Original Communication

Quality of life in patients with benign epilepsy with centro-temporal spikes

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ABSTRACT

Quality of life (QL) in patients with benign epilepsy with centro-temporal spikes (BECTS) is still controversial. Learning disabilities and atypical BECTS could play a significant role in determining unfavourable outcome related to well-being status in these patients. From a cohort of 45 patients with BECTS, diagnosed between 1992 and 2006, we studied long-term outcome (6.8-23.1 years; mean 13.2 years) and QL in 18 patients (4 females, 14 males; mean age 20.1 years) by i) 36-item short form health survey (SF-36) for physical and mental health and ii) semi-structured interview for QL developed using the categories of psychosocial outcomes identified from Wirrell *et al.* and integrated with well-being indicators (BES) elaborated by the Italian institute of statistics (ISTAT). Interview scores were studied according to the main clinical and Electroencephalogram (EEG) variables obtained by non-parametric tests. Seizure remission was confirmed in all patients. SF-36 scores, adjusted for age and sex, were within the average of the Italian population throughout the sample for the physical component, the physical functioning and the role limitations due to physical health (RP), and in most of the patients for mental component (78%) and other scales: bodily pain (72%), vitality (83%), role limitations due to emotional problems (83%), mental health (89%), general health (94%), social functioning (94%). Lower scores for physical component summary were found in patients with atypical BECTS (p = 0.004) and in patients with generalized epileptic EEG abnormalities (p = 0.04); the latter moreover showed lower scores according to general health (p = 0.009) and vitality (p = 0.009). No differences were found according to the other epilepsy variables, learning disabilities, and socioeconomic status of parents. Poor involvement in cultural activities and signs of school maladjustment (grades repeated and suspended from school) were more common in patients with language disorders and learning disabilities and requiring special educational need and/or rehabilitation therapy. In conclusion, whereas mean values of QL scores in most of our patients overlap with those of general population, poorer rates occur in patients with atypical BECTS, generalized epileptic EEG abnormalities, language disorders and learning disabilities.

KEYWORDS: benign epilepsy with centro-temporal spikes, quality of life, prognosis

ABBREVIATIONS

ADHD	:	Attention deficit hyperactivity disorder
AED	:	Antiepileptic drug
BECTS	:	Benign epilepsy with centro-temporal spikes
EEG	:	Electroencephalogram
ESES	:	Electrical status epilepticus during sleep
JRA	:	Juvenile rheumatoid arthritis

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QL	:	Quality of life
SF-36	:	36-item short form health survey
PF	:	Physical functioning
RP	:	Role-physical
BP	:	Bodily pain
GH	:	General health
VT	:	Vitality
SF	:	Social functioning
RE	:	Role-emotional
MH	:	Mental health
PC	:	Physical component
MC	:	Mental component

INTRODUCTION

Benign epilepsy with centro-temporal spikes (BECTS) is the most common idiopathic focal epilepsy in children with well defined electro-clinical feature [1-3]. Seizure onset is between 4 and 13 years in children with normal neurological development. Seizures consist of sensitive-motor signs and symptoms mainly in the orofacial region, usually during sleep. The EEG shows typical epileptic abnormalities characterized by synchronous and asynchronous diphasic high-amplitude spikes and sharp waves in the centro-temporal areas [4]. Atypical BECTS have been long described as characterized by early onset, developmental delay, neuropsychological problems, unusual seizure types (generalized seizures, status epilepticus), and atypical EEG abnormalities [5]. Benign outcome has been widely confirmed according to seizure remission [4-7], while the evolution related to academic achievement and quality of life is still controversial [6, 7]. Unfavourable outcome of the well-being status in these patients may be determined by learning disabilities [6] and atypical BECTS [5]. The aim of this study was to analyse the long-term outcome according to seizure remission, academic achievement and quality of life (QL) in a group of patients with BECTS.

