

Use of Paediatric Epilepsy Side Effects Questionnaire (PESQ) for Early Detection of Adverse Effects of Anti-Epileptic Drugs in Children with Epilepsy

Girish Nanoti*, Shantanu Shembalkar**, Prafulla Shembalkar***

Abstract

Objectives: To use the Paediatric Epilepsy Side Effects Questionnaire (PESQ) for identifying adverse effects of anti epileptic drugs (AEDs) in children with epilepsy. **Methods:** Patients meeting the inclusion criteria (patients of epilepsy aged 2-20 years, newly diagnosed, already under treatment) filled the PESQ during their first and subsequent visits. The two sets of data were compared & statistically analysed. **Results:** 57 patients completed the study. The PESQ scores: the total score and the scores of the 5 individual scales were calculated and compared. The occurrence of each adverse effect was noted for the first and subsequent visit. **Conclusion:** the PESQ doesn't take time, is cheap, easy to use for the identification, quantification and assessment of adverse effects.

Keywords: PESQ; Epilepsy; Adverse Effects; Quality of Life (QOL); Paediatric Epilepsy; Epilepsy Questionnaire.

Introduction

Epilepsy is one of the most common neurological disorders in children, and is the third leading neurological cause of disability worldwide [1]. WHO and the international league against epilepsy estimate that 34 million out of 40 million people with epilepsy live in developing countries [2]. Population based studies report prevalence rates of 3.6 to 4.2 per 1000 for children in developed countries [3, 4] and approximately double these in developing countries [5, 6, 7].

Epilepsy treatment is based on antiepileptic drugs (AEDs). The selection of AEDs is based on efficacy and adverse effects. In some patients, multiple AEDs are required. Hence factors like pharmacokinetics, cost and sex are also considered while selecting a

drug [8].

The Food and Drug Administration (FDA) defines an adverse effect as any side effect associated with the use of a drug, whether or not considered related to its mechanism of action [9].

The traditional monitoring method uses repeated serum drug level measurements. The cons of this are:

- 1) In India, facilities for *serum drug level measurements* aren't widely available and are costly. Measurements for newer drugs like Leveteracetam, Clobazam, etc aren't available.
- 2) *Adverse effects don't always correspond with serum drug levels.* Different people have different sensitivities to AEDs. Lower doses might be effective in one person while higher doses might be required, tolerated and be apparently safe in another [10].

Some AED adverse effects like skin rashes, gum diseases can be identified easily [10]. However, many of them aren't as noticeable and are 'subclinical' with their identification relying solely on reporting by the patient. These include cognitive and general neurological effects like memory difficulties and concentration problems. Identification can be hard due to time constraints of the physician and the presence of multiple symptoms. Patients may be reluctant to voice their complaints out of respect for the doctor or worry over being labelled a 'complainer'.

Author Affiliation: *Associate Professor, Department of Paediatrics, NKP Salve Institute of Medical Sciences and research center, Digdoh Hills, Hingna Road, Nagpur 440019, Maharashtra, India. **Student, Lata Mangeshkar hospital and NKP Salve Institute of Medical Sciences and research center, Digdoh Hills, Hingna Road, Nagpur 440019, Maharashtra, India. ***Director of Neurology, Getwell Hospital and research center, Dhantoli, Nagpur 440012, Maharashtra, India

Reprint Request: Girish Nanoti, Plot No.37, Venkatesh nagar, Khamla Road, Nagpur -440025, Maharashtra, India
E-mail: gir65suv@yahoo.co.in

They might confuse an adverse effect with a symptom of the disease [11]. Previous studies have shown that asking direct questions about an adverse effect is more effective than the patient telling about it himself / herself [12].

Detecting the cause of an adverse effect is hard due to co-existing seizure activity, mental health problems and concurrent medications. Thus, a standardized questionnaire to assess AEDs' adverse effects could be helpful. The epilepsy care quality, especially in a developing country like India, can be improved by regular use of a cheap and low-tech method - a side-effects questionnaire [18]. The Paediatric epilepsy side effects questionnaire (PESQ) was designed to do so.

The PESQ has standard terms, measures which quantify adverse effects. In the same way as the number of seizures is used to measure the efficacy of AEDs, the PESQ is used to measure drug toxicity. It is easy, takes a few minutes and when used with other medical information, gives a whole picture of the adverse effects. It was used validly as an AED adverse effect measure [19]. It has 5 scales- cognitive, motor, behavioural, general neurological, weight and a total score. Scores on each scale range from 0 (nonexistent adverse effects) to 100 (high adverse effects).

