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Original Research Article

Arabic translation and cultural adaptation of Liverpool Adverse Events Profile (LAEP) among a sample of epileptic older adults

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Abstract

Purpose: *To validate and culturally adapt Liverpool Adverse Events Profile (LAEP) in Arabic among a sample of elderly patients with epilepsy.*
Methods: *The face and content validity of the Arabic version of LAEP was ensured by a group of healthcare professionals. Undemented elderly patients (≥ 60 years) with seizure disorders, who are on a single antiepileptic drug (AED), were recruited from two tertiary care centers in Riyadh, Saudi Arabia. Factor analysis was performed to check the construct validity. The reliability was measured using Cronbach's alpha method.*
Results: *Seventy-four patients met the inclusion criteria and were interviewed. Most of the participants had generalized seizures (67.57 %), and were either illiterate or with elementary school education (62.16 %). Their mean age was 68.9 years, and 51.35 % were male. About two-thirds of the participants were on either carbamazepine or levetiracetam (66.22 %). Six factors were extracted from the Arabic version of LAEP. Cronbach's alpha of the Arabic version of LAEP was 0.84. The mean overall LAEP score was 28.9.*
Conclusion: *The Arabic version of LAEP demonstrates good validity and reliability. Similar studies should examine its validity and reliability among different epileptic patient populations.*

Keywords: *Adverse drug event, Epilepsy, Older adults, Cronbach's alpha, Liverpool Adverse Events Profile, Seizure disorders, Carbamazepine, Levetiracetam*

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INTRODUCTION

Epilepsy is one of the most prevalent neurological disorders affecting 70 million people worldwide [1]. Lifetime prevalence rate of epilepsy in developing countries is reported to be almost twice of that in the developed countries (10.4 *vs* 5.8 per 1000 population) [1]. Similar to developed countries in Saudi Arabia, the overall prevalence of epilepsy in 2001 was reported to be 6.54 per 1000 population (95 % confidence interval, 5.48 to 7.60) [2]. The same study reported the prevalence rate in Saudi adults older than 60 years of age to be 5.56 per 1000 population.

Epilepsy is a complex condition which tends to be subject to delays in diagnosis as the

symptoms the patients display may not be always associated with textbook clinical symptoms [3]. This is even more complicated when it comes to older adults as this population is particularly exposed to atypical clinical manifestations [4]. As brain function changes with age, epilepsy episodes become less frequent and may be complicated with uncommon symptoms such as memory loss [5]. Age is a known risk factor for epilepsy with reported annual incidence rate of 10.8/1000 patients in patients older than 65 years [6,7]. The etiology of new onset epilepsy among older adults is usually linked to unknown causes [5]. Other causes could be related to cerebrovascular disease or neurodegenerative diseases (e.g., Alzheimer's) [5,7].

The management of epilepsy in older adults is highly challenging due to a multitude of factors. Drug-related factors that change with age include efficacy, pharmacokinetics, co-medications and medication side effect profiles [4,8]. Indeed, the medication regimen in the geriatric population is often complicated by three main challenges; namely, heightened sensitization to drug action, reduction in physiological elimination function and poly-pharmacy which may lead to drug-drug interactions or reduced drug absorption [9]. All these factors contribute to the increased prevalence of adverse events among the elderly, which is reported to be as high as 30 % [9].

As opposed to drug serum level monitoring, it is now standard to monitor antiepileptic drugs (AEDs) using clinical assessment of seizure and incidence of adverse events [10]. As adverse effect reporting relies greatly on patient reported measures, the best way is to use systemic standardized patient reported measures for AED related symptoms [11]. The Liverpool adverse events profile (LAEP) was developed to assess adverse effects of AEDs [10]. The scale presents several items common with AEDs as a checklist of symptoms reported in the last 4 weeks rated on Likert scale responses. It is composed of 19 questions. The LAEP makes it possible for clinician to capture subjective symptoms reported by the patient in a measurable way [10]. LAEP was developed and validated back in 1994 among English speaking patients with epilepsy in the United Kingdom [12]. However, it was later translated and validated in different countries and languages [13-17]. Although LAEP has been translated and validated for use in some non-English speaking populations [13-17], to our knowledge, there are no studies reporting the use of LAEP in Arab populations. The aim of this study was to translate, validate and use LAEP in the geriatric population with epilepsy in Saudi Arabia.

