Parental view of epilepsy in Rett Syndrome

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Abstract

Few instruments exist to measure the impact of epilepsy on the quality of life in Rett Syndrome (RS). Methods: We attended to describe seizures characteristics, parental opinion and quality of life related in RS by using a newly developed self administered questionnaire, postal sent to parents of French Association for Rett Syndrome (AFSR). Results: Two-hundred completed questionnaires were returned. Mean age of patients was 14.8 ± 8.1 years [3–42]. Parents reported that 70% of children had epileptic and non-epileptic seizures and mean age at first seizures was 7.3 ± 5.1 years [1–24]. No statistical difference was found between the ages of first seizures, diagnosis of epilepsy and introduction of treatment. Seizures had a negative impact on child and family’s life (68% of cases), strongly correlated to the existence of generalized, prolonged, cyanotic and drug-resistant seizures, on the child’s level of alertness and progress in communication skills and psycho-social consequences such as fear of seizures, and difficulties to find home care aids. Conclusions: We identified major concerns of parents with RS that determine the impact of seizures on children and their family’s quality of life. Our results suggest that in order to improve seizures management in RS, better information should reduce fear about seizures and should improve the quality of life of RS.
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Keywords: Rett Syndrome; Epilepsy; Parental opinions; Quality of life; Questionnaire

1. Introduction

Rett Syndrome (RS, MIM 312750) is a childhood neurodevelopmental disorder of genetic background [1] that affects females almost exclusively. After an early period of apparently normal development (until 6–18 months of life), this disorder results in profound intellectual impairment, reduction of speech, purposeful hand movements and reduced brain growth [2–5].

RS is one of the most frequent causes of mental retardation in females with a prevalence of 0.88 per 10,000 females in 5- to 18-year-olds [6] and an incidence of 0.558–1.09 per 10,000 females by 12 years of age [6,7]. Mutations in the methyl-CpG-binding protein 2 (MECP2) have been identified in 70–90% of RS patients, making this major if not the only cause of RS [5,7–12].

After a few years, RS patients can also develop seizures which may or may not be epilepsy related. EEG is invariably abnormal after about 2 years of age. Vari-
ous seizure types are commonly observed in RS. The prevalence of seizures varies considerably in published reports ranging from 30% to 80%, and it is sometimes difficult to distinguish epileptic from non-epileptic events often associated with RS [13,14].

In daily family life, epilepsy is often a threatening and heavy burden that creates ongoing problems. When epilepsy is diagnosed, parents concerns are mainly concentrate on the impact of epilepsy on the child and her family’s quality of life. Many published reports show that epilepsy affects quality of life of children with epilepsy and their family. However, no quality of life scales are available for mentally retarded children with epilepsy [15,16].

To date, the impact of epilepsy on the quality of life of RS patients and her families has never been studied. In order to provide detailed information on the seizures characteristics and their impact on quality of life in RS, we performed an extensive socio-medical survey among members of the French association for Rett Syndrome (AFSR).

2. Methods

2.1. Study design

A questionnaire designed to elicit responses about epileptic and non-epileptic seizures (hereafter referred to as “seizures”) description and their impact was sent to all members of the French Association for Rett Syndrome (AFSR) network. A list of items describing the types of concerns likely to be experienced by the families in relation to their child’s seizures was developed. Items were selected from the literature [17–19] and interviews with clinicians and parents from the AFSR.

2.2. Sample

The 340 members of AFSR group with a child affected by RS were requested to complete an anonymous questionnaire.

2.3. Demographic and clinical variables

The questionnaire requested information about the diagnosis of RS including the age of the child and the age at diagnosis of RS. Questions were also asked about the age at first seizures and the age at diagnosis of epilepsy. The severity of the seizures was evaluated according to their frequency and duration, and the presence of cyanosis. Based on responses, seizures were categorized as to whether they occurred daily, weekly, monthly or yearly. In relation to treatment, the questions were the age of introduction of treatment, the number of anti-epileptic drugs tried, the number of anti-epileptic drugs that failed.