We plan to study, the possibility of using the PESQ [19] in a clinic and whether it'll improve care and quality of life (QOL) in a cost effective manner.

Objectives

1. To identify, assess and follow up on adverse effects in children with epilepsy using PESQ.

Methods

The *observational prospective cohort study* lasted two months in which an analysis of PESQs of patients (newly diagnosed as well as already taking treatment) coming to the Paediatrics department of Lata Mangeshkar Hospital and Neurology department of Getwell Hospital & Research Institute, Nagpur was done. Ethical clearance from the institutional ethics committee was obtained. The study was completed with 57 patients. A total of 63 patients were taken at the beginning of the study, however 6 of them were excluded due their absence and inability to maintain contact with them.

Inclusion Criteria

1. Age: 2-20 years.

2. Epilepsy patients (newly diagnosed as well as already taking treatment) and attending the paediatrics department of Lata Mangeshkar Hospital and Neurology department of Getwell Hospital, Nagpur.

Exclusion Criteria

1. Patients with febrile seizures.

The Steps in the Study were

- a. History, clinical examination, investigations and treatment details were collected.
- b. Informed consent was taken from the patient if above 18 years of age and from the patient's caretaker if below 18 years.
- c. PESQ was completed by the patient or the caretaker during 2 visits.
- d. The interval between the entry in the study and the exit was 6-8 weeks.
- e. A final assessment was done at the end of the study using standard error of mean^[20].

Results

The study had 57 patients, 13(22.8%) of them were females and 44(77.2%) were males.

The age group distribution is shown in Figure 1.

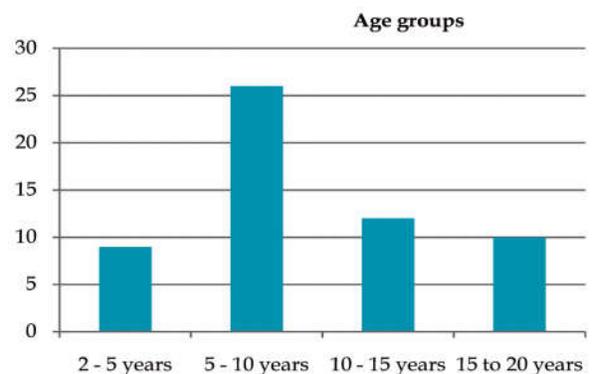


Fig. 1: Age groups of the patients

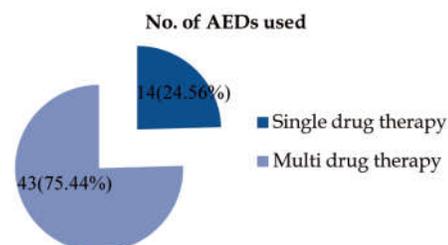


Fig. 2: Multi drug therapy vs. single drug therapy

14(24.56%) patients were on single drug therapy and 43(75.44%) on polydrug therapy (Figure 2).

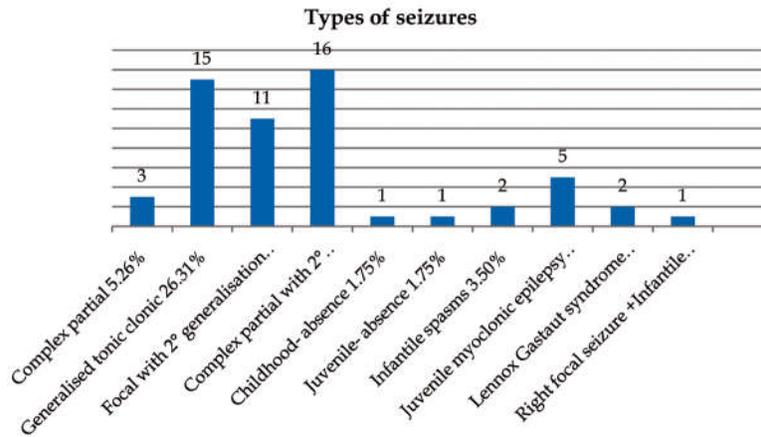


Fig. 3: Types of seizures & their frequency

Table 1: PESQ scores, means, standard deviation, standard Error of mean and significance