METHODS

Instrument and measurement

LAEP is a 19-item self-reported questionnaire, designed to measure the frequency of AEDs side effects experienced by epileptic patients within the past 4 weeks. LAEP covers both CNS and non-CNS related adverse effects, scored on 4-point Likert scale as follows: 1 (always a problem), 2 (rarely a problem), 3 (sometimes a problem) and 4 (never a problem). The total scores range from 19 to 76; scores ≤ 45 indicates mild to moderate adverse effects, and reaches the toxic level if the total score exceeds 45 [18-20].

LAEP translation and validation

The LAEP was first forward translated by a bilingual healthcare professional whose native language is Arabic. The Arabic version of LAEP was then backward translated by another bilingual healthcare professional whose native language is English. No significant differences were found in the backward translated version and the original English version. The Arabic version of the LAEP was then reviewed by two health outcomes researchers and a neurologist for face and content validity. The final Arabic version of LAEP was then approved by all the research team after addressing all the comments. The reliability of LAEP was checked using the Cronbach's Alpha method. The international approved guidelines for translation, adaptation, and validation of self-reported screening instruments were adhered to in this study [21].

Data collection

A medical chart review was performed in the departments of neurology at two tertiary care centers in the city of Riyadh, Saudi Arabia. Patients were considered eligible for inclusion in the study if they were diagnosed with seizure disorders regardless of the seizure type, aged ≥ 60 years, cognitively able, and on a single AED. Eligible patients were then contacted by three healthcare professionals to get their consent for a telephone interview after explaining the study's objectives. Once the patients consented, they were interviewed. The interview included questions about patients' sociodemographic (e.g., age, gender and education), and clinical characteristics (e.g., type of seizures & antiepileptic drug used) besides LAEP questions.

Ethical approval

The study was approved by King Saud University College of Medicine and King Faisal Specialist Hospital and Research Center institutional review boards in Riyadh, Saudi Arabia. For ethical reasons, the data were code, and no patient identifiers were used. The study complied with the guidelines of Declaration of Helsinki (DOH) ethical standards for medical research [22].

Statistical analysis

Descriptive statistics were conducted using t-test and Chi-square test. Factor analysis was also conducted to explore the number of factors that can be extracted from the Arabic version of LAEP. Statistical significance was defined by $p < 0.05$. All analyses were performed using a statistical software (SAS, version 9.2, SAS Institute Inc, Cary, NC, USA).

RESULTS

Out of 131 patients, who met the inclusion criteria and were contacted, 74 patients (56.5 %) consented to participate in the study and were interviewed. The mean age of participants was 68.9 years. Approximately, 50 % of the participants were male and illiterate. Almost 26 % of the participants experienced at least one seizure episode within the past 6 months, however, the majority were seizure free. About two-thirds of the participants had generalized seizures and the remaining had partial seizures. Most of the participants were on either carbamazepine (36.49 %) or levetiracetam (29.73 %). Participants' characteristics are shown in Table 1.

The frequencies of the adverse AED effects based on LAEP are shown in Figure 1. Adverse effects that were reported as always or sometimes on the LAEP were as follows: Disturbed sleep (29.73 %), upset stomach (25.67 %), aggressiveness (22.98 %), sleepiness (22.79 %), Memory problems (20.27 %), headache (20.27 %), nervousness (18.2 %), weight gain (18.2 %), hair loss (17.57 %), depression (17.57 %), restlessness (16.22 %), difficulty in concentration (16.22 %), unsteadiness (12.17 %), blurred vision (10.82 %), trouble with mouth or gum (10.81 %), shaky hands (9.46 %), tiredness (8.1 %), skin problems (6.75 %), and dizziness (5.4 %). The mean scores of LAEP items are presented in Table 2. The overall mean score of LAEP was 28.9, ranging between 19 and 56.

Table 1: Sociodemographic and clinical characteristics of participants

Characteristic	Participants (n=74)
Age (yr)	68.9 ± 7.4
Gender	
Male	38 (51.35)
Female	36 (48.65)
Education	
Illiterate	37 (50)
Elementary school	9 (12.16)
Intermediate school	4 (5.41)
High school diploma	8 (10.81)
Associate degree	7 (9.46)
Bachelor degree or more	9 (12.16)
Experienced seizures in the past 6 months	19 (25.68)
Type of seizure	
Generalized	50 (67.57)
Partial	24 (32.43)
Antiepileptic drug (AED)	
Phenytoin	12 (16.22)
Carbamazepine	27 (36.49)
Valproic acid	11 (14.86)
Lamotrigine	1 (1.35)
Levetiracetam	22 (29.73)
Topiramate	1 (1.35)

Data are expressed as mean ± standard deviation for age and in frequency and percentage for other variables

