

01 – LECTURE**L1:1****NUTRITIONAL ASPECTS OF THE MOSAIC OF RHEUMATIC AUTOIMMUNE DISEASES. A RECIPE FOR THERAPY?**Yehuda Shoenfeld^{1,2} and Shani Dahan¹, Yahel Segal¹¹Zabludowicz Center for Autoimmune Diseases, Sheba Medical Center, Tel-Hashomer, affiliated with the Sackler Faculty of Medicine, Tel-Aviv University, ISRAEL;²Incumbent of the Laura Schwarz-Kipp chair for research of autoimmune diseases, Sackler Faculty of Medicine, Tel Aviv University, ISRAEL.

Today, we are facing a new era of digitization in the health care system, and with increased access to health care information has come a growing demand for safe, cost-effective and easy to administer therapies. Dietary habits have a crucial influence on human health, affecting an individual's risk for hypertension, heart disease and stroke, as well as influencing the risk of developing of cancer. Moreover, an individual's lifestyle choices can greatly influence the progression and manifestation of chronic autoimmune rheumatic diseases. In light of these effects, it makes sense that the search for additional therapies to attenuate such diseases would include investigations into lifestyle modifications. When considering the complex web of factors that influence autoimmunity, it is not surprising to find that several dietary elements are involved in disease progression or prevention. In this Review, several common nutritional components of the human diet are presented, and the evidence for their effects on rheumatic diseases is discussed.

02 – FIRST SESSION: Early Rheumatoid Arthritis**S1:1****EPIDEMIOLOGY AND ENVIRONMENTAL FACTORS IN EARLY RA**Iain McInnes
University of Glasgow

The underlying aetiology of RA is now well recognised to reflect a complex interaction of genetic predisposition, epigenetic changes, environmental factors and time. There remains a considerable stochastic element which may represent unknown factors or true randomness. The key environmental factors include smoking, other pulmonary irritants, environmental pollution, obesity, alcohol intake. Contextual elements including educational attainment, employment and social status, are also implicated. Outcomes in the treatment of early disease are also strongly influenced by socio-environmental factors. As such elucidating these pathways, their mechanistic impact and relative importance may teach us not only about the aetiology of RA, but will also likely influence the way in which therapeutic strategies are assembled in future.

S1:2**EARLY RHEUMATOID ARTHRITIS**G.R. Burmester

Charité - University Medicine Berlin, Berlin, GERMANY

Objective. Rheumatoid Arthritis (RA) usually starts insidiously with sometimes only one to a few swollen joints, morning stiffness and non-specific constitutional symptoms including fatigue and a flu like feeling. The immediate recognition of RA and treatment still represents a challenge. Nevertheless, we have now realized that there appears to be an optimal time "window of opportunity" of 4 – 6 months after symptom start when least damage occurs upon early treatment.

Design and Method. In the recent past, new treatment strategies have dramatically changed the course of rheumatoid arthritis. If recognized early and treated promptly as well as continuously, many patients can achieve remission, despite the still unmet need in treatment-resistant patients. Novel concepts of immediate diagnosis, the subsequent treat to target (T2T) approach with tight monitoring and control as well as setting the high goal of a stringently defined remission have

been developed. Thus, our primary goal must be to find ways to rapid optimal care to utilize the tremendous new therapeutic armamentarium in rheumatology.

Results. Accordingly, the EULAR recommendations for management of early arthritis have been updated to aid in the management of a still undefined but suspected synovitis even prior to the diagnosis of definite RA or another joint disorder. They suggest that patients presenting with arthritis (any joint swelling, associated with pain or stiffness) should be seen by a rheumatologist within 6 weeks after the onset of symptoms. Risk factors for persistent and/or erosive disease should be assessed including number of swollen joints, acute phase reactants, rheumatoid factor, ACPA and imaging findings (ultrasound) to aid in management decisions. Patients at risk of persistent arthritis should be started on DMARDs as early as possible. Smoking cessation, dental care, weight control, assessment of vaccination status and management of comorbidities should be part of overall patient care.

Conclusions. In this lecture, new insights into the management of early RA using targeted therapy approaches employing classical and novel medications will be described and the potential impact of precision medicine in this still challenging disease will be outlined.

ReferenceBURMESTER GR, POPE JE: Novel treatment strategies in rheumatoid arthritis. *Lancet* 2017; 389: 2338-48.**Keywords:** early rheumatoid arthritis, diagnosis, treatment.**S1:3****MANAGEMENT OF EARLY RHEUMATOID ARTHRITIS - FROM GUIDELINES UP TO THE LAST TREATMENT ISSUES**

Bernard Combe,

Rheumatology department, Lapeyronie Hospital, Montpellier University, Montpellier, FRANCE

The management of early arthritis has changed considerably in the past few years under the influence of new concepts for diagnosis and new effective therapies. Conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs) have been shown to slow disease progression in chronic inflammatory arthritides such as RA and PsA. Furthermore, biological(b) DMARDs have demonstrated rapid and sustained disease control associated with an arrest of joint destruction. A large body of evidence points to the usefulness of very early DMARD-start for early chronic inflammatory arthritis, preferably before the onset of erosions, in order to reduce or even prevent the risk of (further) joint damage and disability. Also, the assessment and tight monitoring of patients with early arthritis serves to better adapt therapeutic strategies. Beyond doubt, the treatment goal of early arthritis should now be: clinical remission and prevention of joint destruction.

Patients with early arthritis should be identified and referred to rheumatologists to confirm the presence of arthritis, the diagnosis and its prognosis and initiate appropriate treatment strategies based on these findings. Furthermore, management of early arthritis should include more than drug treatment alone, with education, shared decision making and the role of allied health professionals as important themes.

EULAR has recently updated the 2007 recommendations for the management of early arthritis to address all these different aspects (1).

Reference1. COMBE B *et al.*: 2016 update of the EULAR recommendations for the management of early arthritis. *Ann Rheum Dis* 2017; 76: 948-59.**S1:4****MANAGEMENT: NON PHARMACOLOGICAL ASPECTS AND UNMET NEEDS**

Zoltán Szekanez

University of Debrecen, Faculty of Medicine, Department of Rheumatology, Debrecen, HUNGARY

According to therapeutic recommendations, early RA requested both pharmacological and non-pharmacological treatment modalities. In this review, we will discuss the most important non-pharmacological approaches including evidence-based physiotherapy, exercise, rehabilitation and dietary interventions. In addition, special issues, such as surgery, vaccination, pregnancy and breastfeeding will also be covered.

03 – FIRST SESSION: Early Rheumatoid Arthritis**OC1:1****VACCINATIONS IN INFLAMMATORY ARTHRITIS PATIENTS**

S. Khan, O. Kamal, R. Visevic, T. Duffy, M. Barry

Rheumatology Department, Connolly Hospital, Blanchardstown, Dublin 15, IRELAND

Objective. Patients with autoimmune inflammatory rheumatic diseases (AIIRD) are at increased risk of contracting infections. This risk is further increased by immunosuppressive disease-modifying agents.

Introduction. The vaccination status of patients should be assessed early in the course of work up for patients with AIIRD. Tetanus toxoid an. Efficacy is reduced by immunosuppressive medications. Preferentially vaccinations should be administered during stable disease to minimise flare-ups and side effects. They can be given while patients are on biologics but ideally before B cell depletion. Live attenuated vaccines should be avoided.

