AB1036

FEATURES OF KIDNEY FUNCTION AND URODYNAMICS AT PATIENTS WITH CHRONIC GOUT BASED ON COMPLEX RENAL SCINTIGRAPHY DATA

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Background: One of the frequent manifestations of gout is the gout nephropathy. For assessment of the urinary system functional reserves and the risk of renal failure routine analyses of urine in combination with a sonography are often not enough. Modern technology of the systemic examination of nephrourological status based on complex renal scintigraphy (SENS-CRS) was developed in the laboratory of radioisotope diagnosis in «N.N. Blokhin National Medical Research Centre» and realised as an automated workplace. SENS-CRS technology is designed for assessment of the urinary system functional reserves and the risk of renal failure at all macrostructural levels, and allows lowest radiation doses (0.6 mSv for one patient).

Objectives: To define features of kidney function and urodynamics at patients with chronic gout based on the complex renal scintigraphy (CRS) data.

Methods: 59 medical records of patients with gout (2007–2011) were analysed retrospectively. Most of the patients (95%) were men, average age was 54.4±9.5 years. Duration of the disease was 8^{4–11} years. All patients had chronic gouty arthritis, 28% of patients had tophuses. The CRS tests was carried out on a two-detector gamma camera with simultaneous 2 projections recording. ^{99m}Tc-technephore was used, a Russian radiopharmaceutical (RP) from the group of bisphosphonates that has hemodynamics of a glomerulotropic product, concentrating mainly in the nephrons via filtration, with partial (10%–15%) involvement of secretion. Working protocol consisted of a base 21 min (1 min angiophase) study with administration of RP and a delayed 21 min study without administration of RP, but after taking 200–300 ml of water and/or an antispasmodic or diuretic drug to identify persistent urodynamic dysfunction. The interpretation of CRS data is based on a concentrational-hydrodynamic model of urinary excretion and SENS-CRS software. The Statistica 10.0 software was used too.

Results: According to CRS tests patients with gout had, on average, the level of blood cleansing from RP reduced slightly with a trend to a moderate level, and buffer retention of RP labelled blood in extrarenal structures increased. The signs of a relative hemostasis were found against the background of fast excretion accelerated by taking hypotensive drugs. Quantitative analysis of CRS data allows to estimate sustainability of relative urine delays in the pyelocaliceal system (PCS): in 70% of patients residual urostatics in the renal parenchyma and groups of calyx remained relatively stable, and the urostatics signs in the renal pelvis were disappearing. This result means that there could be a latent increased residence time of substances such as uric acid as well as nephrotoxic drugs in the kidney parenchyma. This requires control of correct drugs dosage and when prescribing repeated therapy courses.

Conclusions: The SENS-CRS technology provides the quantitative assessment of kidney blood cleansing from RP and concentrational function of parenchyma as well as unique quantitative indicators of urodynamic delays in all parts of urinary tract. This kind of functional diagnostics allows to monitor parenchyma and urinary tract condition promptly and with lowest radiation doses, apply therapeutic measures to prevent more severe kidney dysfunction and refer patients to a specialist consultation.

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AB1037

RELATIONSHIP BETWEEN CALCIUM PYROPHOSPHATE DIHYDRATE CRYSTAL AND OPERATED KNEE OSTEOARTHRITIS -GENDER SPECIFIC ANALYSES-

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Background: Calcium pyrophosphate dihydrate (CPPD) crystal deposition disease is a common arthritic disorder in mainly elderly patients. CPPD crystals are found in multiple joints in association with severe cartilage degeneration in osteoarthritis (OA). The knee is a key target site for both CPPD crystals and OA. CPPD crystals are also one of the common types of crystals causing crystal-induced inflammatory arthritis. There is a need to elucidate factors that can cause progression of knee OA. To address this question, we investigated the relationship between CPPD crystals and operated knee OA.

Objectives: We investigated the relationship between CPPD crystal and operated knee OA separated by gender.

Methods: Three hundred sixty-six unicompartmental knee arthroplasty (UKA), total knee arthroplasty (TKA) and high tibial osteotomy (HTO) (average age 73.3: male 59: female 307) were performed for over grade III knee OA classified by Kellgren-Lawrence grading scale from 2010 to 2017. At the operation, joint fluids

were collected and elucidated the CPPD crystal using polarising microscope. We evaluated the relationship between CPPD crystals, and age, body mass index (BMI), C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), matrix metalloproteinase-3 (MMP-3) at the operation. We defined the osteophyte formation degree (OFD) as grade 0–3¹. We also defined the lower extremity alignment as varus (femorotibial angle: FTA ≥180°), neutral (170°≤FTA<180°) and valgus (FTA <170°). The relationship between CPPD crystals, and osteophyte formation and lower extremity were also evaluated.

