and PON1 levels were measured. The MPO/PON1 ratio was calculated as a dysfunctional HDL marker. Cardiology notes of the patients were examined to detect patients who also have CAD.

Results: The mean age of the patient and control groups were 54.6 ± 11.3 and 52.0 ± 10.0, respectively (p:0.107). The mean DAS28 score of the patients was 2.77 ± 0.96. There were no significant differences between two groups in TC, TG, HDL and LDL (p> 0.05). MPO, PON1 and dysfunctional HDL levels were significantly higher in the RA group compared to control group (p <0.001, p <0.023, and p <0.001; respectively).

Dysfunctional HDL levels were higher in 44 RA patients with CAD compared to 86 RA patients without CAD (p = 0.002). 58 patients with active RA had higher dysfunctional HDL levels compared to 72 patients with remission (p = 0.002). There was a positive correlation between DAS28 scores and dysfunctional HDL levels (rho: 0.357, p < 0.001).

Conclusion: Our study shows that, although there is no abnormality in lipid profile parameters, dysfunctional HDL levels were higher in patients with active disease than patients with RA in remission and RA patient with CAD than without CADs. This condition could be associated with CAD in RA patients. Disturbance as a result of inflammation on HDL functions such as inhibition of LDL oxidation and reverse cholesterol transport, could be the cause of CAD in RA patients. As a result screening of conventional cardiovascular risk factors in RA patients with normal lipid panel might be inadequate. Therefore as an additional parameter, dysfunctional HDL are promising to evaluate cardiovascular risk of RA patients.

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FRI0023

CARDIOVASCULAR RISK AND VITAMIN D DEFICIENCY IN PATIENTS WITH RHEUMATOID ARTHRITIS IN THERAPY WITH TNF-ALPHA INHIBITORS

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Background: Cardiovascular disease is the main cause of mortality and morbidity in patients with rheumatoid arthritis (RA). Correlation between vitamin D deficiency and atherosclerosis in patients with rheumatoid arthritis is a subject of medical interest.

Objectives: We studied the correlation between vitamin D deficiency, body mass index (BMI) and carotid intima-media thickness (CIMT) in patients with rheumatoid arthritis with anti tumor necrosis factor-alpha (TNF-α) therapy.

Methods: Our study included 75 RA patients with anti-TNF-alpha therapy (Adalimumab, Infliximab, Etanercept) and 30 RA patients with DMARDs (Methotrexate/Leflunomide). The patients were diagnosed with RA according to ACR/EULAR (2010) classification **criteria**.

CIMT was measured using high-resolution Doppler ultrasonography. CIMT ≥ 0.9 mm is considered as a marker of atherosclerosis. Vitamin D deficiency was defined as serum 25-OH-vitamin D level <20 ng/mL. Other parameters included are age, body mass index (BMI=18.5-24.9kg/m²- normal weight; BMI≥25kg/m²- overweight) and disease activity (DAS28<2.6: remission; DAS28=2.6-3.2: low disease activity, DAS28=3.2-5.1: moderate disease activity; DAS28>5.1: high disease activity).

Patients with current use of vitamin D supplements were excluded.

Results: The anti-TNF group included 29 patients with Adalimumab (38.7%), 25 with Etanercept (33.3%) and 21 patients in treatment with Infliximab (28%). Their mean age was 52.0 years.

We evaluated patients at baseline and after 12 months with treatment.

In anti-TNF group we found 9 patients (12%) with normal BMI and normal vitamin D level correlated with high CIMT (p=0.001), 21 patients (28%) with overweight and normal vitamin D level correlated with high CIMT (p=0.003), and 31 patients (41.3%) with overweight and low vitamin D level correlated with high CIMT (p=0.001). 14 patients (18.7%) with normal vitamin D level and normal weight (9) or overweight (5) were correlated with normal CIMT (p=0.01).

In DMARDs group we followed the same correlation. Patients with normal BMI and normal vitamin D level had a low correlation with CIMT increase (p=0.01). Patients with overweight and low vitamin D level had a significant correlation with CIMT increase (p=0.003) than group with anti-TNF-alpha therapy.

After 12 months of therapy, patients treated with Adalimumab had lower CIMT levels than patients treated with Etanercept.

Conclusion: Rheumatoid arthritis patients treated with TNF inhibitors and with vitamin D deficiency but with normal BMI have been correlated with lower increase of CIMT than patients with DMARDs therapy. Normal vitamin D level was associated with low increase of CIMT in these patients. Deficiency of Vitamin D associated with overweight are risk factors for carotid atherosclerosis in patients with RA.

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FRI0024

AA AMYLOIDOSIS AND LUNG DISEASES IN RHEUMATOID ARTHRITIS – A POSTMORTEM CLINICOPATHOLOGIC STUDY OF 147 PATIENTS

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Background: Systemic AA amyloidosis (AAa) is one of the most important complications of rheumatoid arthritis (RA) [1].

A wide spectrum of lung diseases may complicate RA or associate with RA [2-4].

Objectives: The aim of this study was to determine the influence of AAa on lung diseases related or not related to RA.

Methods: We studied 161 random autopsy patients with RA [1]. RA was confirmed clinically according to the criteria of the ARA [5]. Tissue samples of the lungs were available for histological evaluation of 147 patients.