PHP310

Achieving key objectives in rare diseases healthcare policy in Spain: Contribution from a Dravet Syndrome Working Group

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BACKGROUND & OBJECTIVES

Dravet Syndrome (DS) is a severe, epileptic encelopathy that begins in infancy,[1] is characterised by intractable seizures,[2] and can be associated with significant mortality. Death may occur at any age, but more frequently during childhood.[3] Diagnosis of DS is difficult, and the epidemiology, patient flow, burden of disease, and disease management is not clearly established. This study aims to shed some light on these topics and to elucidate main unmet needs for DS in Spain and propose actions that could contribute to meeting key healthcare (HC) objectives from the Spanish National Strategy for Rare Diseases (RRDD). These objectives are: 1. Improvement of the information available on RRDD and strengthening existing registries; 2. Prevention and early detection, promoting the role of the primary care (PC) physician in diagnosis, facilitating derivation processes, and improving access to diagnostic tests; 3. HC assistance, guaranteeing continuum of HC provision across care levels; 4. Guaranteeing timely access to orphan drugs at national level; 5. HC provision, promoting coordination between authorities and institutions and promoting awareness campaigns; 6. Increasing research on RRDD; and 7. Promoting continued training to PC physicians and specialised care.

METHODS

Literature review from international (ie, Pubmed, Google Scholar, and Cochrane) and national (ie, Medes) sources. Information obtained was supplemented and validated through interviews with 8 Spanish experts in DS management and later used to establish a two-round consultation Delphi study including 19 specialists (9 neuro-paediatricians, 9 neurologists/epileptologists, and 1 primary care physician) from 17 different centres spread across 7 regions. Results were validated via an Advisory Board meeting that included 10 DS specialists (7 neuro-paediatricians and 3 neurologists/epileptologists) in Spain.

RESULTS

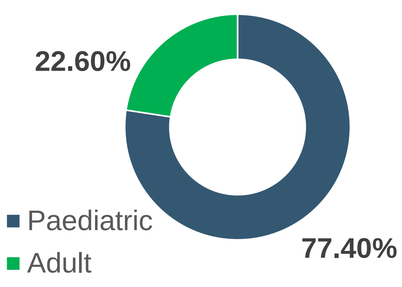
Epidemiology

348-540 estimated DS patients in Spain*

*Prevalence estimation range based from results from the Delphi study (low end of the range) and published DS incidence in the literature, adapted to Spanish population using INE data[4] (high end of the range).

- DS affects both genders **equally**.

Figure 1. DS patient age at diagnosis



Burden of disease

Survival	**Survival could be related to age at diagnosis**, as mortality is associated with the earliest stages of the disease. Experts stated that life expectancy could be 60 years, but no formal data is available.
Quality of life	Physicians noted that DS patients **had extreme problems with self-care** and with **usual activities such as work, family, or leisure activities.** These problems were more pronounced in adult patients.
Resource use	The **average number of yearly physician visits was higher among paediatric vs adults patients**: Emergency Department (7 vs 3), Neuro-paediatricians (5 vs 2), Primary Care (7 vs 4), Neurologist/Epileptologist (4 vs 5), Rehabilitation (5 vs 4), Psychologist (6 vs 4), and Speech Therapist (8 vs 5).