	Mean	Standard deviation	Standard error of mean	Significance*
Total score 1st visit**	41.58	46.97	6.22	Yes
Subsequent visit	58.67	44.90	5.95	
PESQ scale 1	Mean	Standard deviation	Standard error of mean	Significance
Cognitive 1 st visit	15.25	17.09	2.26	No
Subsequent visit	15.89	12.13	1.60	
PESQ scale 2	Mean	Standard deviation	Standard error of mean	Significance
Motor (1 st visit)	16.66	25.53	3.38	Yes
Subsequent visit	11.42	19.07	2.52	
PESQ scale 3	Mean	Standard deviation	Standard error of mean	Significance
Behaviour(1 st visit)	15.20	13.43	1.78	Yes
Subsequent visit	24.15	19.74	2.61	
PESQ scale 4	Mean	Standard deviation	Standard error of mean	Significance
General	7.28	8.61	1.14	Yes
Neurological (1st visit)				
Subsequent visit	11.50	11.94	1.50	
PESQ scale 5	Mean	Standard deviation	Standard error of mean	Significance
Weight changes (1 st visit)	4.21	9.43	1.25	Yes
Subsequent visit	11.05	13.45	1.78	

The means and standard deviations for the total PESQ score and 5 scales for the first & subsequent visits are as shown in Table 1.

*If the observed difference between the two means is >1.96 times the standard error of difference, it is

significant and may be due to influence of an external factor [20].

**Total PESQ score is calculated as-((N-19)/95)*100, where N = sum of the scores of all 5 PESQ scales.

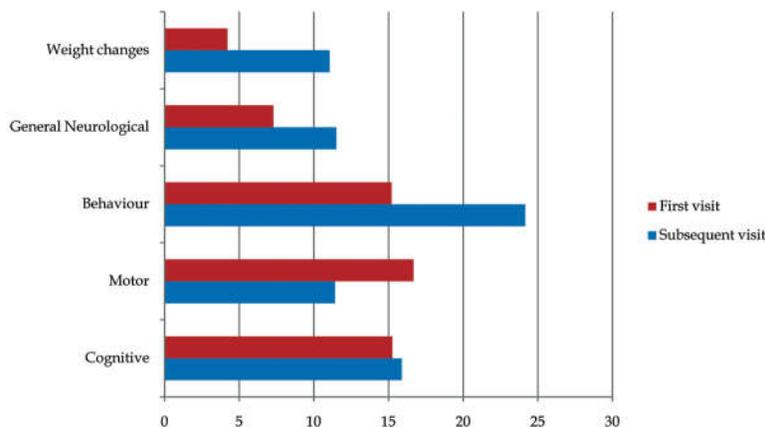


Fig. 4: Mean scores of the 5 PESQ scales: first and subsequent visit

The average total score of the PESQ in the first visit was 41.58(\pm 46.97) and that for the follow up was 58.67(\pm 44.90). The average score for the cognitive scale was not statistically significant, being 15.25(\pm 17.09) for the first visit and that 15.89(\pm 12.13) for the subsequent one. The average score for the motor scale showed a statistically significant drop from 16.66(\pm 25.53) for the first visit to 11.42(\pm 19.07) for the subsequent visit. The average score for the behavioural scale showed a statistically significant

increase from 15.20(\pm 13.43) for the first visit to 24.15(\pm 19.74) for the subsequent visit. The average score for the general neurological scale increased in a statistically significant manner from 7.28(\pm 8.61) for the first visit to 11.50(\pm 11.94) for the subsequent visit. The average score for the weight changes scales showed a statistically significant increase from 4.21(\pm 9.43) for the first visit to 11.05(\pm 13.45) for the subsequent one.