2.4. Health related quality of life and impact of epilepsy

Parents were asked if seizures had an impact on their child’s life, if they impaired her social skills, prevented her from walking or decreased her activity and interaction with the social environment. They were also asked if seizures affected their family life, were worrying to the family or increased difficulties in finding in home or out of home respite or permanent accommodation. They were asked rate the problem associated with their child’s epilepsy as major, moderate, or unimportant. They were also asked to score seizure control and the response to treatment as very resistant, moderately resistant or less resistant. Finally, they had to assess the quality of information they had been provided in relation to seizures as good, average or poor.

2.5. Statistical analysis

For quantitative variables, medians or means with standard deviation were calculated. For categorical variables, the percentages for each modality were calculated. When the proportion of missing data on a variable exceeded 20%, the variable was excluded from analysis. Multivariate analysis was applied using cross tabulation method and factor analysis. The percentage from maximum deviation, an index of tie between modalities of a contingency table was used to construct profiles, set of modalities of response which were in attraction with a modality with descriptive variables. Comparative tests between groups using the Student’s t test for quantitative variables and the \( \chi^2 \) test for categorical variables were performed.

3. Results

A total of 200 (59%) out of the 340 families completed their questionnaire and mailed it back within the survey period.

3.1. Demographic and clinical variables (Table 1)

The 200 patients had a median age of 13 years [3–42 years] with a quarter older than 20 years. The median age of diagnosis of RS was 6 years [1–29 years] and 40% of the patients were older than 10 years at diagnosis.

Among the 200 questionnaires collected, 31 patients didn’t have seizures and 159 had seizures. Among them, 140 (70%) provided usable information on the “epilepsy” status whereas 16 questionnaires had with missing data, and three with false negative answers after statistical coherence analysis.

First seizures occurred between the age of 1 and 24 years (median 6 years). The majority (54%) had the first seizure before the age of 5 years, 29% between 5 and 10 years, and 15% after 10 years. The diagnosis of epi-
lepsy was more frequently confirmed before 5 years (52%), 37% between 5 and 10 years, and 14% after 10 years, with a median age of 6 years. Just over three quarters of parents (76%) reported that the diagnosis of epilepsy had been easy to make and a half (51%) reported that seizure activity had been recorded on EEG.

Seizures were mostly generalized (64% of cases), usually polymorphic (59%), and reported to be associated with a transient loss of the consciousness by 69% and with cyanosis by 56% of families. Nearly a half (44%) of families reported that seizures were associated with falling. In 46% both day and night-time seizures occurred. Their median duration reached 15 min [range 0.3–120 min]. The median number of seizures per month was 10 [range 1–100]. Seizures were reported to occur daily in 5.7% of patients, weekly in 23% and monthly in 21%. Seizures were mostly irregular in frequency (69%) and tended to persist (63% of children still have fits at a median age of 13 years) despite treatment.

One-hundred and twenty-three children (88%) were on antiepileptic treatment with 73 (52%) on a combination of two anti-epileptic drugs. The mean number of drugs used was 2.39 ± 0.71 [range 1–4]. From the onset of epilepsy and the initiation of the treatment, an average of three anti-epileptic medications had been tried. Fifty-one families provided information on their child’s current treatments. Valproate was used in 56% cases, lamotrigine in 26%, clobazam in 21% and carbamazepine in 18%.

### 3.2. Health related quality of life and Impact of epilepsy into day to day life

Fifty-four percent of the parents reported that seizures represented a major problem for their child, 31% a moderate problem and for 7% they were unimportant. Eighty-five percent of the parents considered that seizures mainly have affected their child’s learning and behaviour with major consequences on their child’s level of alertness (in 49% of cases) and evolution of social skills (in 39%). As for motor function, seizures inhibited their ability to walk in 27% of cases.

Globally, among the 140 responders with seizures, seizures impacted adversely on family life in 68%, with it being considered a major problem for 54% of the families. Seizures created fear (68%), and difficulty in finding a baby-sitter or respite home care aids (55%), but did not generate problems to find a permanent rehabilitation institute (only 15% had problems).

