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Brief Communication

Translation, cross-cultural adaptation, and validation of the Bulgarian version of the Liverpool Adverse Event Profile

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ABSTRACT

Background: Adverse effects (AEs) of antiepileptic drugs (AEDs) affect the quality of life of patients with epilepsy and their outcomes. There are no questionnaires or studies on the reliability and validity of instruments measuring AEs of AEDs in patients with epilepsy in Bulgarian language.
Purpose: The aim of the present study was the translation, cross-cultural adaptation, and validation of the LAEP in the Bulgarian language in order to use it in the Bulgarian-speaking population in providing a reliable instrument for the clinical monitoring of patients with epilepsy.
Methods: One hundred thirty-one patients (57 men and 74 women, mean age: 40.13 ± 13.37 years) took part in the investigation. The internal consistency and test–retest reliability were tested by Cronbach's α and ICC estimations. The convergent construct validity was tested by estimating the correlation of the LAEP-BG with the QOLIE-89 and the discriminant validity by evaluating the difference between LAEP-BG scores and clinical parameters such as the type of epilepsy using Kruskal–Wallis ANOVA.
Results: The LAEP-BG showed high internal consistency and reliability. The Cronbach's α of the total scale was 0.86. No significant differences between the Cronbach's α coefficients of the total LAEP-BG and original English, Chinese, Spanish, Korean, and Portuguese–Brazilian versions of the questionnaire were observed. The ICCs, which evaluate the test–retest reliability, were higher than the recommended value of 0.75 and determined the strong positive correlations between the first and second examinations. The creation of two subscales "Neurological and psychiatric side effects" and "Non neurological side effects" of the LAEP-BG proposed by us showed good internal consistency (Cronbach's α of 0.85 and 0.71, respectively). The LAEP-BG scores significantly correlated with other questionnaires such as the Quality of Life in Epilepsy Inventory—89 (QOLIE-89) and showed a good discriminative validity between groups with different levels of self-assessed AEs of AEDs.
Conclusion: The Bulgarian version of the Liverpool Adverse Event Profile (LAEP) is a reliable and valid tool in assessing the patient-reported AEs of AEDs and their impact on the patient's outcome.

1. Introduction

Epilepsy is a multifaceted chronic disorder with diverse and complex effects on the QOL of the patient [1]. High rates of AEs and intolerability of AEDs are important predictors of poor QOL in epilepsy and patients' outcome [2]. There are many studies on AEs of AEDs and instruments used to evaluate them [3–9]. According to the literature, the LAEP questionnaire is one of the standardized instruments to assess patient-reported AEs of AEDs. The LAEP is an instrument to measure the total side effects of a medication regimen and to quantify patients' perceptions of the most common negative side effects of AED treatment [3,10]. There are valid and available versions of the LAEP in the English, Spanish, Chinese, Korean, and Portuguese languages [3,11–14]. Questionnaires or studies on the reliability and validity of instruments measuring AEs of AEDs in patients with epilepsy in Bulgarian language do not exist.

The aim of the present study was the translation, cross-cultural adaptation, and validation of the LAEP in the Bulgarian language in order to use it in the Bulgarian-speaking population in providing a reliable instrument for the clinical monitoring of patients with epilepsy.

2. Methods

The study group consisted of 131 consecutively enrolled patients out of a total of 449 screened patients from the Epilepsy Department of the University Hospital of Neurology and Psychiatry "St. Naum", Sofia, Bulgaria. The patient selection was based on several criteria: (1) diagnosis of epilepsy according to the ILAE criteria for more than 1 year; (2) age of more than 18 years; (3) lack of cognitive impairment, tested with a Mini-

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Mental State Examination score ≥ 28 when used as a screening scale, and sufficient reading ability; and (4) stable doses of antiepileptic drugs (AEDs) for at least 3 months prior to study entry. Patients with another progressive neurological or psychiatric disease or some other chronic severe physical comorbidity (diabetes, asthma, or heart, renal, or hepatic failure, etc.) on stable concomitant medication were excluded from the investigation.

All subjects were volunteers and gave a signed informed consent to participate in the study, which was approved by the local Ethics Committee of Medical University — Sofia and conducted in accordance with the ethical standards of the Declaration of Helsinki. The participants were free to withdraw from the study at any time. All patients were asked to fill out two questionnaires: the LAEP-BG scale and the Bulgarian version of the QOLIE-89 questionnaire validated by Viteva et al. [15].

The Bulgarian version of the QOLIE-89 consists of 89 questions divided into seventeen domains: seizure worry, medication effects, health perceptions, health discouragement, work/driving/social function, language, attention/concentration, memory, overall QOL, emotional well-being, role limitations: emotional, role limitations: physical, social isolation, social support, energy/fatigue, physical functioning, and pain.

The original LAEP scale consists of 19 questions that are presented as a checklist of symptoms experienced in the past 4 weeks, rated using Likert scale responses [16]. With the consent of the author, the original English version of the LAEP questionnaire was translated into Bulgarian by two independent medical experts with very good knowledge of English and good experience in adaptation of clinical tests. It was afterwards retranslated into English by two independent translators who were unaware of the original LAEP version. No major differences between the two translations were found. In order to identify problems in comprehension or cultural specificities, the preliminary Bulgarian version of the LAEP which was edited according to the rules of the Bulgarian language was administered to a pilot sample of ten patients with epilepsy attending the clinic. All questions were well-accepted. The patients filled in the final questionnaire in the hospital in our presence. They understood all the items and did not find any difficulty in answering the questions.