MATERIALS AND METHODS

From a cohort of patients with epilepsy admitted to the epilepsy centre, Department of Pediatrics and Child Neuropsychiatry, Sapienza University of Rome from 1986 to 2012, 46 patients matched with the diagnosis of BECTS. 35 (21 discharged, 14 still followed) of the 46 BECTS patients achieved a follow-up period of at least 6 years;

18 (4 females, 14 males; 11 discharged, 7 still followed) of the 35 selected patients were successfully contacted and agreed for a telephone interview. The interviews were carried out from December 2013 to February 2015. The mean age of the 18 patients at the time of interview was 20.1 years (range 14.2-32.7). Information on seizure remission, academic achievement and QL were collected through 36-item short form health survey (SF-36, Italian version) for physical and mental health [8] and by Wirrell-modified 15-item interview [9]. The socioeconomic level of patients or parents updated at the time of the follow-up was also explored. Informed consent was obtained from all subjects. All phone interviews were conducted by a child neuropsychiatrist (Panunzi. S.).

SF-36 questionnaire

SF-36 for physical and mental health is a short-form health survey with 36 questions and it is derived from the general health survey of the medical outcomes study by Stewart and colleagues [10, 11]. The SF-36 includes 36 items addressing eight health concepts: physical functioning, social functioning, physical role limitations, emotional role limitations, mental health, energy/vitality, pain, and general health. The two summary scores are the physical component and the mental component summary. It is one of the most widely used generic measures of health-related quality of life and has been shown to discriminate between subjects with different severity levels of the epilepsy [12, 13]. SF-36 is also used in follow-up studies for its sensitivity to significant treatment effects in a variety of patient populations [14].

Semi-structured interview for QL

Semi-structured interview was developed using the categories of psychosocial outcomes identified from Wirrell *et al.* [9] and integrated with well-being indicators elaborated by the Italian institute of statistics - ISTAT (Table 1). Two main areas were investigated. Firstly, the possible persistence and the consequent effect of the seizures on the subject's life. The second part examined education and training, jobs and economic well-being, family and social relationships, cultural participation, conduct and legal problems (including substance abuse), and subjective well-being.

Table 1. Psychological variables assessed.

Variables
1. Effects of epilepsy on present life (none, low, moderate, severe)*
2. Occurrence of seizures after discontinuation of therapy (yes, no)
3. Taking antiepileptic drugs after discontinuation of therapy (yes, no)
4. School* - Junior high school - Context class (regular, grate repeated) - Learning difficulties
5. Higher education* - High school - Type - Maturity (diploma, is attending, left) - If you left (diseases, etc.) - University (graduate, is attending university, he left university) - If you left (diseases, etc.) - Postgraduate university courses
6. Behavior* - Ever considered a behaviour problem by parents or teachers, defined as a repetitive and persistent pattern of behavior involving aggression to people or animals, destruction of property, theft, or serious violations of rules - Ever suspended from school
7. Legal problems (yes, charged but no conviction, conviction, no)*
8. For women, previous pregnancy* - If unplanned, age at pregnancy
9. Substance use* - Alcohol use (no, mild/moderate, heavy) - Substance abuse (no, yes)
10. Relations with family and friends* - Relationship with family members (close, normal, distant) - Relationship with friends (many, few, loner) - Satisfaction for family relationships (dissatisfied, fairly satisfied, satisfied, very satisfied) - Satisfaction for friendships (dissatisfied, fairly satisfied, satisfied, very satisfied)
11. Participation and involvement in cultural activities in the 12 months before the interview - Three or more of these activities: cinema, theatre, museums and/or exhibitions, archaeological sites, monuments, classical music concerts, opera, concerts and other music; reading the newspaper at least three times per week; read at least four books; DVD at home at least once a month)

Table 1 continued..

12. Relationship with partner*
- Involvement in a current romantic relationship
- If not, ever involved in previous relationship
- Ever separated or divorced (if applicable)
- Current living arrangements (with spouse or friends, with their parents or alone)
13. Employment*
- At present
- Number of months worked last year
- Type of job
- Job satisfaction
14. Financial security*
- If not a full-time student (self-sufficient, dependent on parents, dependent on partner, or the state)
15. Subjective well-being
- Satisfaction for their own life (0-10)
- Satisfaction for leisure (dissatisfied, fairly satisfied, satisfied, very satisfied)

*Variables reported by Wirrell *et al.* 1997 [9].