The parents rated their level of information on epilepsy as good (26%), average (46%) and bad (17%). Two-thirds of parents received their information from the doctors, 14% from the parent’s association ASFR and 24% from various sources.

Multivariate analysis showed clearly two typologies of awareness: one with a close association between the severity of the seizures (generalized, prolonged, cyanosis, polymorphic, drug-resistant) and the high impact of epilepsy on the child (developmental consequences of seizures on communication and social skills, level of alertness, and ability to walk), the other with a low severity of the seizures associated with less impact of epilepsy on the family (the fear about seizures, the psycho-social impact such as the difficulties of keeping the child, and the bad quality of the information). Furthermore, the poor level of parents’ information on seizures was also associated with a negative perception of impact of seizures on child’s development and her family.

### 4. Discussion

This is the first study to have systematically examined the impact seizures on quality of life of patients with RS and their families from the parents’ perspective. The results of this study support the fact that seizures associated with RS represent one of the major concerns for the majority of families with a child with RS and that for over half it is a frequent and a worrying problem.

Today, there is increasing awareness of the importance of assessing physical, psychological, social and behavioural well-being in childhood epilepsy [15,16]. Health related quality of life (HRQoL) measurements are essentially subjective and refer to the patient’s (or parents’) perception of well being and functions in terms

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**Table 1**

Sample socio-demographic and clinical characteristics

<table>
<thead>
<tr>
<th>Characteristics (n = 200)</th>
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<tbody>
<tr>
<td><strong>Socio demographic</strong></td>
<td></td>
</tr>
<tr>
<td>Mean age (years)</td>
<td>14.76 ± 8.13 [3–42]</td>
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<tr>
<td>Mean age of diagnosis of RS (years)</td>
<td>8.79 ± 7.32 [1–29]</td>
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<tr>
<td><strong>Epilepsy history</strong></td>
<td></td>
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<tr>
<td>Mean age of first seizures (years)</td>
<td>7.32 ± 5.10 [1–24]</td>
</tr>
<tr>
<td>Mean age at diagnosis of epilepsy (years)</td>
<td>7.44 ± 5.71 [1–37]</td>
</tr>
<tr>
<td>Mean age of first introduction of anti-epileptic drugs (years)</td>
<td>7.25 ± 5.78 [1–37]</td>
</tr>
<tr>
<td>Mean number of anti-epileptic drugs currently used</td>
<td>2.39 ± 0.71 [1–4]</td>
</tr>
<tr>
<td>Mean number of anti-epileptic drugs tried from the beginning</td>
<td>3.36 ± 2.25 [1–12]</td>
</tr>
<tr>
<td>Actual combination of more than three drugs (%)</td>
<td>16.4</td>
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<tr>
<td><strong>Clinical features</strong></td>
<td></td>
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<tr>
<td>Mean number of seizures per month</td>
<td>10 [1–100]</td>
</tr>
<tr>
<td>Mean number of different types of seizures</td>
<td>2.71 ± 0.83 [1–5]</td>
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<tr>
<td>Prolonged seizures &gt;15 min (%)</td>
<td>51.0</td>
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<tr>
<td>Seizures associated with cyanosis (%)</td>
<td>37.1</td>
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<tr>
<td>Seizures resistant to antiepileptic drugs (%)</td>
<td>30.7</td>
</tr>
<tr>
<td>Polymorphic seizures</td>
<td>59.3</td>
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</tbody>
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Quantitative variables are expressed by means ± standard deviation [min – max] or median as indicated.
of physical, mental and social domains. However, these instruments have only been validated for the assessment of HRQoL in epileptic patients without mental retardation of any aetiology. Here, we developed a questionnaire based on a list of concerns that had been developed from parents’ interviews by the French Rett Syndrome Association (AFSR) and clinicians as well as from a review of the literature [17–19]. Therefore items selected for this questionnaire had maximal content validity. However, the main limitation of this survey was that because we used a predefined questionnaire with all parameters studied predefined, there were no open questions which could have provided the opportunity for additional, richer and more explanatory information.