The mortality rate of AIIRD patients dying from pulmonary infections is higher than the general population, and therefore EULAR recommends vaccinating these patients against Influenza and pneumococcal. The aim of the study was to assess how many of our inflammatory arthritis patients received vaccinations for these two agents. Hepatitis A and B vaccination is recommended in high risk groups only, and varicella zoster (VZ) for patients prior to Rituximab, as it causes reactivation of previous VZ.

Design and Method. A prospective study.

100 patients with AIIRD patients filled in a questionnaire on the day of their outpatient appointment. The following parameters were included.

- ID number
- Sex
- Age
- Diagnosis
- Oral DMARDs
- Biologics
- Vaccination received /not
- Name of the vaccination
- Year of vaccination
- Who recommended it? GP (General Practitioner) /rheumatologist.

Results. 60% of patients were female, while 40% were male.

Mean age was 55 year (age range 27–89 years).

The majority of patients (52%, n=51) were not on oral medication, 37% were on oral DMARDs, while 11 were on non-steroidal anti-inflammatory drugs (NSAIDs). 62% of the patients were on Biologics.

The majority of patients had received a vaccination (52%). 47% mentioned the name of vaccination received. The majority (60%, 31/52) were advised by Rheumatology to receive a vaccine, while 40% (21/52) were advised by their GP.

Of the 52% patients, who received the Flu vaccine 11 also received the pneumococcal vaccine.

Approximately one third of patients (31%) receive the flu vaccine annually.

Conclusions. The vaccination process can be further improved by better communication with GPs and advise at each rheumatology review.

Keywords: inflammatory arthritics, biologics, vaccination.

OC1:2**MULTICENTER CROSS-SECTIONAL STUDY OF PATIENTS WITH RHEUMATOID ARTHRITIS IN GREECE. RESULTS FROM A COHORT OF 2,491 PATIENTS**

Thomas K¹, Lazarini A¹, Kaltsonoudis E², Drosos A², Papalopoulos I³, Sidiropoulos P³, Katsimbri P¹, Boumpas D¹, Tsatsani P⁴, Gazi S⁴, Grika EP¹, Vlachoyiannopoulos PG¹, Fragkiadaki P¹, Tektonidou M¹, Sfikakis PP¹, Karagianni K⁵, Sakkas L⁶, Pantazi L⁶, Boki KA⁶, Dimitroulas T⁷, Garyfallos A⁷, Kasimos D⁸, Evangelatos G⁹, Iliopoulos A⁹, Georganas C¹⁰, Vounotrypidis P¹⁰, Areti M¹⁰, Melissaropoulos K¹¹, Georgiou P¹¹, Delis K¹⁰, Mavragani K¹, Bournazos I¹⁰, Katsifis G¹², Mavromatis C¹⁰, Kitas GD^{1,13}, Vassilopoulos D¹

¹Joint Rheumatology Program, National and Kapodistrian University of Athens, School of Medicine, Athens; ²Rheumatology Clinic, University of Ioannina, Ioannina; ³Clinical Immunology and Allergy Department, University of Crete, Heraklion; ⁴Rheumatology Unit, KAT Hospital, Athens; ⁵Department of Rheumatology, University of Thessaly, Larissa; ⁶Rheumatology Unit, Sismanoglu

Hospital, Athens; ⁷4th Department of Medicine, Aristotle University, Thessaloniki; ⁸401 General Military Hospital, Athens; ⁹Rheumatology Unit, NIMTS Hospital, Athens; ¹⁰Private Practice; ¹¹Rheumatology Unit, Agios Andreas Hospital, Patras; ¹²Rheumatology Unit, Navy Hospital, Athens; ¹³Hygeia Hospital, Athens, GREECE.

Objective. Data regarding the current profile of patients with rheumatoid arthritis (RA) in Greece are scarce. The purpose of this study was to describe the characteristics, complications, treatment patterns and comorbidities, as well as the preventive strategies, such as vaccination, in a large sample of RA patients in Greece.

Design and Method. Multicenter (15 hospitals, 6 private offices), cross-sectional epidemiologic study held by the RA Study Group of the Greek Rheumatology Society (June 2015 to May 2016). Data were collected via a specific printed and web-based form.

Results. 2,491 RA patients were recruited: 80% female, mean age: 63.1 years and mean disease duration: 11.8 years, 96% of them were followed at referral centers. Fifty-two percent were RF and/or anti-CCP positive, while 41% had erosive disease. Regarding treatment, 82% were on synthetic conventional DMARDs, 42% on biologic DMARDs (anti-TNF: 22%, non-anti-TNF: 20%) and 40% on corticosteroids with a mean daily dose of 5 mg of prednisone. Despite therapy, remission or low disease activity was documented in only half of patients (52%), whereas the rest maintained moderate or even high disease activity (36% and 12%, respectively). The most frequent comorbidities were arterial hypertension (42%), dyslipidemia (33%), osteoporosis (29%), diabetes mellitus (15%) and depression (12%). A history of malignancy was recorded in 5.5%, while 9.5% had a history of serious infection. Latent tuberculosis (positive tuberculin skin test and/or IGRA) was diagnosed in 14.3% upon screening. Regarding chronic viral infections, 6% had a history of herpes zoster, while the respective prevalence for chronic HBV and HCV infection were 2% and 0.7%, respectively. Only 36% and 52% of the participants had ever been vaccinated for Streptococcus pneumoniae and influenza, respectively.

Conclusions. This is the largest recent epidemiologic study that provides detailed data regarding the characteristics of RA patients in Greece, mostly followed by referral centers. Despite being on therapy, half of the patients still had ongoing moderate or high disease activity, while preventive vaccination was rather limited. A follow-up study of this large cohort of patients is under way and is expected to provide more data regarding the disease's course and its comorbidities.

Keywords: rheumatoid arthritis, comorbidities, therapy.

OC1:3**THE ROLE OF DIET ON RHEUMATOID ARTHRITIS: WHAT DO CLINICAL TRIALS TELL US?**S. Petersson¹, E. Philippou^{1,2}, C. Rodomaris³, E. Nikiphorou^{4,5}

¹Department of Life and Health Sciences, University of Nicosia, Nicosia, CYPRUS; ²Diabetes and Nutritional Sciences Division, King's College London, London, UNITED KINGDOM; ³University of Nicosia Medical School, Nicosia, CYPRUS; ⁴Academic Rheumatology Department, King's College London, London, UNITED KINGDOM; ⁵Rheumatology Department, Whittington Hospital, London, UNITED KINGDOM

Objective. Evidence supports that dietary interventions or supplements are associated with rheumatoid arthritis (RA); either as risk factors for disease onset or triggers for disease flare/progression. We aimed to systematically review the evidence from clinical trials in order to better understand the role of diet in various aspects of disease.

Design and Method. A systematic search for relevant papers (1946-17 July 2017) was performed on Medline and Embase via the OVID SP platform using the following terms: Rheumatoid arthritis or arthritis, rheumatoid or inflammatory arthritis and diet or diet therapy or dietary supplement(s) or dietary intake or nutrition or nutritional supplements or nutrient or nutrients or nutrient uptake or vitamin or vitamin uptake or fasting or diet restriction or "Diet, Food and Nutrition".