Table 2: Frequency and percentage of adverse effects Adverse effect Frequency & percentage Cognitive 1st visit (no. of patients out of 57) Subsequent visit (no. of patients out of 57)

Cognitive	Adverse effect	1st visit (no. of patients out of 57)	Frequency & percentage Subsequent visit (no. of patients out of 57)
	1.Slow thinking	23 (40.35%)	32 (56.14%)
	2.Memory problems	30 (52.63%)	30 (52.63%)
	3.Confusion	31 (54.38%)	39 (68.40%)
	4.Poor school results	31 (54.38%)	35 (61.4%)
	5.Decreased concentration	27 (47.36%)	33 (57.89%)
	6.Attention difficulties	24 (42.10%)	39 (68.42%)
	Motor	1st visit	Subsequent visit
	7.Unstable walking	23 (40.35%)	13 (22.80%)
	8.Poor coordination, clumsiness	21 (36.84%)	14 (24.57%)
	9.Falling(not seizure)	16 (28.07%)	13 (22.80%)
	10.Speech difficulties	20 (35.08%)	16 (28.07%)
	Behavior	1st visit	Subsequent visit
	11.Agression	44 (77.19%)	42 (73.68%)
	12.Hyperactivity	30 (52.63%)	39 (68.42%)
	13.Personality change	7 (12.28%)	23 (40.35%)
	General neurological	1st visit	Subsequent visit
	14.Drowsiness, sleepiness	17 (29.82%)	25 (43.85%)
	15.Fatigue, tiredness	27 (47.36%)	29 (50.87%)
	16.Dizziness, light headedness	3 (5.26%)	8 (14.03%)
	17.Headaches	20 (35.08%)	17 (29.82%)
	Weight changes	1st visit	Subsequent visit
	18.Increase in appetite	15 (26.31%)	20 (35.08%)
	19.Weight gain	5 (8.77%)	16 (28.07%)

The PESQ not only detects adverse effects but also shows improvements due to AEDs.

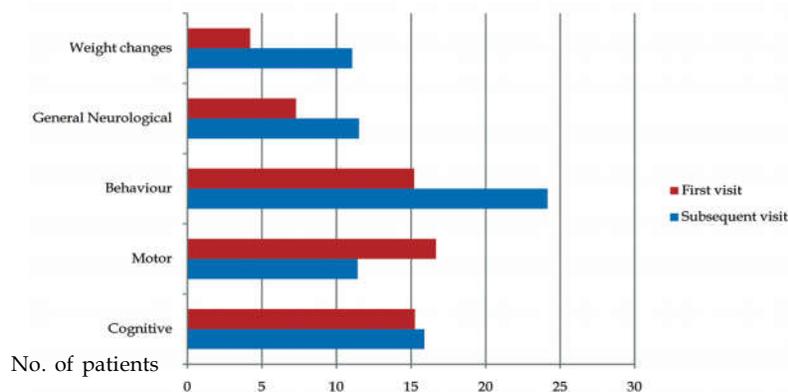


Fig. 5: Cognitive scale: first vs. subsequent visit

The cognitive scale of the PESQ showed increased attention difficulties, decreased concentration, poor

school results, confusion and slow thinking (figure 5).

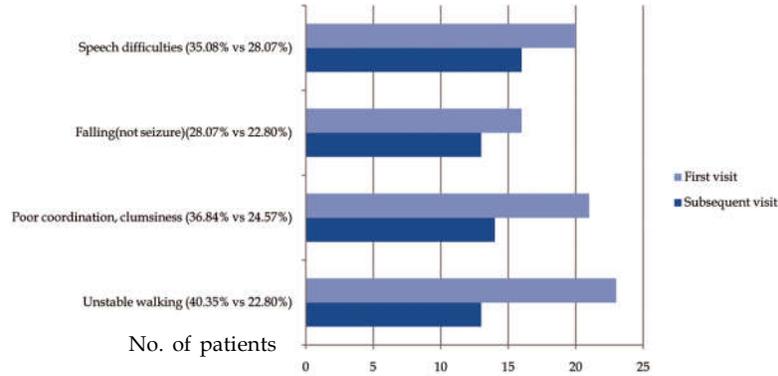


Fig. 6: Motor scale: first vs. subsequent visit

The motor scale of the PESQ showed decreased coordination, clumsiness and unstable walking speech difficulties, falling (not due to seizures), poor (Figure 6).