The main clinical and EEG data of studied patients are summarized in table 2. Data obtained from the interviews were compared with the following clinical and EEG features: family history for seizures, sex, seizure onset, occurrence of no typical BECTS seizures and/or electrical status epilepticus during sleep (ESES), antiepileptic drug (AED) therapy (number of drugs, duration), time between first and last seizure, seizure free period and drug free period at interview time, generalized EEG epileptic activity, locations of EEG focal epileptic activity other than centro-temporal, side of focus, and EEG epileptic activity evolution. Moreover, patients affected by atypical BECTS were identified according to Callenbach *et al.* [5] on the basis of the following criteria: age at onset < 4 years, developmental delay or learning difficulties at inclusion, other seizure types, and atypical EEG abnormalities.

Associated disturbances were studied according to type (language disorders, learning disabilities, behaviour disturbances), onset (before or after seizure onset) and severity level (rehabilitation therapy, scholastic assistance, disorders pre-existing seizure onset and to repeat classes). Parental socio-economic status was determined by Hollingshead score [15]. Briefly, the Hollingshead index of socioeconomic status, administered to parents, is a survey designed to assess social status in four domains: marital status, retired/employed status, educational attainment, and occupational level. It estimates the position of an individual or a nuclear family in five classes: class 1 (< 19.5); class 2 (20-29.5); class 3 (30-39.5); class 4 (40-54.5); class 5 (> 55). Higher scores correspond to higher socio-economic status.

All statistical analyses were performed using StatSoft Inc. (Tulsa, OK, USA 2010) STATISTICA (data analysis software system), version 9.1 for Windows. Chi square test was used for dichotomous variables, with Yates correction when required. Mann-Whitney nonparametric test and nonparametric correlation analysis (Spearman) were performed for continuous variables. A p value of 0.05 was considered to indicate statistical significance. All enrolled patients or their parents provided informed consent prior to participation, and the study was approved by the institutional review board at Sapienza University of Rome.

Table 2. Clinical and EEG data of studied patients.

Clinical features	Mean ± SD	
Age at first examination	6.6 ± 1.8 years	
Age at seizure onset	6.0 ± 2.0 years	
Age at start of therapy	6.6 ± 2.0 years	
Duration of disease	3.2 ± 1.8 years	
Therapy duration	7.8 ± 2.5 years	
Time of remission	6.5 ± 3.2 years	
Age at remission	9.1 ± 2.3 years	
Seizure-free period	11.0 ± 4.6 years	
Age at AED discontinuation	14.5 ± 2.4 years	
Free-period from therapy	6.4 ± 4.2 years	
Age at the time of interview	20.1 ± 5.5 years	
	N	**%**
Sex (males)	14	78
Family history of epilepsy	11	61
Seizure onset > 4 years	17	95
Secondarily generalized seizures	9	50
IQ		
Normal	14	78
Borderline	4	22
Associated disorders (Language, Learning)	8	44
Preexisting disorders	8	44
Rehabilitation	7	38
Educational support	5	28
EEG features		
Prevailing side of epileptic abnormalities		
Right	9	50
Left	8	44
Bilateral	1	6
Frontal foci	4	22
Other foci	10	55
Occurrence of generalized abnormalities	12	67
ESES	5	28

Table 2 continued..

Epileptic abnormalities at the end of follow-up		
Remission	15	83
Reduction	3	17
Socio-economic status (Hollingshead classes)*		
Class 1	4	22
Class 2	7	39
Class 3	6	33
Class 4	1	6
Class 5	0	--

*Index of Hollingshead, 1975 [15].