Table 2: Mean score of LAEP items

Adverse effect	Mean ± SD
Unsteadiness	1.5 ± 0.8
Tiredness	1.3 ± 0.7
Restlessness	1.5 ± 1.0
Feelings of anger or aggression to others	1.7 ± 1.0
Nervousness and/or agitation	1.6 ± 0.9
Headache	1.6 ± 0.9
Hair loss	1.5 ± 0.9
Problems with skin	1.3 ± 0.7
Double or blurred vision	1.4 ± 0.8
Upset stomach	1.7 ± 1.1
Difficulty in concentrating	1.5 ± 1.0
Trouble with mouth or gums	1.3 ± 0.8
Shaky hands	1.4 ± 0.8
Weight gain	1.6 ± 1.0
Dizziness	1.2 ± 0.6
Sleepiness	1.8 ± 1.2
Depression	1.5 ± 1.0
Memory problems	1.6 ± 1.0
Overall score	***28.9 ± 8.9***

Using factor analysis, six factors were extracted using the eigenvalue cutoff point of ≥1 (Figure 2). The factors were labelled as follows: (1) Psycho-motor symptoms (dizziness, unsteadiness, headache, hair loss, and upset stomach); (2) Neuro-somatic symptoms(double or blurred vision, memory problems, problems with skin,

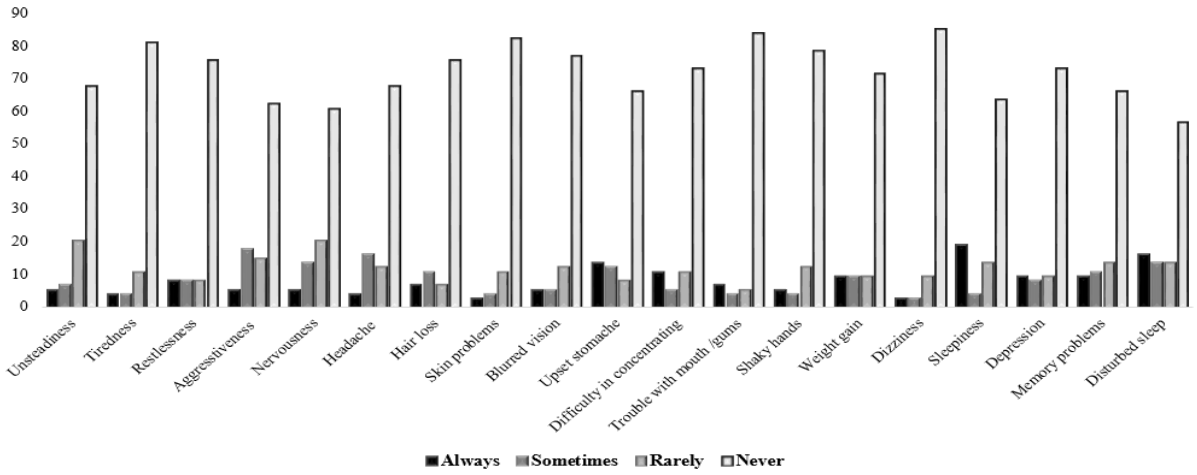

Figure 1: Frequency of AED adverse effects based on LAEP scale

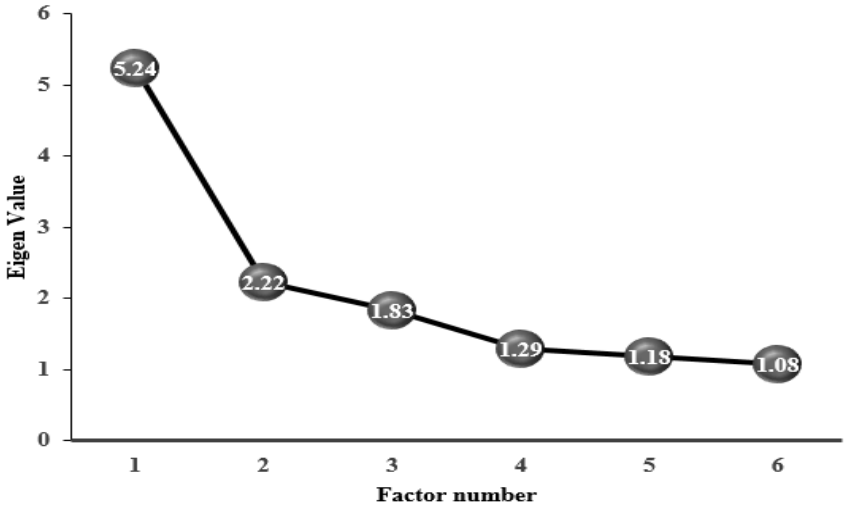

Figure 2: Scree plot of the number of factors that can be extracted from the Arabic version of LAEP and their Eigen values

