ECYSCO : A European Cohort dedicated to cystinosis

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Aims/Purpose:

Specific treatment by cysteamine to treat cystinosis decreases renal and extrarenal complications frequency. Recently, new treatments for cystinosis were available with an extended-release formulation of cysteamine and a new formulation of eye drops. The aim of this project was to describe the natural history of the disease and long-term clinical manifestations.

Methods

We set up a European, multi-centre, longitudinal, non-interventional cohort, ECYSCO, that uses observational study methods to collect uniform data. 243 patients with a confirmed diagnosis of cystinosis and followed in 25 French and 5 European centers (Belgium, Italy, Spain and Germany) were included. Data were collected on the secure RaDiCo platform, via an e-CRF (REDCap).

Results

Data from 180 patients (50.0% male) were analyzed. Median age at diagnosis was 1.3 years [IQ 0.8; 1.9], with earlier diagnosis since the 1980s, but no further improvement in the 2000s. Genetic analysis was available for 174 patients: 57 (32.8%) presented with homozygous 57kb deletion in the *CTNS* gene, 71 (40.8%) with heterozygous 57kb deletion associated with another variant and 46 (26.4%) with other variants. The type of variant had no impact on the age at diagnosis. Median age at cysteamine start was 1,6 years (IQ 1.0-3.0). An improvement on age at treatment start was observed after the 1990s. All but 6 patients were treated with cysteamine. 71 patients received immediate release formulation (Cystagon®) and 103 received extended release formulation (Procysbi®). Median white blood cell cystine level was correct at 1.2 nmol ½ cystine/mg protein (IQ 0.59; 2.20). The median duration of treatment was 21.5 years [IQ 11.7; 31.1]. 167 (95,9%) patients also received cysteamine ocular gel, Cystadrops®.

Median age at inclusion was 19.08 years (IQ 10.43; 31.41). At that time, 104 patients (57.8%) had kidney failure. There was no impact of genotype on age at kidney failure. Median age at kidney failure was 12.9 years [IQ 9.9; 18.0]. A 5-year gain in renal survival was observed after the 1990s. 102 patients (56.7%) received a kidney transplant. Among these transplanted patients: 76 (74.5%) received 1 transplant, 23 (22.5%) received 2 consecutive transplants, and 3 (2.9%) received 3. Median eGFR in the remaining patients was 58.9 ml/min [IQ 40.4; 82.2]. Extrarenal manifestations included hypothyroidism in 61 (33.9%) patients, diabetes mellitus in 11 (6.1%), skeletal manifestations in 73 (40.5%), myopathy in 32 (17.8%), and neurological disorders in 22 (12.2%). At inclusion, 36 patients had no kidney failure and no extra-renal complication.

Conclusion

Cystinosis is a good example of a pediatric disease with multiorgan involvement extending into adult care. More than half of patients are adults and have reached kidney failure even if age at renal replacement therapy start has increased. The frequency of extra-renal manifestations demonstrates the importance of a multidisciplinary follow up of these patients.