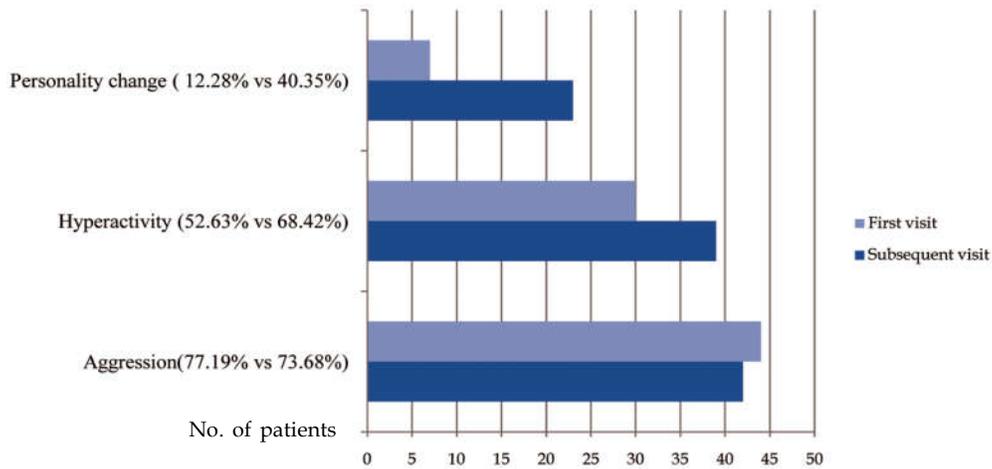


Fig. 7: Behaviour scale: first vs. subsequent visit

The behaviour scale of the PESQ identified slight reduction in aggression (Figure 7). increased personality change, hyperactivity and a

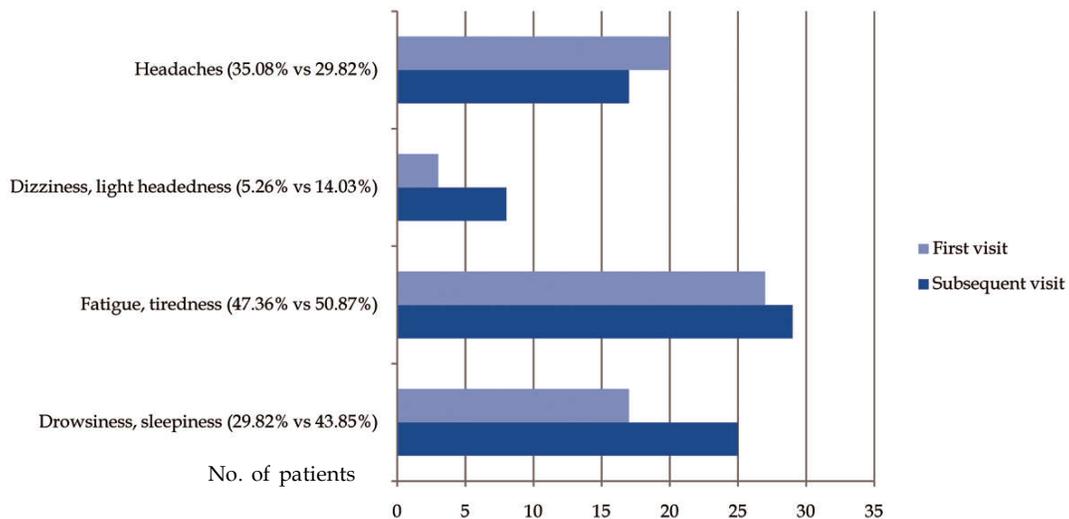


Fig. 8: General Neurological scale: first vs. subsequent visit.

The general neurological scale of the PESQ showed tiredness, drowsiness and sleepiness (Figure 8). reduced headaches and increased dizziness, fatigue,

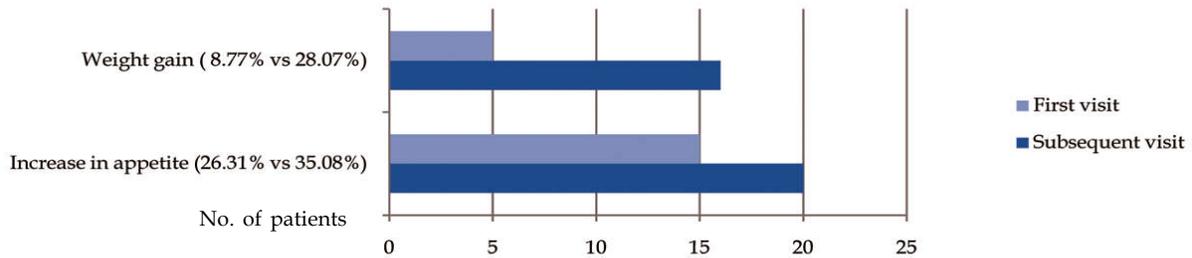


Fig. 9: Weight changes scale: first vs. subsequent visit

Weight gain and an increased appetite were picked up by the PESQ (Figure 9).