Even though only 59% families mailed back their questionnaire, among these 200 answers, there were a relatively low number of non-responses and little missing or incoherent data. We do not have information on the 41% non-responders, but it might be related to the fact that these children didn’t have seizures and as a consequence, parents didn’t feel concerned with seizures related quality of life. The population of RS studied comes from the French parent support association (ASFR) which is likely to be representative of RS in general. The AFSR association was set up in 1990 and RS children of the member parents comprise a broad range of ages and clinical stages (1–45 years; clinical stages II, III, IV). Since RS was only identified as a disorder in the early 1980s [2,3], diagnosis is likely to have been made relatively late in the oldest girls whose parents are in the ASFR. This probably explains why the age of the population and the age at RS diagnosis are higher in the present study than usually described.

Of our 200 answers, 70% were reported to exhibit seizures. This overall reported prevalence of seizures in our patients was relatively high, considering the great variability epilepsy reported in the literature ranging from 30% to 80% [13,14]. The age of onset of seizure (54% before 5 years) in our group is consistent with previous studies of epilepsy in RS, which show that seizures had a median onset at age 4 years in most patients and below 12 years in 80% [13,14]. Compared with the epilepsies in severe mental retardation in general, this age of onset is a significantly later (4 years in RS versus 0.8 years in mental retardation) [20], but similar to population-based studies of all epilepsy in children aged 3.5–4 years [21]. In our series, 88% of the children with seizures received an anti-epileptic treatment and were most commonly on two anti-epileptic drugs. From the onset of epilepsy, an average of three anti-epileptic drugs had been tried. Based on these data, our patients seem to have more drug-resistant epilepsy than usually described since previous series usually described as 30% used two anti-epileptic drugs and 10% with three anti-epileptic drugs. However, in the same study, 54% of females have intractable and severe epilepsy while in 46% the epilepsy was controlled [13]. Due to the high number of non-responses to the question relating to the names of the medication, our information relating to treatment needs to be treated with caution. To date, no evidence has been provided regarding the superiority of any specific drug or combination of drugs in seizure control in RS [13]. The literature does suggest that generally these commonly used anti-epileptic drugs have little impact on child alertness and behaviour [22,23], that we did not have the capacity to examine in this study.

This survey shows that seizures represent one of the major concerns of parents of RS children. Half the parents claim that seizures represent a major problem. Parameters of severity of seizures are strongly reported as the main cause of impact on quality of life, such as generalization, polymorphism, prolonged duration, the association with cyanosis, and drug resistance. It is important to mention however that these parameters of severity are not correlated with delayed diagnosis of epilepsy or delayed introduction of anti-epileptic drugs. These findings can be compared with parental worries about epilepsy in a healthy child or with epilepsy associated with severe mental retardation. In a healthy child, ongoing seizure activity has major effects on mental health, social functioning, general health perceptions, and epilepsy specific concerns such as seizure worries, medication effects and social functions [15–17,24]. With a severe intellectual impairment such as RS, many of these issues are not relevant and grossly, only epilepsy specific concerns are reported by relatives [25,26]. For example, in Angelman Syndrome, where only one study has reported parental views, the main concerns were the seizure activity and side effects of anti-epileptic drugs on their child’s alertness and behaviour. However, parents were not asked about the impact of epilepsy on either the life of their child or the family [27].

Here, we show that seizures in RS impact adversely on both the child’s and family’s quality of life, especially when seizures are associated with impaired social development and reduced alertness. Parents strongly report that epilepsy is associated with a negative impact on communication and social skills, level of alertness and ability to walk which are often preserved in RS without epilepsy. On the other hand, multivariate analysis of correlated responses demonstrate that these parameters are also associated with parameters that affect the family quality of life such as fear about seizures and the psycho-social impact of epilepsy leading to difficulties in the general management of the child. Finally, poor social outcome is also correlated with bad quality of the information about epilepsy. Theses results suggest that in order to improve epilepsy management in RS, better information should reduce fear about epilepsy and should improve the quality of life of RS with epilepsy.
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References


