

THU0458 READY OR NOT? CHANGES IN THE CLINICAL PROFILE OF GOUT PATIENTS OVER THE LAST 25 YEARS

S.P. Chinchilla^{1,2}, I. Urionaguena³, F. Perez-Ruiz^{1,2,3}. ¹University of the Basque Country, Bilbao; ²Arthritis Research Group, BioCruces Health Research Institute; ³Rheumatology Division, Hospital Universitario Cruces, Barakaldo, Spain

Background: The number of publications associated to gout, as well as the prevalence of the disease, has increased in recent years. Gout is a rising cause of hospital admissions and emergency consults. More so in patients with comorbidities, it has even replaced rheumatoid arthritis as the principal rheumatological condition causing admissions (1). Some questions arise in this setting: What are the characteristics of our patients? How have they changed over the past years? **Objectives:** To analyze possible changes in the epidemiologic, clinical and biochemical profiles of gout patients during a period of 25 years.

Methods: Data was collected from a prospective cohort of gout patients, from a crystal arthritis clinic in a tertiary hospital, with a reference population of half a million inhabitants. A period of 25 years was reviewed, between 1992 and 2016 ($n=1137$), with further division into five quinquennia (Q) for comparison purposes. When entering the cohort, epidemiologic, clinic, laboratory and imaging data are systematically collected. Variables susceptible to change in time were considered: age, gender, gout specific clinical data (articular pattern, presence of tophi), previous admissions due to gout, comorbidities and association with other conditions. Quantitative variables were analyzed with ANOVA and Bonferroni correction; qualitative variables with chi-square test. Inclusion of patients to the cohort was approved by the hospital ethics committee. Results from extreme quinquennia are reported (1stQ: 1992–1996/5thQ 2011–2016 or 2ndQ: 1997–2001/4th: 2006–2010). All results are statistically significant unless stated otherwise.

Results: Differences were observed amongst the periods of five years and age at first visit (1stQ: 54.1±10.9/5thQ: 64.6±13.8 years); gender (1stQ: 2.6%/5thQ: 12.2% of women, respectively). There were no differences when comparing with years of disease evolution before the first visit.

Initial comorbidities: important differences pertaining the prevalence of cardiovascular disease were observed (2ndQ: 26.3%/5thQ: 43.2%), as well as renal disease (1stQ: 16.7%/5thQ: 45.2%), hypertension (1stQ: 27.3%/5thQ: 75.1%) and hyperlipidaemia (1stQ: 50.6%/5thQ: 61.2%)—although this was not the case for Diabetes Mellitus. There was difference amongst periods and association with acute episodes of calcium pyrophosphate arthritis (1stQ: 3.8%/5thQ: 5.9%).

Initial clinical characteristics: differences were found in presentation with tophi (2ndQ: 23.6%/4thQ: 40.1%); polyarticular disease (1stQ: 32.9%/5thQ: 41.3%); hospital admission on the year prior to inclusion (1stQ: 14.5%/5thQ: 24.4%); use of diuretics (1stQ: 6.4%/5thQ: 45.9%); and uricaemia, the latter with no relevant clinical significance.

Conclusions: The profile of gout patients has notably changed in the past 25 years: we have elder, more complex patients, with higher rates of hospital admissions, with severe forms of disease and important comorbidities. When considering these results, we believe that a substantial proportion of gout patients will require specialized attention in the coming years.

References:

[1] Lim SY, Lu N, Oza A, et al. Trends in Gout and Rheumatoid Arthritis Hospitalizations in the United States, 1993–2011. *JAMA*. 2016 Jun 7;315(21):2345–7.

Disclosure of Interest: S. Chinchilla Grant/research support from: BBK-BioCruces Post Fellowship Research Grant 2016–2017, I. Urionaguena: None declared, F. Perez-Ruiz Consultant for: Amgen, Ardea, AstraZeneca, Grünenthal, Menarini, Speakers bureau: AstraZeneca, Grünenthal, Menarini

DOI: 10.1136/annrheumdis-2017-eular.5459

THU0459 EXPLORING DUAL MODULATION OF GLUT9 AND OAT3, AN APICAL AND BASOLATERAL TRANSPORTERS IN PROXIMAL TUBULES AND EXPERIMENTAL MICE

S.H. Lee, S.B. Kim, D.-S. Oh. *The K-herb Research Centre, Korea Institute of Oriental Medicine, Daejeon, Korea, Republic Of*

Background: Uric acid homeostasis is a set of the balance in glomerular filtration, tubular secretion, reabsorption, and excretion. In the course of cascade, two kinds play a pivotal role: efflux transporters in apical at renal proximal tubular membrane, uptake ones in basolateral at membrane. The former has been of interest in the targets for uricosuric effects, however, dual modulation of the two could keep uric acid balance in stable ways.

Objectives: The aim of this study was to assess the uptake of seven test articles in the course of the expressions of apical/basolateral transporters in potassium oxonate (PO)-treated kidney epithelial cell lines (Caco-2, MDCK, LLC-PK1) and ICR mice.