Results: CPPD crystals were detected from 101 Knee OA (27.6%). CPPD(+) rate in female (30.0%: 92/307) was significantly higher than that in male (15.3%: 9/59). There was a significant difference between CPPD(+) and (-) in male about only FTA (186.9°/182.0°). There were significant differences between CPPD(+) and (-) in female about age (76.3/72.4), FTA (182.7°/183.2°), BMI (24.9/26.6). The more severe OFD became, the higher CPPD(+) rate was in female, significantly. CPPD(+) rate in valgus knees (60.9%) was higher than that in varus knees (29.6%) in female significantly.

Conclusions: The European League Against Rheumatism (EULAR) reported that female gender was not a risk factor associated with CPPD crystals². In contrast, a recent study using a relatively large sample size of Japanese cadaveric knees showed a significant correlation for CPPD crystals and female gender³. Our data also showed a significantly high CPPD(+) rate in females. Because our data were based on Japanese patients only, Japanese ethnicity may influence the gender difference in the CPPD(+) population. In addition, the significantly different items in male and female were different. These results may suggest that the mechanism of CPPD deposition may be different by gender.

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AB1038

PHARMACOKINETICS, PHARMACODYNAMICS AND SAFETY OF NC-2500, A NOVEL XANTHINE OXIDOREDUCTASE INHIBITOR, IN HEALTHY JAPANESE MALE SUBJECTS

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Background: Gout flare due to rapid urate reduction after initiating urate-lowering therapy (ULT) is one of the major issues in the therapy, which impairs patients' quality of life and adherence. For the prevention of it, the guidelines in the ACR, the EULAR and Japan recommend initiating ULT with a low starting dose followed by adequate titrations, however it is rare in clinical settings. NC-2500 is a novel orally active xanthine oxidoreductase (XOR) inhibitor in development for the treatment of gout/hyperuricemia. Preclinical studies showed that multiple doses increase the plasma concentration and enhance the urate-lowering effect of NC-2500, suggesting that NC-2500 may decrease the risk of gout flare when initiating the treatment.

Objectives: The aim of this study was to evaluate the pharmacokinetics, pharmacodynamics and safety of NC-2500 in healthy Japanese male subjects.

Methods: A Phase 1, randomised, single-blind, placebo-controlled, single and multiple ascending dose study was conducted. Each cohort consisted of 8 subjects, with 6 receiving NC-2500 and 2 receiving placebo orally. A total of 5 cohorts were studied in the single-dose study (10 mg to 160 mg, fasted conditions) and 4 cohorts were studied in the multiple-dose study (10 mg to 80 mg, fed conditions). The levels of NC-2500 and urate in plasma/serum and urine were assayed at pre-determined time points. Safety and tolerability were assessed by physical examination, vital signs, electrocardiography, clinical laboratory tests and adverse events (AEs).

Results: Following single oral doses of NC-2500, maximum plasma concentration (C_{max}) and area under the plasma concentration-time curve (AUC) increased approximately in a dose-proportional manner except that the increase in the C_{max} at 160 mg was less than dose proportional. The time to reach the C_{max} (T_{max}, median) was at 2.0–3.5 hours post dose and food intake delayed the T_{max} by 1 hour. In the presence of food, NC-2500 absorption appeared to decrease slightly or not be affected. Plasma NC-2500 concentration increased

with multiple doses and the Cmax and AUC on Day 7 at 80 mg were 1.4–1.5 times higher than those on Day 1. NC-2500 was hardly excreted into the urine. Effects of NC-2500 on serum urate (sUA) levels were approximately dose-dependent. The sUA level in the single 160 mg dose cohort decreased by 1.03 mg/dL. Moreover, in the subjects receiving multiple doses of 80 mg, the sUA level decreased gradually over the 7 days with a decrease from baseline of 1.93 mg/dL. The incidence of AEs was similar between NC-2500 and placebo treatments and all AEs were mild in severity.

Abstract AB1038 – Figure 1

Conclusions: From the results, NC-2500 is expected to have potential to resolve the issues of current ULT by its unique urate-lowering property to decrease acute flare, with no or minimal titrations. As for safety, NC-2500 was considered safe and well-tolerated. Furthermore, NC-2500 was hardly excreted through the kidneys, which can be a favourable profile for patients with renal impairment, frequently observed in gout.

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AB1039 DIET MAY PLAY ESSENTIAL ROLE FOR THE SUCCESS OF THE URATE LOWERING THERAPY IN GOUT

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Background: Chronic deposition of monosodium urate crystals, in case of hyperuricemia, is the main cause of the gout.¹ Furthermore, lowering uric acid to the targeted levels is the main therapeutic objective in chronic gout treatment. Uric acid lowering treatment (ULT) has three main arms: Practicing lifestyle modifications, pharmacologic ULT and targeting co-morbid illnesses.² Thus, patients' medical and therapeutic properties may have a role in successful ULT.

