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 nephrological status based on complex renal scintigraphy (SENS-CRS) was developed in the laboratory of radioscopydiagnosis in “N.N. Blokhin National Medical Research Center 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 8.1±11 years. All patients had chronic gouty arthropathy, 28% of patients had tophuses. The CRS tests was carried out on a two-detector gamma camera with simultaneous 2 projections recording. 99mTc-technephore was used, a Russian radiopharmaceutical (RP) from the group of biuret compounds. The radiourodynamics of the (urine excretion) 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 concentration-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 allowed to estimate sustainability of relative urine delays in the pyelocutaneous system (PCS), in 70% of patients residual urostasis in the renal parenchyma and groups of calyx remained relatively stable, and the urostatic 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 nephrotic 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 concentration functional 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.

Disclosure of Interest: None declared


PHARMACOKINETICS, PHARMACODYNAMICS AND SAFETY OF NC-2500, A NOVEL XANTHINE OXIDASE 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 patient's 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 oxidase (XO) inhibitor. 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 (Cmax) and area under the plasma concentration-time curve (AUC) increased approximately in a dose-proportional manner except that the increase in the Cmax at 160 mg was less than dose proportional. The time to reach the Cmax (Tmax, median) was 2.0–3.5 hours post dose and food intake delayed the Tmax by 1 hour. In the presence of food, NC-2500 absorption appeared to decrease slightly or not be affected. Plasma NC-2500 concentration increased.