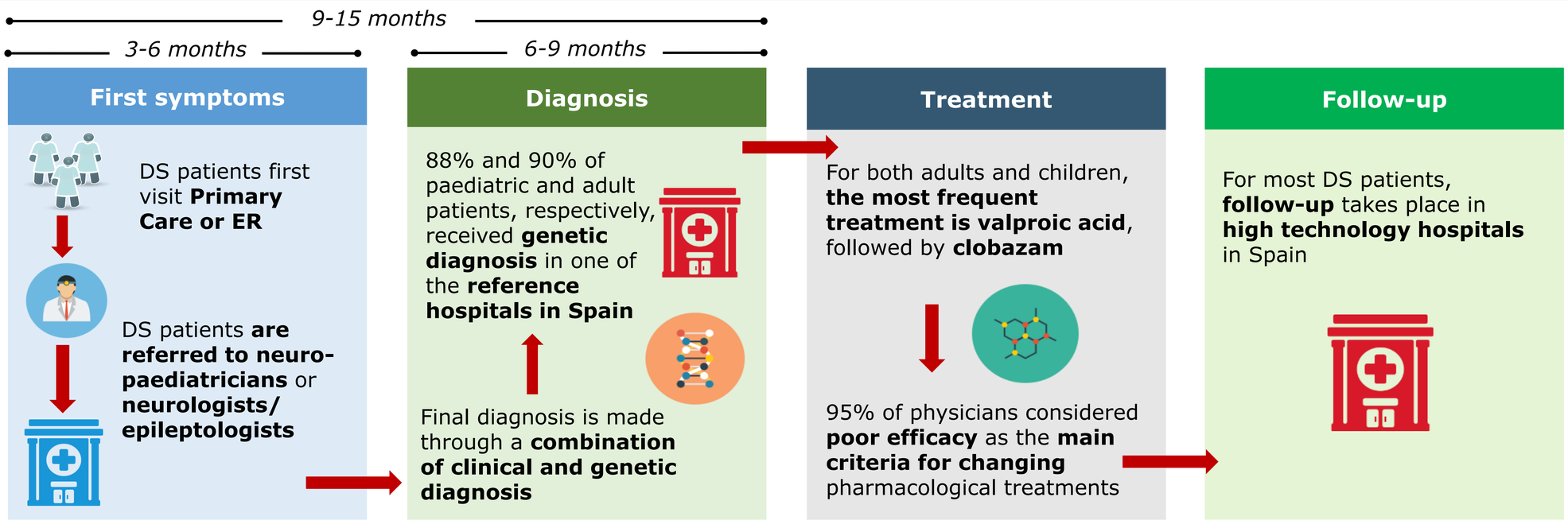
DS patient flow

Figure 2. DS patient flow diagram in Spain

There is a **significant delay** in reaching **DS diagnosis** in Spain

The DS **genetic test** is only **available** in a few **high technology hospitals**

Most **DS patients** are **managed by neuro-paediatricians**



Disease management

- Genetic testing has been used in Spain since 2003. Regional/hospital **access to the test is variable** with only two hospitals having the test available *"in situ"* and the **time to obtain the genetic test results also varies widely** between public and private centres (up to 6 months vs. 1 month, respectively).
- **Clinical criteria for diagnosis are well defined** in Hattori 2008.[5] **No clinical guidelines exist** for DS in Spain, although there are some protocols in certain hospitals.
- **Experts agreed on a ranking of treatments** based on importance and frequency of use (**Figure 3**). The treatments are the same for paediatric and adult patients.
- The main reason for changing pharmacological treatment is **poor efficacy,** defined as the occurrence of multiple seizures in a year.
- **Early diagnosis and treatment** can **improve** patient **status and prognosis**.

Figure 3. DS treatment ranking in Spain

1st	**Valproic acid**
2nd	Clobazam
3rd	Stiripentol
4th	Topiramate
5th	Other

Key unmet needs for DS in Spain

1. Robust epidemiological data.
2. Consensus for patient diagnosis and management.
3. Training of HC professionals.
4. Wider availability and faster test results for genetic testing.
5. Better disease awareness.
6. Disease *continuum* management (paediatric to adulthood).
7. Availability of more effective treatments.

Proposed actions

1. Perform an epidemiological study and establish an epidemiologic register.
2. Generate a national consensus to be incorporated at regional and hospital level.
3. Establish a validated training programme for PC and ER paediatricians to improve prognosis and outcomes.
4. Revisit timely access to and results from genetic testing.
5. Develop a disease severity model that includes quality of life aspects.
6. Establish a best practice framework for patient management from primary care.
7. Continue efforts in development, approval, and timely access to new treatments.

CONCLUSIONS

DS is a disease that can lead to death and is currently neither well diagnosed nor correctly treated. Main unmet needs include: robust epidemiologic data, patient diagnosis, management, specific training for HC professionals, availability of the genetic tests, disease awareness, disease *continuum* management, and the availability of more effective treatments. The above proposed actions are fully aligned with the 7 strategic lines within the Spanish NHS Strategic Plan for RRDD.

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