Results. Out of 1952 articles screened, 53 were included. Twenty-five papers focused on specific diets; n=5 studied the effects of the Mediterranean Diet (MD), n=5 of vegetarian, n=5 of vegan diets, n=4 of elemental or peptide diets, n=1 ketogenic diet and n=7 on other dietary changes (restrictions, elimination diets or changes in dietary fats). Eighteen papers studied the effects of dietary supplements, namely n=3 fatty acids, Vitamin K, Vitamin D alone or in combination with calcium or antioxidants on disease flares. Five papers studied a combination therapy of diet and dietary supplements. Nine studies explored the effect of fasting (n=1 focused on Ramadan fasting). There was heterogeneity across all clinical trials examined, both in design and type of dietary intervention. Yet, the

evidence points towards an overall beneficial effect on disease with supplementation with n-3 fatty acids, MD, vegetarian diets or fasting.

Conclusions. This review highlights the heterogeneity of studies on diet and RA. Existing evidence supports a role for diet and specific supplements in managing RA. Yet, there remains a need for more objective evidence to inform on the efficacy and the appropriate duration of specific diet interventions and/or supplements in RA.

Keywords: diet patterns, dietary interventions, dietary supplements.

OC1:4

FACTORS ASSOCIATED WITH PROGRESSION TO INFLAMMATORY ARTHRITIS IN THE FIRST-DEGREE RELATIVES (FDR) OF INDIGENOUS NORTH AMERICAN (INA) RA PATIENTS

H. El-Gabalawy¹, I. Smolik, X. Meng, V. Anaparti, S. Tanner, D. Robinson

University of Manitoba, Winnipeg, CANADA

Objective. INA have a high prevalence of RA (2-5%) based on gene-environment interactions. We have defined a key molecular mechanism underlying HLA-DRB1 disease susceptibility in this population (Scally *et al.*, *Ann Rheum Dis* 2017). This population also exhibits a high prevalence of smoking, periodontal disease, and obesity. To better define risk of RA development, we have longitudinally followed the FDR of INA RA patients and examined the impact of vitamin D levels.

Design and Method. A cohort of 569 INA FDR were followed for a mean of 81.3±47.7 months. At baseline, and yearly, data are obtained regarding joint symptoms, medications, comorbidities, and presence of synovitis. ACPA and RF are measured in a clinical lab. Onset of inflammatory arthritis (IA) is defined as the presence of one or more swollen joints in typical RA-like locations. Serum samples were tested for 25-OH vitamin D3 levels by ELISA.

Results. At baseline, the cohort of 569 FDR had 61% females and a mean age of 36.5±11 yrs.; 41 (7%) and 79 (14%) were ACPA and RF positive, respectively; 14 (2%) were double positive. After a median follow up of 11.2 yrs, 15 individuals developed IA, giving an annual transition rate of 0.9% per year. At baseline IA were younger than non-transitioners (NT) (31 vs. 37 yrs, $p=0.07$); 6/15 (40%), 6/15 (40%), and 3/15 (20%) were ACPA+, RF+, and ACPA+/RF+, respectively. D3 levels were significantly lower in winter (n=60) compared to summer (n=60) months (66±63 vs. 81±86, $p=0.01$). There was no clear relationship between ACPA and/or RF positivity and D3 levels. Analysis of multiple samples from IA study subjects indicated that time in storage had a major effect on D3 levels ($r = -0.68$, $p < 0.0001$).

Conclusions. The frequency of seropositivity and rates of IA development in INA FDR is substantially higher than that reported in most other populations. Analysis of the impact of D3 levels on risk of RA development is confounded by the effects of time in storage for the serum samples.

Keywords: preclinical, vitamin D, risk factors.

OC1:5

SALT CONSUMPTION MAY BE A RISK FACTOR FOR THE DEVELOPMENT OF ARTHRITIS

L. Carmona¹, E. Salgado²

¹Instituto de Salud Musculoesquelética, Madrid, SPAIN;

²Complejo Hospitalario Universitario de Ourense, Ourense, SPAIN

Objective. There is a link between cardiovascular diseases and inflammation. Our objective was to analyze whether salt intake may be a risk factor for arthritis.

Design and Method. Cross-sectional study of baseline year of the SUN (Seguimiento Universidad de Navarra), a cohort launched in 1999 to study the influence of diet, habits, and physical activity on diseases. Participants are recruited from universities and scientific societies. Daily sodium intake was calculated using a formula that includes the amount of sodium in foods and the average of pinches of salt (1 pinch = 1 gr of sodium). Arthritis was ascertained by self report. The association of sodium intake and arthritis was investigated by logistic regression to estimate odds ratios with 95% confidence intervals (CI), and further adjusted by covariates.

Results. The sample included 18,555 individuals (mean age 38 years, 60% women) whose median total daily sodium intake was 3.47 (P25-75: 2.63 - 4.55) grams, and of whom 392 self-reported a diagnosis of arthritis. Individuals with

self-reported rheumatoid arthritis were older, more frequently women, weighted more, and smoked more. The odds for self-reported arthritis increased with the amount of daily sodium intake when adjusted for sex, and age (odds ratio for the 4th quartile of total sodium intake 1.4; 95% CI, 1.1 to 1.9, $p=0.02$). After adjustment for potential confounders (age, sex, total energy intake, physical activity, prevalent hypertension, prevalent cardiovascular prevalent disease, prevalent diabetes, prevalent cancer, body mass index, following a special diet, snacking between meals, and smoking), the significant association was maintained (adjusted odds ratio 1.5; 95% CI, 1.1 to 2.1, $p=0.03$). A linear trend test included in the multivariate analysis revealed a significant association of sodium intake with the diagnosis of rheumatoid arthritis in a dose-dependent manner ($p=0.02$). When sodium intake was adjusted for total energy intake through the residuals method, the association was replicated (adjusted odds ratio 1.4; 95% CI, 1.1 to 1.9, p for trend=0.006).

Conclusions. Although the association needs confirmation in a longitudinal setting, high salt intake is associated with arthritis in a dose-dependent manner. Correction may have an impact on the rate of arthritis.

Keywords: epidemiology, diet, risk.

OC1:6

DIETETIC THERAPY AND RHEUMATOID ARTHRITIS

L.N. Denisov

V.A. Nasonova Research Institute of Rheumatology, Moscow, RUSSIA

Objective. To study nutritional status of patients with rheumatoid arthritis (RA), effect of some nutritional products of the course of the disease and to develop basic principles of dietetic therapy.

Design and Method. The study included 118 patients, 68 of whom entered the experimental group and had specially composed diet and 50 patients of control group had general diet. Study of the dynamics of dietetic effect on clinical symptoms and functional statute of joints depending on the degree of activity of the inflammatory process.

Results. Nutritional statute demonstrated I-III degree of obesity in 32% of patients, decrease of C vitamin in 88% with severe deficiency in 45%, β - carotene deficiency in 52%, B12 - in 46%, B1 - in 95%, B6 - practically in 100%. We revealed also the disturbance of mineral metabolism. Among nutritional products negatively influencing RA patients were cereals and meat with high fat content. Positive dynamics of clinical symptoms was noted: arthralgia in experimental group considerably decreased as compared with the control group ($p < 0.001$), morning stiffness ($p < 0.001$), articular index decreased ($p < 0.001$). Positive dietetic effect also was revealed on subjective and objective symptoms of functional condition and digestive organs, level of arterial pressure. Concentration of cholesterol and triglycerides statistically reliably decreased ($p < 0/05$), acute phases of blood proteins - transferrin ($p < 0.05$), α - antitrypsin ($p < 0.001$), orozomuroid (< 0.001), immunoglobulins IgG ($p < 0.01$), IgM ($p < 0.05$). Total assessment of the results by geometrical representation using algorithm "CORA-3" demonstrated that dietetic therapy in RA patients increases the efficacy of complex therapy by 33.5% as compared with the control group.