and trouble with mouth or gums); (3) Behavioral symptoms (feelings of anger or aggression to others, and nervousness and/or agitation); (4) Mental disturbance symptoms (tiredness, disturbed sleep, depression, and restlessness) (5) Hypersomnia symptoms (weight gain and sleepiness); and (6) dementia-like symptoms (shaky hands and difficulty in concentrating). The Kaiser-Meyer-Olkin measure of sampling adequacy suggested that the study sample was factorable (KMO = 0.67). The internal consistency of the Arabic version of the LAEP was good (Cronbach's alpha = 0.84). Table 3 shows the names of the extracted factors with their items, eigenvalues, and communalities.

DISCUSSION

For many decades, therapeutic drug monitoring (TDM) has been and still the cornerstone in optimizing the dosage regimen of AEDs in order to control seizures and minimize their side effects [22]. However, with the advent of the patient-centered care era, which has been taking root recently, healthcare researchers and providers alike are beginning to believe more in patient reported outcomes (PROs) [23]. Questionnaires and scales that measure patients' experiences with different treatment strategies including medications are gaining ground in clinical practice over the last two decades [24]. Questionnaires such as the LAEP that quantify patients' perceptions and experiences with medications in primary care are widely used nowadays [10-12]. In this study we aimed to translate and validate for the first time the LAEP in Arabic, which is a widely used questionnaire to quantify patients' experienced side effects with AEDs. However, we decided to focus on the geriatric patient population (≥ 60 years) due to the fact that this segment of patients is largely ignored and faces tremendous problems with

Table 2: Extracted factors from Arabic version of LAEP

Adverse effect	Factors						Communalities (h2)
	Psycho-motor symptoms	***Neuro-somatic symptoms***	***Behavioral symptoms***	***Mental disturbance symptoms***	***Hypersomnia symptoms***	***Dementia-like symptoms***	
Dizziness	0.76						0.67
Unsteadiness	0.73						0.67
Headache	0.69						0.62
Hair loss	0.68						0.58
Upset stomach	0.67						0.66
Double or blurred vision		0.79					0.74
Memory problems		0.71					0.58
Problems with skin		0.66					0.67
Trouble with mouth or gums		0.65					0.73
nervousness and/or agitation			0.95				0.93
Feelings of anger or aggression to others			0.94				0.94
Tiredness				0.69			0.62
Disturbed sleep				0.67			0.48
Depression				0.59			0.59
Restlessness				0.47			0.51
Weight gain					0.76		0.65
Sleepiness					0.75		0.64
Shaky hands						0.87	0.81
Difficulty in concentrating						0.46	0.73

medication adherence especially AEDs as well as in communication with healthcare providers [25]. Further, elderly patients may become more susceptible to the adverse effects of medications due to their diminished physical reserve [7-8].

Similar to previous studies, the Arabic version of the LAEP demonstrated good reliability (Cronbach's alpha = 0.84) [13-17]. In addition, the face and content validity was checked by multiple healthcare professionals and deemed to be good. However, six factors were retained from the factor analysis that was performed to check the construct validity of the Arabic version of LAEP contrary to Baker *et al* and other validation studies that retained 3 factors only [13-17]. This could be explained by language differences and the fact that only elderly patients were included in the study.

In this study, the lowest and highest LAEP scores were 19 and 56, respectively. However, the mean LAEP score was 28.9, which is significantly lower than the ones reported in other studies, and suggests that the majority of patients in the study experienced low grade adverse AEDs effects [13-17]. This can be due to the fact that only patients on a single AED were included in the study as well as the tolerance to the AEDs adverse effects that patients might have developed over the years of treatment. Disturbed sleep, upset stomach, aggressiveness, sleepiness, memory problems and headache were the most commonly reported symptoms among more than 20 % of the participants.

Limitations of the study

Although this study is the first to validate the LAEP in Arabic, it has several limitations. First, only patients on a single AED were included in the study. Second, the study was limited to elderly patients (≥ 60 years) only. Third, the sample size of the study is small. Therefore, the results of this study have limited generalizability.

CONCLUSION

An Arabic version of LAEP has been has been established. It demonstrates good validity and reliability and makes it easier to screen Arabic speaking epileptic patients for common side effects of AEDs. Future studies should examine the validity and reliability of the Arabic version of LAEP among different epileptic patient populations.

DECLARATIONS

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Conflict of Interest

No conflict of interest associated with this work.

Contribution of Authors

The authors declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by them.

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