Objectives: We evaluated the demographic and therapeutic properties; co-illnesses and disease features of the patients that would relate with the success of ULT. Then, we compared these parameters between the gout patients with successful ULT and inadequate ULT.

Methods: 66 gout patients on pharmacologic ULT were enrolled to the study. Non-adherence to pharmacologic ULT was accepted an exclusion criteria. Demographic and therapeutic features; co-illnesses and disease features of the patients were obtained during the study. Then, we compared these parameters between the patients with successful ULT and inadequate ULT.

Results: Adherence to diet was found different between groups (OR, 7.00; CL% 95 2.27–21.56). All other features including maximum allopurinol dosage were similar. Only one patient from successful ULT group and none of the patients in inadequate group had an drinking habit.

Abstract AB1039 – Table 1. Demographic properties, therapeutic features and laboratory values of the patients

	Successful ULT n=32	Inadequate ULT n=34	p
Gender (M/F)	29/3	28/6	0.47
Age	60.3±13.1	55.8±11.8	0.14
Body mass index	27.2±9.8	27.8±8.9	0.32
Diabetes mellitus n(%)	7 (21.9)	11 (32.4)	0.24
Hypertension n(%)	19 (59.4)	18 (52.8)	0.39
Chronic cardiac disease* n(%)	9 (28.1)	6 (17.6)	0.23
Hyperlipidemia n(%)	1 (3.1)	2 (5.9)	0.52
Chronic kidney disease n(%)	6 (18.8)	3 (8.8)	0.20
ACE inhibitors/AT II blockers n(%)	18 (56.3)	13 (38.2)	0.14
Beta-blockers n(%)	5 (15.6)	4 (11.8)	0.72
Diuretics n(%)	5 (15.6)	5 (14.7)	0.91
Acetylsalicylic acid n(%)	5 (15.6)	3 (8.8)	0.46

Abstract AB1039 – Table 2. Disease and treatment features of the patients

	Successful ULT n=32	Inadequate ULT n=34	p
Pretreatment SUA (mg/dL)	9.47±1.6	8.8±1.6	0.18
Maximum allopurinol dosage (mg)	290.6±92.8	313.8±134.8	0.75
Adherence to diet n(%)	26 (81.2)	13 (38.2)	<0001
Chronic gout arthritis n(%)	8 (25.0)	11 (32.3)	0.56
Tophus n(%)	5 (15.6)	2 (5.8)	0.25
Erosion n(%)	7 (21.8)	7 (20.5)	1.00

Conclusions: We found that diet was the only factor that relate with success of ULT while patients were on pharmacologic ULT. So, clinicians should emphasise the importance of all part of ULT including diet with informing patients about the nature of disease and benefits of ULT during visits.

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AB1040 IS GOUT A CHRONIC INFLAMMATORY DISEASE OF A LOW LEVEL OF ACTIVITY?

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Objectives: To determine the presence of physical, laboratory and ultrasound (US) signs of inflammation on the affected joints, but also on the joints that in the clinical sense never showed an inflammatory reaction in the intercritical gout period.

Methods: This prospective study included 43 patients (pts.) with diagnosis primary gout (20 with and 23 without acute gout attacks). The research included: demography; medical history; laboratory analyses: sedimentation of erythrocytes (ESR), C reactive protein (CRP), and serology; physical: detect tender and swollen joint; and US examination detect synovial fluid and hypertrophy, Power Doppler (PD) signal and "double contour" sign on the wrist, first metatarsal joint (MTP1), tibiotalar (TT) joint and knee.

Results: A physical examination showed presence of 78% tender and 43% swollen joints in the group pts. with acute gout attack, but also 23% pts. had painful and 10% swollen joints in the group without acute gout attack (p<0.001). In the group with acute gout attacks the mean ESR was 32.80 mm/L, value CRP was 8.20 mg/L and leukocytes (Le) (9.09 × 10⁹/L), and in the group without acute gout attacks SE was 21.60 mm/L median CRP was 6.40 mg/L and also a higher average Le (8.39 × 10⁹/L). So we found that there was no statistical difference (p>0.5) in the laboratory parameters (ESR, CRP and Le) between the groups. There was also no statistically significant difference in the findings of US signs of "double contour" (p>0.5), synovial fluid and hypertrophy (p>0.05), per group, but the presence of PD signal statistics was more often observed in a group of patients in an acute gout attack (p<0.05), table 1.