Including of diet into complex RA therapy allowed us to drop the dose of voltaren by 25-50mg, ibuprofen by 400-600mg, prednisolone by 1.25-2.5mg. Frequency of intraarticular injections of diprospan was by 2.5 times lower in experimental group (6 patients out of 68 - 8.8%) as compared to the control group (11 patients out of 50 - 22%).

Conclusions. Including of the diet manipulations into the complex therapy of RD demonstrated positive dynamics of clinical disease manifestations, immunological and biochemical parameters which allowed us to decrease the dose of anti-inflammatory drugs and developing of adverse events.

Keywords: rheumatoid arthritis, nutritional products, dietetic therapy.

04 – Mediterranean Diet in the 3rd Millennium

L2:1

MEDITERRANEAN DIET IN THE 3RD MILLENNIUM: JUST PREVENTION OR EVEN THERAPY?

Antonia Trichopoulou

Substantial evidence has verified the Mediterranean diet (MedDiet) nutritional adequacy, long-term sustainability, and effectiveness for preventing several diseases, as well as increasing longevity. The Mediterranean diet is a scientific concept that reflects the traditional dietary pattern that prevailed in the olive tree-growing areas of the Mediterranean basin before the mid-1960s, that is, before globalization had its influence on lifestyle, including diet. In the current context of assessing the health effects of overall food patterns rather than of single nutrients or foods, the MedDiet has become a scientific topic of high interest due to evidence that has directly supported substantial health benefits. This includes prospective studies and some large trials with hard clinical endpoints. Such high-quality evidence is not available for any other dietary pattern (1).

There is accumulating evidence that Med Diet, beyond its preventive role, could have been beneficial for some chronic diseases offering safe and effective alternative treatments that not only provide symptom relief but also slow the development of the disease. Indeed, MedDiet has been linked with reductions in joint inflammation in patients with rheumatoid arthritis (2). Data from the Osteoarthritis Initiative indicate that adherence to the Mediterranean diet is associated with better quality of life (3) and in another study there was a significant improvement in knee flexion and hip rotation for those who adhere to MedDiet (4). Greater adherence to the traditional MedDiet is associated with a significant reduction in mortality among individuals diagnosed with coronary heart disease (5). Making changes to the diet and adopting a more Mediterranean-style diet might be one simple first option that people or practitioners could consider as a way of managing reflux (6). Study results support the hypothesis that a “Mediterranean-like” diet is associated with a lower coronary artery calcification -progression and lower degree of coronary artery calcification in men and women (7).

Thus, the evidence for the therapeutic and prognostic aspects of MedDiet is still limited, but is steadily accumulating, and should be studied as an alternative tasty and pleasant option towards health improvement on an individual and population level.

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05 – Epigenetic Effects of the Mediterranean Diet

L3:1

EPIGENOMIC EFFECTS OF MEDITERRANEAN DIETARY COMPONENTS

Ana Arpón, Omar Ramos-Lopez, Fermín I. Milagro, José-Ignacio Riezu-Boj, M. Ángeles Zulet, J. Alfredo Martínez

Purpose. Epigenetic marks, including DNA methylation, are related with body homeostasis and might be modulated by environmental factors such as dietary exposures. Indeed, some dietary components have demonstrated to mediate metabolic effects through methylation processes. Searching relationships between methylation status and Mediterranean diet in terms of adherence to MedDiet and specific foods and nutrients, such as extra-virgin olive oil (EVOO), nuts, fatty acids, and folate (a micronutrient whose intake is associated to MedDiet), could add further insights to the influence of the diet on the epigenome.

Methods. An initial cross-sectional analysis (folate) was conducted in 47 obese subjects from the RESMENA study (Spain). A subset of 36 representative individuals were selected for the second analysis (adherence to MedDiet, EVOO, nuts, and fatty acids) within the PREDIMED-Navarra study with three intervention groups in high-cardiovascular risk volunteers: MedDiet supplemented with EVOO, MedDiet supplemented with nuts and a low-fat control group. DNA methylation in peripheral white blood cells (PWBCs) was analyzed by microarray approaches.

Results. In the initial cross-sectional analysis, low folate intake was associated with adiposity and insulin resistance in obese individuals. Interestingly, folate deficiency was related to lower methylation levels of the *CAMKK2* gene, which in turn, has been implicated in diet-induced obesity, glucose intolerance, insulin resistance, and inflammation. In the second analysis, changes in methylation levels of eight genes related to inflammation and immunocompetence (*EEF2*, *COL18A1*, *IL4I1*, *LEPR*, *PLAGL1*, *IFRD1*, *MAPKAPK2*, and *PPARGC1B*) correlated with adherence to MedDiet, suggesting a possible beneficial effect of MedDiet on health through anti-inflammatory actions mediated by epigenetic mechanisms. Additionally, one CpG site (cg01081346-*CPT1B/CHKB-CPT1B*) associated with intermediate metabolism emerged due to changes in methylation after the intervention with the different supplemented diets. Interestingly, this CpG was also related with polyunsaturated fatty acids intake, showing a role for specific fatty acids on epigenetic regulation.

Conclusions. MedDiet and some specific foods or nutrients relevant in MedDiet patterns are able to induce methylation changes in several PWBCs genes related to inflammation, intermediate metabolism, adiposity and insulin resistance. These findings contribute to understand nutriepigenetics interactions, concluding that methylation processes may mediate some beneficial health effects of MedDiet or specific food components.

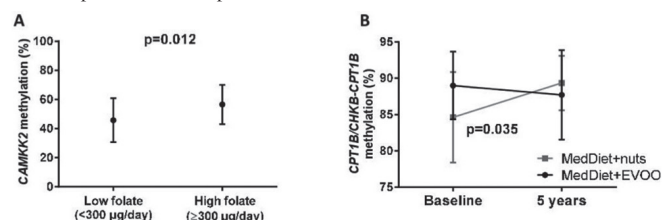


Figure. A) Means comparison of *CAMKK2* methylation levels between low (n=23) and high (n=24) folate consumptions (Ramos-Lopez O *et al.* Nutrition Research, 2017. DOI: 10.1016/j.nutres.2017.11.007). B) Methylation mean and SD of each dietary group at baseline and at 5 years for cg01081346 (*CPT1B/CHKB-CPT1B*). (Arpón A *et al.* *Ann Nutr Metab* 2017; 71 (Suppl. 2): 450). Both analysis were performed using Student's t test ($p < 0.05$).

06 – SECOND SESSION: Gouty arthritis and dismetabolism

S2:1

NUTRITIONAL ASPECTS – INCLUDING WEIGHT LOSS – FOR GOUT: AN UPDATE FROM CLINICAL EPIDEMIOLOGY

S.M. Nielsen, H. Bliddal, L.E. Kristensen, R. Christensen

Musculoskeletal Statistics Unit, The Parker Institute, Bispebjerg and Frederiksberg Hospital, Copenhagen, DENMARK

Background. According to the current guidelines, one of the overarching principles for the management of gout is advice regarding lifestyle. Many specific nutritional recommendations exist, however, for many of these recommendations, high quality evidence may be lacking. An example being weight loss, which is commonly recommended for gout, but the effect had not been evaluated in a systematic review until recently.

