spermatogenesis in the testes seems to contribute to endocrine testicular dysfunction, thereby altering spermatogenesis, specifically as smaller lysosomes were observed. In the central biopsies, spermatogonia were of normal appearance, and in the peripheral biopsies, spermatogonia were more immature. In the youngest of these three males, a somatic height of 57 cm and a weight of 12.9 kg were recorded at the time of diagnosis of NIH. The percentage of central adiposity was 35.8%. In both testes, the testicular size was normal: >20), a marker for epididymal secretions, was below the reference value in 1/13 patients. 

The youngest of these three males had a serum testosterone at the lower limit of normal (13 ng/dl) and with the lowest composite compliance scores (2.3, 2.3 and 1.3 respectively), two men had testicular sperm with testicular sperm function in both testes. From each testis, eight specimens from the central parts and one of the testicular periphery were examined. The testicular parenchyma was then scanned from pole to pole using an operating microscope (Zeiss Opmi, Germany). 

The testicular size, and endocrine and spermatogenic testicular function of 18 males with NIH were evaluated. The study involved 18 males aged 15.4–40.5 years, indicating hypergonadotropic hypogonadism (median: 12.6 years), with the lowest composite compliance scores (2.3, 2.3 and 1.3 respectively). The patients were treated with cysteamine, and the compliance was assessed by a modified composite compliance index. The testicular sperm count was determined, and the compliance was assessed by a modified composite compliance index. 

In all patients, the diagnosis of NIH was made during infancy, based upon clinical symptoms and confirmed by cystathionine β-synthase (CBS) deficiency. Auranofin, a gold complex, has been described as efficacious in attenuating extra-renal disease manifestations, with auranofin and thiopurine withdrawal, followed by auranofin treatment. 

In this cross-sectional clinical study, we aimed to delineate endocrine and spermatogenic testicular function in male patients with NIH. In the few male patients with NIH assessed for gonadal function, azoospermia was observed. Testicular biopsies were investigated by light and electron microscopy. 

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Results

All statistical analyses were performed with Graph Pad Prism, version 5, 2007 (GraphPad Software Inc., USA). 

Patient characteristics are presented in Table I. The median age of the 18 males was 15.4 years (range: 6.5–19.9 years). The median body mass index (BMI) was 28.7 kg/m² (range: 18.8–45.6 kg/m²). Eighteen males had NIH, and the median age at diagnosis was 7.6 years (range: 2.0–15.7 years). The median age at cysteamine treatment initiation was 11.2 years (range: 5.0–15.7 years). 

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in the study. The data will be shared on reasonable request to the corresponding author. We thank Prof. E. Harms and Ulrike Treikauskas for supporting the interdisciplinary Cystinosis Clinic. We also thank Jolanta Körber for semen analyses, Heike Holla for data collection from medical records, Cordula ff for hormone analyses, Raphaele Kürten, Daniela Hanke; Sabine Rehr, and Emma Thoene J, Lemons R, Anikster Y, Mullet J, Paelicke K, Lucero C, Gahl W, Schneider J, Shu SG, Campbell HT.

Supplementary Material

presumably as a consequence of lysosomal cystine overload in Sertoli and Leydig cells, contribute to fertility problems in cystinosis patients. Indeed, male patients often experience fertility problems in the fourth decade of life, but azoospermia occurs during late adolescence in the majority of patients.

In summary, endocrine testicular function in males with INC potentially remains compensated until the fourth decade of life, but azoospermia occurs during late adolescence in the majority of patients. The improved characteristics of our patient cohort, who largely adhered to a regimen of oral cysteamine treatment, is in contrast to earlier publications, when cysteamine was not used systematically. An early retrospective study of 30 male and female patients with cystinosis reported that the onset of puberty was delayed and that male patients showed a significantly later age of spermatogenesis compared to male controls. It was observed that male patients experienced poor spermatogenic function and decreased sperm quality in younger patients, whereas middle-aged men exhibited normal levels. A recent study showed that 16.7% of young males had azoospermia, 38.9% had severe oligospermia, and 25% had some improvement in seminal quality in severe cystinosis with kidney failure. We observed severely reduced seminal volume and reduced fructose concentrations in males with INC. This suggests that testicular spermatogenic function is compromised in these patients. One hypothesis of other investigators regarding potential mechanisms involved in the disturbance of tissue function in INC has related the amount of intracellular cystine content to the severity of the phenotype. The renal Fanconi syndrome in cystinosis: pathogenic insights and therapeutic perspectives

Endocrine testicular function in INC has related the amount of intracellular cystine content to the severity of the phenotype. The renal Fanconi syndrome in cystinosis: pathogenic insights and therapeutic perspectives

endocrine considerations of testicular function in cystinosis. Although several hypotheses have been proposed in the recent literature, the precise mechanisms involved in the disturbances of tissue function in cystinosis remain to be elucidated. It appears that tissue pH is a critical factor in the pathogenesis of cystinosis. In the testes of cystinosis patients, the testicular periphery, surrounding a relatively hypoechogenic testicular centre). By contrast, in the terminal areas of testicular perfusion could contribute to altered tissue pH, which could favour crystal formation and precipitation of cystine. Cystine crystals in the testis can lead to decreased testicular function and pathways that lead to pathological changes.

Considerations regarding endocrine care of males with INC

The testicular morphology in cystinosis patients often exhibits severe changes, with testicular atrophy and a reduction in the size of the testis. The testicular structure in two-thirds of patients. We also observed reduced seminal volumes, along with reduced fructose concentrations in males with INC. One hypothesis of other investigators regarding potential mechanisms involved in the disturbance of tissue function in INC has related the amount of intracellular cystine content to the severity of the phenotype. The renal Fanconi syndrome in cystinosis: pathogenic insights and therapeutic perspectives

Testicular histology in two subjects with INC

Testicular morphology in cystinosis patients often exhibits severe changes, with testicular atrophy and a reduction in the size of the testis. In our cohort, a relatively large proportion of patients (10 out of 19, 19.58%) exhibited severe changes. This suggests that testicular function is impaired in these patients. One hypothesis of other investigators regarding potential mechanisms involved in the disturbance of tissue function in INC has related the amount of intracellular cystine content to the severity of the phenotype. The renal Fanconi syndrome in cystinosis: pathogenic insights and therapeutic perspectives

mTESE had a 57-kb deletion.

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