Pediatric Epilepsy Side Effects Questionnaire (PESQ)						
Please rate the severity of side effects the patient has experienced during the past 4 weeks by placing an "X" in the appropriate box. Do not include problems related to seizures or long-term problems. Each line should have one and only one mark.						
Side effect related ONLY to seizure medicine	Not present (1)	Low Severity (2)	Low-moderate severity (3)	Moderate severity (4)	Moderate-high severity (5)	High severity (6)
1. Slow thinking						
2. Memory problems						
3. Confusion						
4. Poor school results						
5. Decreased concentration						
6. Attention dif? culties						
7. Unstable walking						
8. Poor coordination, clumsiness						
9. Falling (not seizure)						
10. Speech dif? culties						
11. Aggression						
12. Hyperactivity						
13. Personality change						
14. Drowsiness, sleepiness						
15. Fatigue, tiredness						
16. Dizziness, lightheadedness						
17. Headaches						
18. Increase in appetite						
19. Weight gain						

Scoring for Pediatric Epilepsy Side-Effects Questionnaire (PESQ)

Instructions

Step 1: Item-by-Item Responses

Please check the data for missing responses. If the patient has completed all items, use Worksheet A. If the patient has missing responses, use Worksheet B.

Note: If participants choose multiple response choices for the same question or they skip a

question, do not assign the question a response value (i.e., leave it blank) and consider it missing.

Step 2: Scaled Scoring (if no items are missing-Worksheet A)

Scaled scores are obtained for each domain by using the equations found for each scale. The formula below is used to calculate scaled scores:

$$\text{SCALED SCORES} = \frac{\text{Sum of responses} - \text{Minimal Possible sum (n} \times 1)}{\text{Maximum possible sum (n} \times 6) - \text{Minimum possible sum (n} \times 1)} \times 100$$

Example: For a scale comprising four items, such as the Motor scale of the PESQ, and on the basis of the six-point scale used, the calculation method is:

- Minimum possible sum: 4 items \times 1 point = 4
- Maximum possible sum: 4 items \times 6 points = 24

If the participant who completed the questionnaire obtains 4 points (e.g., 2 points for #7 + 2 points for #8 + 1 point for #9 + 4 points for #10), the result is:

$$\text{SCALED SCORE} = \frac{9 - 4}{24 - 4} \times 100 = \frac{5}{20} \times 100 = 25 \text{ for the Motor scale}$$

Step 3: Missing Values (See Worksheet B)

For all scales, the number of items needed to score the scale is specified. Please follow the directions for Worksheet B to score this measure if items are missing.

Scaled Scores Worksheet A

Cognitive

1. ____
2. ____
3. ____
4. ____
5. ____
6. ____

Cognitive Scaled Score = $(\text{_____} - 6)/30 = \text{___} \times 100 = \text{_____}$
Raw Cognitive Item Total

Motor

7. ____
8. ____
9. ____
10. ____

Motor Scaled Score = $(\text{_____} - 4)/20 = \text{___} \times 100 = \text{_____}$
Raw Motor Item Total

Behavioral

11. ____
12. ____
13. ____

Behavioral Scaled Score = $(\text{_____} - 3)/15 = \text{___} \times 100 = \text{_____}$

Raw Behavioral Item Total**General Neurological**

14. ____
 15. ____
 16. ____
 17. ____

$$\text{General Neurological Scaled Score} = \left(\frac{\text{____} - 4}{20} \right) \times 100 = \text{____}$$

Raw General Neurological Item Total

Weight

18. ____
 19. ____

$$\text{Weight Scaled Score} = \left(\frac{\text{____} - 2}{10} \right) \times 100 = \text{____}$$

Raw Weight Item Total

Total PESQ score:

$$\text{Total PESQ Scaled Score} = \left(\frac{\text{____} - 19}{95} \right) \times 100 = \text{____}$$

Total of All Items

Scaled Scores Worksheet B -MISSING ITEMS

If you are unable to compute the scaled score for a particular scale due to too many missing items, please continue on to the next scale and then follow directions for the Total PESQ scoring.