Purpose. To present the evidence for lifestyle changes, including many nutritional aspects, by using our recent systematic review of weight loss for overweight and obese gout patients (1) as an exemplar.

Methods. Guidelines including nutritional recommendations were searched in Medline (via PubMed). For each guideline, the quality of the evidence for the nutritional recommendations was evaluated. In our systematic review of weight loss, we searched six databases for longitudinal studies reporting the effect of weight loss in overweight/obese gout patients. Risk of bias was assessed using the tool Risk of Bias in Non-Randomised Studies of Interventions (ROBINS-I) (2). The quality of evidence was assessed and interpreted using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology (3).

Results. In the current guidelines, we found that the recommendations regarding nutritional aspects (such as avoidance of alcohol and sugar-sweetened drinks, and intake of low-fat dairy products) are generally based on low quality evidence. For the systematic review of weight loss for overweight/obese gout patients, a thorough search resulted in 3991 potentially eligible studies, of which 10 were included (including one randomised trial). Interventions included diet with or without physical activity, bariatric surgery, diuretics, metformin or no intervention. Mean weight losses ranged from 3 kg to 34 kg. Clinical heterogeneity in study characteristics precluded meta-analysis. The effect on serum uric acid (sUA) ranged from -168 to 30 µmol/L, and between 0% and 60% patients achieved sUA target (<360 µmol/L). Six out of eight studies (75%) showed beneficial effects on gout attacks. Two studies indicated dose-response relationship for sUA, achieving sUA target and gout attacks. At short term, temporary increased sUA and gout attacks tended to occur after bariatric surgery. The most frequent risk of bias was 'Bias due to confounding', with four studies rated critical, five studies rated serious, and only one study rated low risk of bias. For a beneficial effect of weight loss, we evaluated the overall quality of evidence to be low for sUA, moderate for achieving sUA target and low for gout attacks.

Conclusions. In the current guidelines, the nutritional recommendations are generally based on low quality evidence. In the case of weight loss, the available evidence is in favour of weight loss for overweight/obese gout patients, with low, moderate and low quality of evidence for effects on sUA, achieving sUA target and gout attacks, respectively. At short term, unfavourable effects may occur. Since the current evidence consists of a few studies (mostly observational) of low methodological quality, there is an urgent need to initiate rigorous prospective studies (preferably randomised trials).

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S2:2

THE EARLY DISEASE: CLINICAL FEATURES AND DIAGNOSTIC TOOLS

Sivera Francisca

Rheumatology Dpt, Hospital General Universitario Elda, Elda (Alicante), SPAIN

Gout's pathogenic hallmark is the deposition of monosodium urate crystals within and around joints. This deposit is asymptomatic, until the first gout flare occurs. However, even when no flares have taken place, crystal deposit might not be innocuous. There is no standardized definition of how long 'early' gout lasts; time frames of two years from the first flare have been used. Early diagnosis and adequate management strategies are key to success in gout. Whether hyperuricemia should be treated before symptoms occurs is still controversial.

S2:3

MANAGEMENT: FROM GUIDELINES UP TO THE LAST TREATMENT ISSUES

Pascal Richette

Purpose. to give an overview of the international recommendations (Eular, BSR, ACR) for the management of gout, and to describe emerging treatments for both flares and hyperuricemia.

Methods. Systematic literature search in PubMed with MESH terms, and focus on the 2016 Eular recommendations.

Results. The EULAR recommendations comprise 3 overarching principles and 11 key recommendations for clinical practice. Patient education about the pathophysiology of gout and its comorbidities, as well as the existence of effective treatments are important, and understanding the principles of managing acute attacks and eliminating urate crystals by lifelong lowering of the serum urate (SU) below a target level are essential. Advice about lifestyle, diet, weight, and other risk factors, as well as the need to screen for, and manage, comorbidities is emphasized. For the treatment of flares, colchicine, nonsteroidal anti-inflammatory drugs (NSAIDs), and oral or intraarticular steroids, or a combination are recommended. In patients with frequent flares and contraindications to colchicine, NSAIDs, and corticosteroids, an interleukin-1 blocker should be considered. Urate-lowering therapy (ULT) should be discussed from the first presentation of the disease, and SU levels should be maintained at less than 6 mg/dl (360 µmol/l), or less than 5 mg/dl (300 µmol/l) in patients with severe gout. Allopurinol is recommended as first-line ULT with dose adjustment according to renal function. If the SU target cannot be achieved with allopurinol, then febuxostat, a uricosuric, or combining a xanthine oxidase inhibitor with a uricosuric should be considered. All ULTs should be started at low dose and titrated upwards until the SU target is achieved. Unless contraindicated, flare prophylaxis with low-dose colchicine or with NSAIDs at low dosage is recommended during the first 6 months of ULT. In patients with refractory gout, pegloticase can be considered. New drugs inhibiting URAT1 such as lesinurad or Arhalofenate should cover the unmet need for patients with failure to respond or with contraindications to xanthine oxidase inhibitors.

Conclusions. These recommendations and emerging drugs should improve patients care

S2:4

MANAGEMENT. NON PHARMACOLOGICAL ASPECTS AND UNMET NEEDS

L. Punzi, F. Oliviero

Rheumatology Unit, Dept. of Medicine DIMED, University of Padova, ITALY.

Purpose. Gout is the commonest inflammatory arthritis caused by the deposition of monosodium urate (MSU) crystal in joint and other tissues as a consequence of hyperuricemia, a condition so called when serum uric acid (sUA) are > 6.0 mg/dl (360 µmol/L) (1,2). Gout is not a minor disease since it may induce disability and nephropathy, and increase cardiovascular risk (3). Furthermore, it causes relevant consequences on the quality of life (4). Although there are the most favourable conditions to be easily treated, gout remains untreated or poorly managed in the majority of people with gout (5). In addition, treatment of gout is hampered by the low adherence to UA lowering treatment (6).

Methods. With the aim to identify needs for improvement of care and unmet needs, we analysed the specialised literature, especially in the field of non-pharmacological aspects concerning the management of gout.

Results. Most studies underline that an important reason for poor adherence is the significant gaps in knowledge about gout and its treatment not only in people with this condition, but also in the general public and in health-care professionals. However, when people with gout receive full individualized education about gout, tailored to their own information needs and understanding, the adherence is excellent (7). In this context, attention to life-style changes may improve also the adherence to pharmacological treatments.

Non-pharmacological interventions have a relevant role in the management of gout, as underlined by the recent EULAR recommendations (8). Avoidance of risk factors that are known to trigger acute attacks of gout, such as excessive alcohol or red-meat intake, may reduce attack frequency (9). It is noteworthy that purines derived from animal meats confer higher risk of recurrent gout attacks than those derived from vegetable sources. People with gout should be advised to reduce excessive intake of red meat, fish, shellfish and alcohol, especially those rich in added purines, such as beer, lager and whiskey (10). This recommendation should be considered mandatory in the presence of overweight or obese patients. Among foods able to reduce sUA there are cherries, vitamin C at higher doses, non-soy legumes, fresh fruits, and coffees, whereas consumption of sugar-sweetened soft drinks, including fruit juices, increased sUA concentrations (7).

Another mean to reduce sUA is the physical activities, both directly and indirectly, acting on the weight loss. However, an adequate hydration is important, since another unmet aspect is the exposure to low temperatures and dehydration, factors believed to increase the nocturnal risk of gout attacks; dehydration may also explain the increased risk of incident gout in summer months.

