



EDITORIAL

Multidisciplinary units in tertiary referral hospitals to improve management of Wilson disease[☆]



Unidades multidisciplinarias en hospitales de referencia para mejorar la atención de los pacientes con enfermedad de Wilson

Introduction

Wilson disease (WD) is a genetic disease caused by a mutation in the ATP7B protein, which leads to an inability to eliminate copper in the bile, with consequent retention of copper in the liver, and eventually in the nervous system and other organs.¹ If untreated, the accumulation of copper causes the liver disease to progress from simple steatosis to liver cirrhosis, and neurological lesions can appear.^{2,3} Several treatments are available: copper chelators (penicillamine and trientine)⁴ and zinc acetate or sulphate. When given orally, these prevent the absorption of copper from the diet.⁵ When administered in early stages of the disease, the treatment prevents the accumulation of copper and therefore disease progression, and enables treated patients to have a life expectancy similar to that of the age-matched general population.⁶ If, in contrast, the diagnosis is made in advanced stages, a shortened life expectancy is the norm.⁷

WD is included in the category of "rare diseases". With an estimated prevalence of only 25–30 cases per million population, many medical professionals are unfamiliar with the disease, resulting in delayed diagnosis in a large number of cases, and consequently, delays in the start of treatment.

The disease can manifest at any age, and although more than half of cases debut in childhood, it has also been diagnosed in septuagenarians.^{8,9} Paediatricians are, therefore, the specialists who most often face the challenge of diagnosing the disease. Recognising WD is difficult, because it can manifest in a variety of ways: asymptomatic elevation of transaminases; advanced liver disease that onsets with a complication (ascites or gastrointestinal bleeding)¹⁰;

haemolytic anaemia, sometimes accompanied by signs of severe acute liver failure¹¹; neurological manifestations, especially tremor, dysarthria or movement disorders¹²; or in the form of a psychiatric syndrome.¹³ This variability in clinical expression contributes to diagnostic delay and the resulting impact on the severity of the disease. Diagnostic delay also hampers treatment, since patients with neurological symptoms require other measures in addition to pharmacological therapy, such as physical and speech rehabilitation.¹⁴

Medical care of patients with Wilson disease

In most reference hospitals, patients with WD are treated by different specialists (paediatricians, hepatologists or neurologists) with little or no contact with each other. There are very few centres specialised in this disease in Spain that offer comprehensive care, or that enable a patient who has been referred with suspected WD to rapidly undergo all the tests needed to definitively diagnose or rule out the disease.

Follow-up is complex in patients who have already been diagnosed, as it involves monitoring treatment compliance, detecting adverse drug reactions, assessing changes in liver function, checking for improvement or lack of improvement in neurological symptoms, and determining whether other organs are involved. All of this implies the involvement of different specialists, and the need for blood samples for analysis or instrumental procedures to check the evolution of certain changes, such as slit lamp examination to assess the persistence or resolution of Kayser–Fleischer rings following treatment.¹⁵ Psychologists or psychiatrists may at times be needed to assess the impact of the diagnosis of a genetic disease on the patient and their family, and social workers may be required to resolve occupational or social problems caused by the disease.

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Due to the organisation of healthcare services in the Spanish public health system, care of WD patients necessarily involves many visits to different specialists (hepatologists, neurologists, ophthalmologists, phlebotomy centres, psychiatrists and social workers). This fragments the study and follow-up of patients with WD into a succession of time-consuming consultations that result in school or work absenteeism, numerous trips to hospital, and cause the patient and the persons accompanying them considerable inconvenience.

Benefits of multidisciplinary units for Wilson disease

The main aim of creating these units in some reference hospitals would be to ease the burden on patients by reducing the number of visits. Thus, within the framework of a multidisciplinary unit for WD, all visits to the different specialists and all analytical or instrumental examinations required could be coordinated on the same day. This would greatly reduce the number of losses to follow-up of patients who live far from the reference hospital, or whose jobs make it difficult for them to get permission to visit their doctor.

The existence of this type of clinical unit would give patients access to services that are rarely available in general hospitals, such as speech therapy (in patients with neurological WD with speech difficulties), physiotherapy (for correction of dystonia), or experts in genetic counselling. These specialists could be actively integrated into this multidisciplinary unit on a part-time basis.

This type of unit should not only attend patients from the catchment area of the hospital in which it is located, but could answer, either online or by telephone, queries about WD from doctors practising in areas further afield.

Forming part of a multidisciplinary unit focusing on a particular disease will notably improve individual skills, encouraging members to engage in group discussion of cases and to keep up to date with medical literature. It also opens the possibility of conducting therapeutic trials, and applying genetic or biological research procedures. The accumulation of cases with different phenotypic symptoms and genetic patterns would also allow similar units in different locations to network on clinical studies of the natural history of the disease under different therapeutic regimens.

Finally, WD units could help train doctors from their geographical area to recognise factors that should raise suspicion of the disease, thus enabling earlier diagnoses.

Composition of Wilson disease units

A multidisciplinary unit can exist without the need for a designated manager appointed by the hospital. However, someone must be willing to take on a leadership role in order to recruit specialists to the unit, maintain good relationships, and ensure that all members benefit academically. This role should be taken on by the physician with the most motivation to concern themselves with this disease.

The composition of a unit of this type should be determined by the type of hospital in which it is located, but in broad terms should include a paediatrician, a hepatologist, a neurologist interested in movement disorders and

a psychiatrist/psychologist. It is essential that both the paediatrician and the hepatologist are particularly interested in WD, and see all patients with this diagnosis who are treated at the hospital. The ophthalmologist who performs the Kayser–Fleischer ring examinations is a key figure, and should have the experience needed to diagnose WD in patients with non-specific neurological expression and to monitor treatment compliance and therapeutic response. The unit would also benefit from the collaboration of a geneticist interested in this disease, a speech therapist and a physiotherapist. Furthermore, the participation of a case manager to schedule visits with minimal time disruption for patients is essential.

Ideally, to facilitate access by the patient, the WD unit should be located in a single area that includes facilities for collecting biological (blood and urine) samples. Taking into account that the number of patients with WD is low, one morning per week dedicated to the care of these patients should suffice, and staff attached to the unit will be able to devote the rest of the week to their respective duties in their own hospital department.

Furthermore, a WD unit can have a complementary role, collaborating with the biochemistry department in validating laboratory tests for WD markers, ceruloplasmin, blood and urinary copper levels, and quantitation of copper in liver tissue.

All patient data should be entered into a database that would permit research into case studies. The medical staff in the unit should have periodic meetings to discuss the cases of both recently diagnosed patients and those in follow-up, and to draw up diagnostic and therapeutic protocols. Part of the time in these sessions should be dedicated to reviewing and discussing relevant published articles, and a member of the team should be assigned the task of preparing the bibliographic material for these meetings. It would also be useful to invite other physicians from the paediatric, hepatology and neurology departments to attend sessions to familiarise them with the characteristics of a rare disease in their different fields. The experience gained from the national WD reference centre in Paris has shown that these multidisciplinary projects clearly improve the care provided to patients with rare diseases from both a medical and social perspective.^{16,17}

Conflict of interests

None.

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