RESULTS

All patients confirmed their seizure remission for an average of 11.1 years (range 3.2-20.1 years). At the time of the interview all patients had completed middle school, 11 were still attending high school (3 of them had been repeating a class), 5 had achieved high school title (one also had a degree title) and four of them had a job and 2 were about to leave high school (one of them had a job).

SF-36 scores compared with the normal range of Italian population were within the limits for physical component (PC). 4 patients presented lower scores for mental component (MC). Concerning scale scores, physical functioning (PF) and role limitations due to physical health (RP) were normal for all the patients; scores lower than normal range were found for bodily pain (BP) (5 patients), vitality (VT) (3 patients), role limitations due to emotional problems (RE) (3 patients), mental health (MH) (2 patients), general health (GH) (1 patient) and social functioning (SF) (1 patient) (Table 3). When compared with the clinical and EEG features, lower PC scores were found in patients with atypical BECTS (56.09 *vs* 61.65; p = 0.004). Moreover, lower scores in PC, GH, and VT occurred in patients who had presented generalized EEG paroxysmal activity (PC: 55.97 *vs* 60.03; p = 0.04; GH: 49.17 *vs* 61.50; p = 0.009; VT: 44.41 *vs* 56.67; p = 0.009) (Table 4).

Wirrell-modified 15-item interview results are shown in table 5. Fifteen patients (83%) declared that epilepsy didn't affect their life at all. Scores were very low for the presence of behaviour problems, history of heavy drinking, unplanned pregnancy, and relationship with family and friends. Instead, scores were higher for scholastic problems and academic underachievement. Grade repeated, suspended from school, lower level of participation and carrying out cultural activities were more frequent in patients with language disorders, learning disabilities, rehabilitation therapy and scholastic assistance (Table 6).

DISCUSSION

As expected, all the patients confirmed their seizure-free status at the time of the phone interview. Atypical EEG and clinical findings did not condition the seizure outcome, as stressed by Callenbach *et al.* [5]; moreover, none of the 14 patients with atypical BECTS developed epileptic syndromes connected with BECTS spectrum (Landau-Kleffner syndrome, ESES, etc.).

SF-36 health survey scores were within normal range for age and sex-matched Italian population in all our patients for physical component and for 2 of the 8 scales (PF and RP). While most of them scored normal values on all the other SF-36 items, some of them showed rates below the normal range in mental component and the remaining scales. At the time of the phone interview, 2 patients were

Table 3. SF-36 scores of patients compared with the Italian population.

SF-36 scores	Mean ± SD	Normal* N	< -1 SD* N	< -2 SD* N
PF, Physical functioning	51.22 ± 3.3	18	0	0
RP, Role-physical	52.61 ± 3.7	18	0	0
BP, Bodily pain	48.94 ± 10.9	13	4	1
GH, General health	53.28 ± 10.7	17	0	1
VT, Vitality	48.50 ± 11.0	15	2	1
SF, Social functioning	49.78 ± 6.6	17	1	0
RE, Role-emotional	47.17 ± 10.4	16	2	1
MH, Mental health	52.39 ± 10.8	16	2	0
PC, Physical component	57.33 ± 4.4	18	0	0
MC, Mental component	49.10 ± 8.8	14	2	2

*Comparison with the Italian population, adjusted for age and sex.

Table 4. Clinical and EEG variables significantly related with SF-36 scores.

SF-36 scores	BECTS		p*
	Typical (N 4)	Atypical (N 14)	
PC, Physical component	61.65 ± 4.2	56.09 ± 1.5	0.004
	Generalized epileptic EEG abnormalities		
	No (N 6)	Yes (N 12)	
GH, General health	61.50 ± 6.6	49.17 ± 10.9	0.009
VT, Vitality	56.67 ± 6.1	44.41 ± 10.8	0.009
PC, Physical component	60.03 ± 2.1	55.97 ± 4.7	0.04

*Spearman test.

affected by medium degree of back pain and were impaired both on physical and mental components. When SF-36 scores were matched with clinical and EEG characteristics, significantly different scores were obtained. Physical component scores were lower in patients with atypical BECTS and in patients with generalized EEG paroxysmal activity. Moreover, the latter presented lower scores also for general health and vitality.