The importance of weight loss is increasingly emphasised in a number of new studies, and may be useful as educational improvement in a patient with metabolic syndrome and/or other comorbidities.

As regard the patient education, this should be individualized and tailored, together with involvement of the patient in management decisions, as recommended for all chronic conditions.

Conclusions. Many barriers contribute to the frequent disappointing management of gout (11). There is an increasing body of evidences that the education of patients, along with that of physicians, represents a mandatory core for a correct approach to the gout.

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07 – SECOND SESSION:

Gouty arthritis and dismetabolism

OC2:1

EFFECT OF POLYDATIN AND RESVERATROL ON CRYSTAL-INDUCED INFLAMMATION: BENEFICIAL IMPLICATIONS FOR GOUT AND OTHER CRYSTAL-RELATED ARTHROPATHIES

E.Oliviero¹, Y. Zamudio-Cuevas², A. Scanu¹, E. Belluzzi¹, L. Andretto¹, M. Favero¹, A. Lopez-Reyes², G. Ravagnan³, P. Spinella⁴, R. Ramonda¹, L. Punzi¹

¹Rheumatology Unit, Dep. of Medicine, University of Padova, Padova, ITALY;

²Instituto Nacional de Rehabilitación, Mexico City, MEXICO;

³Translational Pharmacology Institute - CNR, Roma, ITALY;

⁴Clinical Nutrition Unit, Dep. of Medicine, University of Padova, Padova, ITALY

Objective. Crystal-induced arthritis is characterized by an intense articular inflammatory reaction accompanied by pain, limited joint function and, chronically, by joint destruction. Although effective drugs are available for these patients, it has been shown that adherence to the Mediterranean diet correlates to lower serum uric acid levels and prevalence of gout. We previously demonstrated that plant catechins have a strong anti-inflammatory effect in crystal-induced inflammation, theorizing that they can improve the course of the disease.

With this study, we aimed to investigate the role of polyphenolic compounds found in grape and wine (resveratrol RES and its precursor, polydatin PD) in crystal-induced inflammation.

Design and Method. THP-1 cells were stimulated with synthetic MSU (0.05mg/ml) and CPP (0.025mg/ml) crystals after a 3h priming with phorbol myristate acetate (PMA) (100ng/ml). RES (100µM) or PD (200µM) were added along with the stimulus or as pretreatment.

The anti-inflammatory effect of the two polyphenols has been assessed through the determination of intra- and extra-cellular IL-1β levels and IL-8 extra-cellular levels, NLRP3 expression, ROS and nitric oxide production, and the evaluation of the phagocytosis process.

Results. RES and PD lead to a marked decrease in IL-1β (3-fold and 5-fold in presence of CPP and MSU respectively) and IL-8 release (2 fold and 3 fold in presence of CPP and MSU respectively). The inhibition of the inflammatory response by polyphenols was more effective after cell pretreatment, as additionally demonstrated by the downregulation of IL-1β mRNA expression. No effect was observed in NLRP3 expression. Instead, both RES and PD showed to modulate IL-1β intracellular levels.

The study on phagocytosis showed a rapid internalization of crystals which was not influenced by the two compounds.

The efficacy of RES on ROS inhibition was more pronounced with respect to PD ($p < 0.05$ crystals vs crystals+RES), while the pretreatment lead to a decreased ROS production in presence of both polyphenols.

Conclusions. The results of this study highlighted the anti-inflammatory potential of grape polyphenols in crystal-induced inflammation. Based upon the data obtained with cell pretreatment, we hypothesize that RES and PD act on specific signaling pathways preventing the inflammatory reaction and that this effect doesnot involve crystal phagocytosis inhibition.

Keywords: crystal-induced inflammation, polyphenols, cytokines.

OC2:2

ANALYSIS OF THE EFFICACY OF LOW PURINE DIET IN GOUT PATIENTS

M.S. Eliseev, S.A. Vladimirov, O.V. Zhelyabina, M.N. Chikina, L.N. Denisov

V.A. Nasonova Research Institute of Rheumatology, Moscow, RUSSIA

Objective. Evaluation of the efficacy of long-term low purine diet in gout patients

Design and Method. 58 gout pts. (males) without urate-lowering therapy were included. Mean age – 48±12 y., disease duration – 14.6 [10.1; 18.8] y., mean follow up period – 4.9±2.0 y. These patients were divided into groups based on low purine diet adherence: those who didn't observe the diet – 40 (69%) pts, and those who observed - 18 (31%) pts. Lab evaluation included monitoring of serum uric acid (sUA) levels. The target sUA levels were established at <360 µmol/l.

Results. At baseline sUA level was 492.8±93.3 µmol/l, body mass index (BMI) – 30.3±4.2 kg/m², chronic arthritis – 18 (31%), frequency of gouty arthritis flares – 4 [2;6] per year, gouty tophi were present in 21 (34%) pts.

By the end of the study sUA level improved from 492.8±93.3 µmol/l to 445±116.3 µmol/l (8%) ($p < 0.05$) in 18 diet observers, BMI decreased from 29.5±6.4 kg/m²

to 28.4±6.7 kg/m² ($p<0.05$). Median frequency of gouty arthritis flares increased from 4 [1;7] to 5 [2;7] ($p>0.05$), the number of pts with subcutaneous tophi increased from 7 (39%) to 13 (72%) ($p<0.05$), the number of pts with chronic arthritis increased from 6 (33%) to 7 (38%) ($p>0.05$).

In 40 non-adherent to diet pts mean sUA level increased from 496.1±99.6 μmol/l to 499.7±100.5 μmol/l ($p>0.05$), BMI increased from 30.7±5.3 kg/m² to 31.2±5.6 kg/m² ($p>0.05$), the number of pts with chronic arthritis increased from 12 (30%) to 32 (80%) ($p<0.05$), median frequency of gouty arthritis flares increased from 4 [2; 6] to 6 [3;8] ($p<0.01$), and the number of subcutaneous tophi increased from 14 (35%) to 34 (85%) ($p>0.05$).

None of the pts achieved the target sUA concentration.

Conclusions. Long-term adherence to low purine diet is associated with significant decrease sUA levels, but fails to achieve the desired target sUA levels and does not slow down the progression of gout.

Keywords: gout, diet, uric acid.

OC2:3

COMBINATION OF LOSARTAN AND ALLOPURINOL IN HYPERTENSIVE PATIENTS WITH HYPERURICEMIA

M. Jordhani, V. Duraj, D. Ruci, J. Seiti

UHC Mother Teresa, Tirana, ALBANIA

Objective. The aim of this study was to evaluate the effect of combination of allopurinol with losartan in hypertensive patients with high levels of uricemia, comparing it to other combinations of allopurinol and other antiHTA (other than losartan and diuretics).

Design and Method. This is a case-control study which involved 107 patients admitted at UHC Mother Teresa, Tirana, Albania for HTA and high levels of uricemia.

Thirty-five patients were treated with losartan and allopurinol. Seventy-two patients were treated with allopurinol and antiHTA other than losartan or diuretics. All patients included in this study were evaluated for their uricemia levels after 2 weeks and then monthly.

Results. One month after the beginning of the therapy, from 35 patients treated with the combination of losartan and allopurinol, 15 patients (42.8%) were observed to have a reduction of 50% or more of their uric acid levels. Eighteen (51.4%) other patients using the same combination had uricemia decreased of 35-49%.