Methods: The selected cell lines were treated with potassium oxonate (0.25 mM) and then modulated by seven test articles, the commercial herbal products (SITK01 through SITK06 and SITT01) at dose range of 0.015–1 mg/mL. To determine efficacious dose range by each test article, three cell lines, Caco-2, MDCK and LLC-PK1 cells were assessed with MTT assay. Forty eight ICR mice were injected intraperitoneally with PO at a dose of 200 and 400 mg/kg and then blood draws were conducted 0, 6, 12, 24, 72 hours after PO administration. The levels of uric acid and transporters were also measured by ELISA assay and Western blotting analysis in those cell lines.

Results: Treatment of SITK01 through SITK03 and SITT01 at concentration (250 mg/mL) decreased the cell viability. The PO-stimulated kidney epithelial cells with SITK01 through SITK03 treatment increased GLUT9 by 2.5 folds and decreased OAT3 by 1.5 folds (versus controls, $p=0.012$, and $p=0.017$, respectively). In PO-treated mice, uric acid levels were increased through GLUT9 and OAT3 transporters. The results indicated that SITK01, SITK02, and SITK03 showed the potential on uricosuric effects in a dual modulation of apical/basolateral sides of kidney epithelial tubular membranes.

Table 1. Protein expression of transporters in apical and basolateral membranes of proximal tubular epithelial cells and potassium oxonate-treated experimental mice

Membrane domain	Functions	Transporters	Caco-2	MDCK	LLC-PK1	Potassium Oxonate-treated mice
Apical	Palpation of excretion	SLC22A12 (URAT1)				++
		SLC2A9 (GLUT9)	+	++	++	++
		ABCG2 (BCRP)				
Basolateral	Inhibition of reabsorption	SLC22A6 (OAT1)		+	++	
		SLC22A8 (OAT3)	+++	+++	+	++

Conclusions: The present findings demonstrated that three commercial herbal products showed potentials to reduce hyperuricaemia-induced condition by changing protein expression levels in a transporter-uptake assay. The OAT3 and GLUT9 could be further investigated as the uricosuric group-targets on the bilateral sides at kidney epithelial tubular membranes.

References:

[1] Fromm MF, König J. Transporters and drug-drug interactions: important determinants of drug disposition and effects. 2015 *Nature Reviews Drug Discovery* 14, 543–560.

[2] Giacomini KM, Lawrence Lin, Sook Wah Yee, Richard B. Kim & Kathleen. SLC transporters as therapeutic targets: emerging opportunities. 2015 *Nature Reviews Drug Discovery* 14, 543–560.

Acknowledgements: This study was supported by the Traditional Korean Medicine R&D program funded by the Ministry of Health & Welfare through the Korea Health Industry Development Institute (KHIDI, Grant # HI16C0864). The commercial products were donated by the virtue of Kracie Pharma, Ltd. and Tsumura & Co.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2816

THU0460 BARRIERS TO GOUT CARE: A SYSTEMATIC REVIEW AND THEMATIC SYNTHESIS OF 120 PROVIDERS AND 480 GOUT PATIENTS FROM QUALITATIVE STUDIES

S.K. Rai^{1,2}, H.K. Choi^{1,2}, S. Choi³, A. Townsend^{1,4}, M.A. De Vera^{1,5}. ¹Arthritis Research Canada, Vancouver, Canada; ²Division of Rheumatology, Allergy, and Immunology, Massachusetts General Hospital, Boston, United States; ³Faculty of Medicine, University of British Columbia, Vancouver, Canada; ⁴Exeter Medical School, University of Exeter, Exeter, United Kingdom; ⁵Faculty of Pharmaceutical Sciences, University of British Columbia, Vancouver, Canada

Background: Despite gout's well-known pathogenesis and the availability of effective urate-lowering therapy (ULT), management remains poor. However, limited research has sought to improve care among this patient population. An in-depth understanding of provider and patient perspectives on barriers to the delivery of optimal gout care is critical to informing the development of evidence-based interventions to effectively improve disease management and patient outcomes.

Objectives: To systematically review and thematically synthesize qualitative studies to date reporting provider and patient barriers to gout management.

Methods: We conducted a mapped search of MEDLINE, EMBASE, Cumulative Index to Nursing and Allied Health Literature, and Social Sciences Citation Index databases and selected qualitative studies reporting provider and patient perspectives on gout management. Thematic synthesis was used to combine the source studies and identify key themes across studies. Two authors independently read and annotated the data and after discussion agreed on an initial coding framework. Concepts were organized into descriptive themes, and the relationships between these descriptive themes were further explored to develop higher-order analytical themes.

Results: Our search strategy retrieved 2,750 articles after the removal of duplicates. After full-text review, 20 studies spanning several geographic settings worldwide (i.e., the US, the UK, New Zealand, Australia, and the Netherlands) met all inclusion criteria and were included in our systematic review. Of these, 16 studies reported gout patient perspectives ($n=480$ patients), while only 7 studies reported provider perspectives ($n=120$ providers, including general practitioners, rheumatologists and other specialists, and allied health professionals). Thematic synthesis identified three predominant interlocking analytical themes among providers: (a) knowledge gaps and management approaches, (b) perceptions and beliefs about gout patients, and (c) system barriers to optimal gout care (Table 1). We further identified four predominant themes among gout patients: (a) limited gout knowledge (e.g., the “curable” nature of gout), (b) attitudes toward taking medication, (c) interactions with healthcare providers, and (d) practical barriers to chronic medication use (Table 1).