Cognitive (You must have at least 4 of 6 items)

1. ____
 2. ____
 3. ____
 4. ____
 5. ____
 6. ____

$$\text{Raw Cognitive Total} = \left(\frac{\text{____}}{\text{____}} \right) \times 6 = \text{____}$$

Sum the items / # of cognitive items completed

$$\text{Cognitive Scaled Score} = \left(\frac{\text{____} - 6}{30} \right) \times 100 = \text{____}$$

Raw Cognitive Item Total

Motor (You must have at least 3 of 4 items)

7. ____
 8. ____
 9. ____
 10. ____

$$\text{Raw Motor Item Total} = \left(\frac{\text{____}}{\text{____}} \right) \times 4 = \text{____}$$

Sum the items / # of motor items completed

$$\text{Motor Scaled Score} = \left(\frac{\text{____} - 4}{20} \right) \times 100 = \text{____}$$

Raw Motor Item Total

Behavioral (You must have 2 of 3 items)

11. ____
 12. ____
 13. ____

$$\text{Raw Behavioral Item Total} = \left(\frac{\text{____}}{\text{____}} \right) \times 3 = \text{____}$$

Sum the items / # of behavioral items completed

$$\text{Behavioral Scaled Score} = \left(\frac{\text{____} - 3}{15} \right) \times 100 = \text{____}$$

Raw Teasing Item Total

General Neurological (You must have at least 3 of 4 items)

- 14. ____
- 15. ____
- 16. ____
- 17. ____

Raw General Neurological Item Total: (_____/_____) *4 = ____

Sum the items / # of general neurological items completed

General Neurological Scaled Score = (____ - 4)/20 = ____ × 100 = ____

Raw General Neurological Item Total

Weight (You must have both items)

- 18. ____
- 19. ____

Weight Scaled Score = (____ - 2)/10 = ____ × 100 = ____

Raw Weight Item Total

Total PESQ score (You must have 14 of 19 items)

Raw Total PESQ Item Score: (_____/_____) *19 = ____

Total of All Completed Items / # of all items completed

Total PESQ Scaled Score = (____ - 19)/95 = ____ × 100 = ____

Raw Total Item Total

Discussion and Conclusion

The cornerstone of epilepsy treatment are AEDs. While AEDs play a big role in the control of seizures, their utility might be outweighed by adverse effects. The selection of AEDs is based primarily on efficacy and adverse effects. In some patients multiple AEDs are required which increases the likelihood of adverse effects [21].

Analysis of the adverse effects of AEDs can be hard due to different descriptive terms and difficulty in gauging their severity. The PESQ uses standard terms, quantifies side effects and provides an objective measurement [19].

The various scales of the PESQ contain measures which detect adverse effects. Cognitive adverse effects like slow thinking, poor school results etc are easily identified. A decrease in motor adverse effects like falling (not seizure related), speech difficulties etc was picked up by the PESQ. An increase in behavioural adverse effects like hyperactivity, aggression etc were detected easily by PESQ. A rise in the general neurological adverse effects like drowsiness, headaches etc was ascertained by the PESQ. Weight changes like weight gain and an increased appetite were discerned by the PESQ, showing a significant increase. These adverse effects are seldom reported spontaneously by the patients themselves. As our

results show these effects were routinely detected by the PESQ. Identifying these adverse effects earlier increases the compliance of the patient to the treatment. Thus, using PESQ for the identification of the adverse effects is superior as compared to spontaneous reporting by the patient.

A major strength of the study was the diversity of the patients regarding age, type of epilepsy, time since the start of treatment and number of AEDs used which makes the possibility of generalising the findings greater. The PESQ is not long and hardly takes a few minutes of time.

It can be used as a device to improve treatment too by allowing the physician to choose or adjust the dose of AEDs to lower adverse effects thus improving the QOL.

Despite the widespread use of AEDs, little research has been done to find cost effective methods to identify and reduce the common adverse effects [15] and the impact of them on health and QOL [16, 17].

There are very few studies for paediatric epilepsy questionnaires either. PESQ can fulfil these unmet needs.

Thus, this study shows that use of a standardized questionnaire like the PESQ, which can be performed quickly & easily, is feasible and a simple tool to assess AED adverse effects.

Funding

This study was not funded.

Competing Interests

None

Limitations

1. The study period was short (two months).
2. The sample size was small due to the short study duration (to extrapolate the results, the study period should be longer and the sample size larger).

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