From 72 patients who were treated with allopurinol and another antiHTA drug other than losartan or diuretics, 25 patients (34.7%) had their uricemia reduced 50% of the first level and 17 patients (23.6%) had it reduced more than 50%.

Conclusions. In this study was found that the combination of Losartan and Allopurinol in patients with HTA and Hyperuricemia causes a greater and faster reduction of uricemia than the combination of allopurinol with any antiHTA drug other than losartan and diuretics.

Keywords: losartan, hyperuricemia, HTA.

OC2:4

ULTRA-LOW DOSE ANTI-INTERLEUKIN1 IN CHRONIC GOUT: A SAFE AND SUCCESSFUL COMBINATION THERAPY WITH LOW DOSE COLCHICINE AND URATE LOWERING AGENTS.

M. Capassoni, F. Galluccio, M. Matucci-Cerinic

AOU Careggi SOD Reumatologia, Firenze, ITALY

Objective. Evaluate the efficacy of low dose anti-IL1 inhibitors administer by sublingual route in gout arthritis with remitting course that cannot be completely controlled with standard therapy regimens

Design and Method. Inclusion criteria was diagnosis of chronic gouty arthritis with remitting course (acute flares in patients with chronic gout and no inter-critical period), high levels of CRP and the need of chronic assumptions of NSAIDs or steroids, with flare at suspension. 20 patients were selected that fulfilled the criteria (Patients intolerant to the study drug, with poor compliance to therapies or to diet, with hyperuricemia or end stage renal disease were excluded from the study).

The study consists of two consecutive parts: an observational part where patients are treated for 6 months with 0.5-1 mg/daily of colchicine and 300 mg/daily of allopurinol. They performed visits at baseline, 3 and 6 months and we collected data about blood tests, VAS score, number of flares, compliance to therapy and adverse events. An experimental part were we added GUNA anti-IL1® (an infinitesimal dilution of anakinra that has has a concentration of 10 fg/mL) 20 drops

administered SL. Again patients performed visits at baseline (which coincides with the last visit of the observational phase), 3 and 6 months and we collected the same kind of data.

Results. At 6 months after introduction of GUNA anti-IL1 all patients, except 1, experienced no flares of disease, levels of CRP became negative and VAS pain

CONTROLLO								
colchicina 0.5-1 mg giorno + allopurinolo 300mg								
	BASELINE		3 MESI		6 MESI		N° FLARE	
	PCR	VAS	PCR	VAS	PCR	VAS		
PZ 1	0,78	6	0,65	5	0,71	6		x
PZ 2	0,69	5	0,72	7	0,67	6		x
PZ 3	0,98	7	0,91	7	0,89	7		xxx
PZ 4	0,67	4	0,75	5	0,71	5		x
PZ 5	1,03	5	1,1	6	0,96	6		xx
PZ 6	0,85	6	0,82	6	0,77	5		x
PZ 7	1,12	8	1,2	8	1,05	8		xxxx
PZ 8	0,71	4	0,68	4	0,73	4		
PZ 9	0,84	5	0,85	5	0,82	5		xx
PZ 10	0,68	4	0,7	5	0,7	5		
PZ 11	0,77	6	0,74	5	0,7	6		x
PZ 12	0,92	5	0,69	5	0,84	7		x
PZ 13	0,59	4	1,35	7	0,9	6		xx
PZ 14	0,62	6	0,75	6	0,98	7		x
PZ 15	0,81	5	0,76	5	0,87	6		x
PZ 16	0,87	6	1,1	8	1,05	7		xxx
PZ 17	1,05	7	1,4	8	0,98	7		xx
PZ 18	0,72	3	0,7	4	0,68	3		
PZ 19	0,76	5	0,95	6	0,84	6		x
PZ 20	0,95	7	0,78	6	0,88	7		xx

SPERIMENTALE								
colchicina 0.5-1 mg giorno + vld antiIL1 + allopurinolo 300mg								
	BASELINE		3 MESI		6 MESI		N° FLARE	
	PCR	VAS	PCR	VAS	PCR	VAS		
PZ 1	0,71	6	0,65	4	<0,5	1		
PZ 2	0,67	6	0,64	5	<0,5	2		
PZ 3	0,89	7	0,79	6	0,52	3		
PZ 4	0,71	5	0,7	4	<0,5	2		
PZ 5	0,96	6	0,9	4	<0,5	2		
PZ 6	0,77	5	0,55	3	<0,5	0		
PZ 7	1,05	8	0,86	5	0,56	3		
PZ 8	0,73	4	0,66	3	<0,5	2		
PZ 9	0,82	5	0,81	4	<0,5	2		
PZ 10	0,7	5	0,65	3	<0,5	0		
PZ 11	0,7	6	0,72	4	0,58	3		
PZ 12	0,84	7	0,68	5	<0,5	2		
PZ 13	0,9	6	0,81	6	<0,5	1		
PZ 14	0,98	7	<0,5	3	1,03	7		x
PZ 15	0,87	6	0,68	4	<0,5	0		
PZ 16	1,05	7	0,9	5	<0,5	2		
PZ 17	0,98	7	0,86	5	<0,5	1		
PZ 18	0,68	3	0,55	2	<0,5	0		
PZ 19	0,84	6	0,6	4	<0,5	1		
PZ 20	0,88	7	0,75	5	<0,5	2		

proteina c reattiva valore normale <0,5 mg/dl
 n° di flare: ogni x indica 1 evento durante il periodo di studio (6 mesi) il flare è stato trattato con FANS o steroidi
 nessun evento avverso
 tutti i pazienti con uricemia <6

Variabile	Media	Dev std	Quartile inferiore	Mediana	Quartile superiore	Minimo	Massimo
PCR_0	0.82	0.15	0.70	0.80	0.94	0.59	1.12
PCR_3	0.88	0.23	0.71	0.77	1.03	0.65	1.40
PCR_6	0.84	0.12	0.71	0.84	0.93	0.67	1.05
VAS_0	5.40	1.27	4.50	5.00	6.00	3.00	8.00
VAS_3	5.90	1.25	5.00	6.00	7.00	4.00	8.00
VAS_6	5.95	1.19	5.00	6.00	7.00	3.00	8.00
d_pcr_3	0.06	0.21	-0.04	0.01	0.11	-0.23	0.76
d_pcr_6	0.02	0.13	-0.07	-0.03	0.05	-0.09	0.36
d_vas_3	0.50	1.05	0.00	0.00	1.00	-1.00	3.00
d_vas_6	0.55	0.76	0.00	0.50	1.00	-1.00	2.00

TRT=Trattamento							
Variabile	Media	Dev std	Quartile inferiore	Mediana	Quartile superiore	Minimo	Massimo
PCR_0	0.84	0.12	0.71	0.84	0.93	0.67	1.05
PCR_3	0.72	0.11	0.65	0.70	0.81	0.55	0.90
PCR_6	0.53	0.12	0.50	0.50	0.50	0.50	1.03
VAS_0	5.95	1.19	5.00	6.00	7.00	3.00	8.00
VAS_3	4.25	1.07	3.50	4.00	5.00	2.00	6.00
VAS_6	1.80	1.58	1.00	2.00	2.00	0.00	7.00
d_pcr_3	-0.10	0.07	-0.16	-0.10	-0.05	-0.24	0.02
d_pcr_6	-0.30	0.15	-0.39	-0.33	-0.21	-0.55	0.05
d_vas_3	-1.70	0.86	-2.00	-2.00	-1.00	-4.00	0.00
d_vas_6	-4.15	1.46	-5.00	-5.00	-3.00	-6.00	0.00

Test wilcoxon signed rank test	
Differenza	P-value
PCR3-PCR0	0.001
PCR6-PCR0	<0.0001
VAS3-VAS0	<0.0001
VAS6-VAS0	<0.0001

scale was significantly reduce (CRP level $p<0.0001$; VAS $p<0.0001$). NSAIDs and steroid consumption was significantly reduced. No adverse events happened.