As in previous studies [5], atypical BECTS in our study do not affect the final outcome regarding seizure remission. While Callenbach *et al*. [5]

did not refer a poorer general health outcome in atypical BECTS, we found lower SF-36 scores for physical component in these patients. Different measures and methods used in the two studies may justify those differences.

Most of the selected clinical and EEG characteristics did not significantly matched with SF-36 scores. In particular neither associated disturbances nor parent socio-economic status were associated to lower SF-36 Scores.

Concerning academic achievement, all the patients had completed middle school, 5 of them also

Table 5. Replies to the questionnaire.

Variables	Yes	
	N	**%**
1. Effects of epilepsy on present life*	3	17
2. Occurrence of seizures after discontinuation of therapy	0	--
3. Taking antiepileptic drugs after discontinuation of therapy	0	--
4. School*		
- Junior high school	18	100
- Context class (grate repeated)	7	39
- Learning difficulties	8	44
5. Higher education*		
- High school	17	94
- Type (lyceum, technical school, professional school, other)	(6, 6, 5, 0)	
- Maturity (diploma, is attending, left)	(5, 11, 2)	
- If you left (diseases, etc.)	(disease 1)	
- University (graduate, is attending university, he left university)	(1, 0, 0)	
- If you left (diseases, etc.)		
- Postgraduate university courses	1	
6. Behavior*		
- Ever considered a behaviour problem by parents or teachers, defined as a repetitive and persistent pattern of behavior involving aggression to people or animals, destruction of property, theft, or serious violations of rules	2	11
- Ever suspended from school	4	22
7. Legal problems*	1	6
8. For women (n. 4), previous pregnancy*		
- If unplanned, age at the time of pregnancy	0	--
9. Substance use*		
- Alcohol use		
- No	0	--
- Mild/Moderate	6	33
- Heavy	0	--
- Substance abuse	2	11
10. Relations with family and friends*		
- Relationship with family members	16	89
- Relationship with friends	11	61
- Satisfaction for family relationships (dissatisfied, fairly satisfied, satisfied, very satisfied)	(0, 7, 7, 4)	

Table 5 continued..

- Satisfaction for friendships (dissatisfied, fairly satisfied, satisfied, very satisfied)	(0, 6, 5, 7)	
11. Participation and involvement in cultural activities in the 12 months before the interview		
- Three or more of these activities: cinema, theatre, museums and/or exhibitions, archaeological sites, monuments, classical music concerts, opera, concerts and other music; reading the newspaper at least three times per week; read at least four books; DVD at home at least once a month)	14	78
12. Relationship with partner*		
- Involvement in a current romantic relationship	4	22
- If not, ever involved in previous relationship	8	44
- Ever separated or divorced, if applicable (n. 13)	0	--
- Current living arrangements (with spouse, friends, with their parents, alone)	(0, 1, 17, 0)	
13. Employment, if applicable (n. 7)*		
- No (at present)	1	14
- Number of months worked in last year (2, 8, 12)	(1, 1, 4)	
- Type of job (unskilled labor, apprentice, clerk or middle manager, upper-level manager, professional)	(0, 2, 3, 1, 0)	
- Job satisfaction (0-5, 5-10)	(3, 3)	
14. Financial security*		
- (self-sufficient, dependent on parents, dependent on partner, or state)	(4, 14, 0, 0)	
15. Subjective well-being		
- Satisfaction for their own life: (0-5, 5-10)	(2, 16)	
- Satisfaction for leisure: (dissatisfied, fairly satisfied, satisfied, very satisfied)	(1, 10, 5, 2)	

*Variables reported by Wirrell et al. 1997 [9].

completed high school, and 1 of them had graduated; 2 patients had left high school and 5 patients had a job. A longer follow-up period is needed to evaluate further academic outcomes and employment degrees, considering that at time of the phone interview 11 patients from our sample were still attending high school. At the Wirrell-modified interview, most of the patients (83%) declared that epilepsy didn't affect their life at all.

