Dravet syndrome (DS) is a rare epileptic encephalopathy with onset during the first year of life in an otherwise healthy infant [1]. The clinical picture is characterized by frequent convulsive tonic-clonic seizures, followed later by non-convulsive seizures, mainly clonic and unatonic, of long duration and frequent status epilepticus [2]. Children with DS have significant developmental disabilities, including cognitive, social, and emotional impairments, which can impact quality of life (HRQoL) [3].

Available treatments are non-cumulative and prognosis is generally poor [2]. As such, children and young persons with DS require intensive care and supervision, which also impacts the HRQoL of their caregivers.

Purpose

Although seizures are the most commonly measured endpoint in clinical trials, there are important impacts of DS which are often overlooked and not measured.

The main objective of the study was to identify a core set of concepts, relevant to the patient and caregiver experience of DS, which could be assessed as outcomes in clinical trials.

This research forms part of a longer term project with the aim of using a core set of outcome measures to define a single measure of improvement/composite endpoint in DS trials.

Results

Concepts Elicited from Interviews: Symptoms

The most commonly reported symptom was seizures, which was elicited by all participants. Types of seizures reported included generalized (n=10), convulsive (n=8), absence (n=7), tonic clonic (n=4), myoclonic and focal (partial) (n=4, respectively). Seizures were reported to last between five seconds and several hours, while frequency, treatment and type of seizure. Frequency of seizures was reported to vary and occur in a series with seizure-free intervals in between.

Seizures were reported to occur with a range of factors, such as temperature rise, crying, fever (n=11), changes in external temperature (n=9), submersion in water (n=7), excitement (n=5) and emotional experience [n=7, respectively; buy specialist equipment (n=2), emotional (n=2), social and physical (n=1); and emotional expression (n=1)].

Concepts Elicited from Interviews: Impacts

A range of impacts on children with DS were identified, most commonly cognitive functioning (e.g. gross motor function (n=11), learning and attention (n=10), respectively), expressive communication (n=9), fine motor function (n=8), receptive communication and emotional experience (n=7, respectively) and behavioural function (e.g. general behaviour, anxiety (n=5), respectively) and emotional expression (n=4, respectively).

Sub-concepts that were less frequently reported included work (n=5), family (n=4), leisure (n=3), treatment (n=3), respectively; buy specialist equipment (n=2), emotional (n=2), social and physical (n=2) and daily activities (e.g. physical (n=2)).

Concepts Elicited from Interviews: Coping Strategies

Participants mentioned a range of coping strategies to help patients and their caregivers to manage the most frequently reported concepts were: home adjustments (n=7), use of assistive aids/devices (n=6), coping strategies related to daily activities (n=5) and preventative behaviours (n=3) and communication (n=3).

Development of Conceptual Model

A conceptual model was developed based on the concepts elicited in the interviews, presenting all the symptoms, trigger, impact and coping strategies concepts. [Figure 2, Figure 3] A wide range of concepts were elicited only by caregivers and not reported by clinicians, highlighting the value of the caregiver perspective in DS. In particular, the following coping strategies were only mentioned by caregivers: management of seizures, coping relating to daily activities, use of assistive aids, preventative behaviours and social support, suggesting that these are not aspects of DS upon which clinicians focus.

Additionally, a wide range of concepts were elicited by caregivers than clinicians, across the following domains; cognitive functioning (e.g. expressive communication), behavioural function (e.g. CFU and anxiety) and secondarily on the child (e.g. social functioning and somatization).

Conclusions

The impact of DS is experienced by patients and caregivers extending beyond the direct impact of seizures. Notably, a wide range of impacts on children with DS and their caregivers were identified.

If the benefit of therapeutic interventions is to be fully understood, it is important that a range of patient- and caregiver-relevant outcome measures are considered.

From this qualitative research the authors identified a core set of caregiver- and patient-reported outcome measures that could be used as a composite endpoint in DS trials.

Further work is underway to understand the cross-cultural validity of these concepts/outcome measures.

There are in use measures, if appropriate, will be included in a randomised controlled trial for a new pharmacotherapy for DS.