Conclusions. Ultra-low dose of anti-IL1 agents added to standard therapy is an effective and safe way to achieve disease remission.

Keywords: gout, chronic, interleukin-1.

OC2:5

SEASONAL VARIATION OF JOINT ASPIRATIONS FOR GOUT AND CPPD IN A COHORT OF ARTROPATHIC PATIENTS WITH EFFUSION

P. Montagna, R. Brizzolara, S. Soldano, M. Cutolo, M.A. Cimmino

Research Laboratory and Academic Division of Clinical Rheumatology, Department of Internal Medicine, University of Genov, Genova, ITALY

Objective. Microcrystalline arthropathies result from microcrystals formation and deposition within the joint. The formation of monosodium urate (MSU) and calcium pyrophosphate (CPP) crystals depends on many physico-chemical factors, which are partly still unknown (1). Various theories on the effect of weather and immune system changes on the chronobiology of the equilibrium and precipitation of MSU crystals have been proposed. Studies describe seasonal variations in acute gouty arthritis, but disagree on timing, with most showing a peak in spring while others showing peaks later in the year (2,3). In this study we evaluated the seasonal variations of joint aspirations for gout and CPPD in a cohort of artropathic patients.

Design and Method. Arthrocentesis was performed in 406 patients with synovial fluid (SF) effusion. SF were analysed for cytological evaluation (including SF leukocyte count and differential count) and crystal detection by compensated polarized microscopy (magnification 400x). Demographic data and clinical features were also collected.

SFs were divided into 3 groups, according to crystal type found (MSU, CPP) or absence of crystals. Month and day of each event were categorized both into four 3-month periods (by seasons) and 12 monthly intervals.

Results. 212/406 (52.2%) patients were female. Median age was 70 years (range 18-96 years). 257 (63.6%) patients showed no crystals in their SFs, 64 (15.8%) showed MSU crystals and 83 (20.5%) showed CPP crystals. The median volume of aspirated synovial fluid was 6 ml (range 1-60 ml). There was a slight seasonality in the result of SF aspirations ($p=0.048$): MSU crystals were more frequent in the autumn and winter, CPP crystals in winter. Number of white blood cells, % of polymorphonuclear cells, and volume of SF showed no seasonality.

Conclusions. The present study shows a slight seasonality in the result of SF aspirations ($p=0.048$): MSU crystals were more frequent in the autumn and winter, CPP crystals in winter. Since most of the SF aspirations were performed during acute attacks, our findings support the view of the seasonality of microcrystalline arthritis.

Keywords: synovial fluid, seasonality, crystals.

OC2:6

GOUT AND METABOLIC SYNDROME

N. Zehraoui, R. Benaziez, N. Blidi, M. Berkache, C. Dahou-Makhloufi

Mohamedlamine Debaghine University Hospital Center, Algiers, ALGERIA

Objective. The potential link between gout and metabolic syndrome (MS) has been suggested.

The MS, also known as X Syndrome or Insulin Resistance Syndrome, includes the presence of several associated metabolic abnormalities (abdominal obesity, hypertriglyceridaemia, low HDL cholesterol, glucose intolerance or diabetes mellitus, hypertension). The objective of this study is to determine the frequency of metabolic syndrome among patients with gout

Design and Method. This was a descriptive, retrospective study, including patients with chronic gout, from the period of 2007 to 2017. All patients included respond to the ACR/EULAR 2015 criteria.

The following parameters were analyzed: demographic data, comorbidities (diabetes, hypertension, dyslipidemia, and BMI).

We used the AACE (American association of clinical endocrinologists) definition to assess the presence of MS.

Results. 40 cases were collected, 82.5% men (sex ratio: 4.7), mean age: 56 ± 13 years. 37.5% of patients had a primary gout, including 3 cases of enzymatic drop and 62.5% had secondary gout. Joint flares were monoarticular in 72.5% of cases, mostly in the lower limb (metatarsophalangeal: 80%).

The main comorbidities observed were: hypertension (47.5%), obesity (35.9%), dyslipidemia (32.5%), diabetes (27.5%).

20% of patients had a moderate kidney failure, and 7.5% presented a severe one. 27.7% had a metabolic syndrome: 29.5% during primary gout and 70.5% during secondary gout.

kidney failure and metabolic syndrome were associated in 40% of cases.

Conclusions. These findings indicate that the prevalence of metabolic syndrome is high among individuals with gout.

Keywords: gout, metabolic syndrome, association.

08 – Metabolic effects of Glucocorticoids

L4:1

METABOLIC EFFECTS OF GLUCOCORTICOIDS: IS THERE A SAFE DOSAGE?

J.W. Bijlsma¹, C. Strehl², F. Buttgeriet²

¹University Medical Center Utrecht, Utrecht, THE NETHERLANDS;

²University Medical Center Charite, Berlin, GERMANY

Objective. To evaluate the effects of glucocorticoids (GC) on metabolic parameters, operationalised as hyperglycaemia / diabetes mellitus (DM) and cardiovascular disease (CVD); and evaluate the balance between efficacy and safety.

Design and Method. A multidisciplinary EULAR task force group of experts including patients was assembled. Databases were systematically searched to identify literature reporting harm of long-term GC therapy. Groups critically reviewed the evidence on the effects on hyperglycaemia / DM and CVD, following a structured questionnaire for final discussion and consensus finding.

Results. Hyperglycaemia / DM: GC therapy represents an additional factor for the development of hyperglycaemia / DM, potentially adding to the risk already conferred by chronic inflammation itself, advanced age and/or high body mass index. A genetic predisposition can increase the risk of DM. Weight loss for obese patients, healthy diet, appropriate exercise and hydroxychloroquine as a therapeutic measure reduce the DM risk.

GC-induced cardiovascular disease: Advanced age, male gender, obesity, hypertension, diabetes, and dyslipidaemia increase the risk for CVD. GC therapy may have an additional negative impact on the cardiovascular system. Patients with high disease activity or functional impairment have increased cardiovascular mortality, but these patients are the more likely to be treated with GC anyway.

Dosages. When given at a dosage of 5 mg/day or below, the benefits in general outweigh the harm; when given at a dosage of 10 mg/day or more, the harm in general outweighs the benefit. For dosages in between 5 and 10 mg/day patient specific characteristics influence the balance between efficacy and safety; especially general CVD risk factors should be taken into account in this situation.

Conclusions. Metabolic effects of GC are a reason for concern, especially when given in dosages above 10 mg/day; below a dosage of 5 mg/day they are rather safe, except in patients with CVD-risk factors.

General preventive/therapeutic measures include healthy diet (low in saturated fat & calories), appropriate physical activity resulting in weight normalization, sodium restriction and cessation of smoking.

This abstract is based on the EULAR task force: Defining conditions where long-term glucocorticoid treatment has an acceptably low level of harm in chronic inflammatory rheumatic diseases. ARD 2016

Keywords: glucocorticoids, metabolic effects, safe dosages