It is well known that BECTS patients may be affected by cognitive problems. Neurodevelopmental disorders are reported in about 40% of patients and include speech sound disorder, language impairment and reading disability [16-20]. In our series, 8 patients (44%) presented learning disabilities. Moreover, other disorders were coexistent in 5 patients (3 language disorders, 1 developmental motor coordination disorder, 2 externalizing problems – attention deficit hyperactivity disorder (ADHD) and oppositional defiant disorder). Seven of them received specific rehabilitation therapies, and 5 of them attended school with the support of special educational interventions.

Table 6. Clinical variables significantly related with items of the interview.

	Grade repeated N (%)	p*
Language disorders		
Yes (n = 5)	4 (80)	0.04
No (n = 13)	3 (23)	
Learning disabilities		
Yes (n = 7)	5 (71)	0.04
No (n = 11)	2 (18)	
Language disorders and Learning disabilities		
Yes (n = 5)	4 (80)	0.05
No (n = 13)	3 (23)	
Rehabilitation therapy		
Yes (n = 7)	5 (71)	0.04
No (n = 11)	2 (18)	
	Suspended from school	
Preexisting disorders		
Yes (n = 8)	4 (50)	0.02
No (n = 10)	0 (--)	
Scholastic assistance		
Yes (n = 5)	3 (60)	0.04
No (n = 13)	1 (8)	
	Poor cultural activities	
Scholastic assistance		
Yes (n = 5)	3 (60)	0.04
No (n = 13)	1 (8)	

*Chi square test with Yates correction.

Wirrell rates on psychosocial outcome items in patients with absence epilepsy and in those with juvenile rheumatoid arthritis (JRA) showed poorer outcome values in epilepsy group [9]. Most of the percentages of the Wirrell items selected for our study rated between the two Wirrell group values [9]. In particular, our percentages were lower than absence group patients and closer to JRA group for behaviour problems, history of heavy drinking, unplanned pregnancy, and relationship with family and friends [9]. Higher scores in these items were significantly related to Wirrell series for patients without remission; long seizure history starting from childhood and going on through adolescence and adult age in unremitted absence seizure patients compared with remitted patients (both our BECTS patients and remitted absence seizure patients) may then influence emotional functioning. Scholastic achievement rates in our sample were close to those of absence seizure patients reported

by Wirrell *et al.* [9]. Thus, the common denominator in these two idiopathic epileptic syndromes of childhood seem to be the possible coexistence of learning difficulties rather than impaired emotional functioning and behaviour problems. Moreover, in the Wirrell study [9], lack of seizure remission did not affect cognitive area; learning disabilities then, seem to be frequently associated with childhood idiopathic epilepsies, but not necessarily related to seizure course.

Among EEG and clinical variables, the only significant differences were found for neuro-psychological disturbances and their severity with scholastic underachievement and also with low level of participation and carrying out cultural activities; no other differences in Wirrell-modified interview results were found regarding neuro-psychological disturbances. In particular, no differences were found for family and social relationships, conduct and legal problems (including substance abuse) and subjective well-being. Moreover no component and scale scores of SF-36 healthy survey were significantly higher when neuropsychological disturbances were present. Thus, in our study, the comorbidity of BECTS with neuropsychological disturbances, even if quite frequent, does not affect general well-being and quality of life. Anyway, it must be mentioned that all the patients with this kind of comorbidity in our cohort were promptly diagnosed and underwent rehabilitation, special education training and whatever they needed in order to cope well with their disabilities. Moreover, all the patients and their parents received psychological support specifically directed to the emotional impact related to epilepsy and associated disturbances, when coexisting.

CONCLUSION

In conclusion, our data confirm the particularly favorable social outcome of BECTS [5, 7, 20, 21]. Since more than half of our patients are still attending high school, further follow-up periods may be useful to confirm the good level of QL over the years.

CONFLICT OF INTEREST STATEMENT

None of the authors has any conflict of interest to disclose.

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