After performing and evaluating the pilot study, we came to the conclusion that three of the items should be modified so that the inventory would become better for our purpose. First, we observed that the word "unsteadiness" had to be changed to "instability". Second, the word "aggression" was replaced by "feeling of anger or aggression". Third, "nervousness" was replaced by "nervousness and/or agitation". The panel of the same experts who participated in the previous phase discussed that no further adaptations were required.

Descriptive statistics were used for calculating the mean scores of the LAEP scale and demographic data. The score distribution of each item was evaluated for investigating the possible ceiling and floor effects (proportions of patients with the best and worst possible scores). The internal consistency of the LAEP scale was determined by estimating the Cronbach's α coefficient. In general, Cronbach's $\alpha > 0.7$ (Nunnally's criterion) indicates high levels of internal consistency [17–19].

The test–retest reliability was evaluated by calculating ICCs. In general, values above 0.75 are indicative of reliability. The Mann–Whitney *U*-tests were used for the estimation of differences between correlation coefficients of items in Bulgarian and other language versions of the scale, where the correlation coefficients were transformed by Fisher transformation.

The convergent construct validity was tested by estimating the correlation of the LAEP-BG with the QOLIE-89 and the discriminant validity by evaluating the difference between LAEP-BG scores and clinical parameters such as the type of epilepsy using Kruskal–Wallis ANOVA.

The analyses were made using the computer software Statistica 8.0 for Windows (StatSoft Inc., USA).

3. Results

The average age of the patients was 40.13 ± 13.37 years, the mean duration of the disease was 15.61 ± 9.45 years, 43.5% were male, and the education level of 89% was relatively high (secondary school — 52% and university education — 37%). The patients with idiopathic epilepsy comprised 19.8% of the sample, with cryptogenic epilepsy 45.8%, and with symptomatic epilepsy 34.4%.

All patients completed the LEAP questionnaire manually, and missing information on any of the items was not observed (analysis of missing data not supplied). The patients declared that all questions were clearly defined and that they had not encountered difficulties in completing the questionnaire.

We used the original questionnaire with 19 items and created three subscales of items in accordance with the classification of Chen et al. [12]: "CNS dose-related side effects," "Non CNS dose-related side effects," and "Psychiatric side effects." The "CNS dose-related side effects" subscale contained 10 items: unsteadiness, tiredness, headache, double/blurred vision, difficulty in concentrating, shaky hands, dizziness, sleepiness, memory problems, and disturbed sleep (theoretical summary score range of 10–40 points). The "Non CNS dose-related side effects" subscale consisted of 5 items: hair loss, skin problems, upset stomach, trouble with mouth/gums, and weight gain (theoretical score range of 5–20 points) and "Psychiatric side effects" 4 items: restlessness, feelings of aggression, nervousness/agitation, and depression (theoretical score range of 4–16 points).

The Cronbach's α of the total scale was 0.86, which indicates high levels of internal consistency. The Cronbach's α values of the three subscales were as follows: "CNS dose-related side effects" — 0.85, "Non CNS dose-related side effects" — 0.71, and "Psychiatric side effects" — 0.44. The Cronbach's α of the third subscale was <0.7 and showed a low internal reliability of this subscale. That was the reason for creating two subscales of the LAEP-BG: the first one consisted of the "CNS dose-related side effects" and "Psychiatric side effects", which are united and named "Neurological and psychiatric side effects" (14 items, theoretical score range of 14–56 points) and the second subscale was the "Non neurological side effects" (5 items, theoretical score range of 5–20 points). The two subscales had good internal reliability. The Cronbach's α for the "Neurological and psychiatric side effects" subscale was 0.85 and for the "Non neurological side effects" subscale 0.71. No significant differences were observed between the Cronbach's α coefficients of the total scale of LAEP-BG and original English (0.89) [3], Chinese (0.92) [12], Spanish (0.84) [11], Korean (0.9) [13], and Portuguese–Brazilian (0.9) [14] versions of the questionnaire. The range of observed scores was 19–66 (theoretical range: 19–76).

Out of 131 patients, 2% had a score of 19 points and 1% had a score of 66 points. Forty-three percent had a score higher than 45 points. The results demonstrated no obvious floor and ceiling effects.

The mean scores, medians, and test–retest reliability of the LAEP-BG determined with the ICCs were presented in Table 1. The ICCs, which evaluate the test–retest reliability, were higher than the recommended value of 0.75 and showed strong positive correlations between the first and second examinations, which prove the reliability of the scale (Table 1).

The convergent construct validity of the LAEP-BG scores for the "Neurological and psychiatric side effects" subscale was high, which demonstrates good reliability of the results related to this category of negative effects of the disease (Table 2).

The Kruskal–Wallis ANOVA with three levels (idiopathic, cryptogenic, and symptomatic types of epilepsy) showed a significant effect in relation to the type of epilepsy on the LAEP-BG total score ($H(2,131) = 6.552$, $p < 0.05$). A post hoc Mann–Whitney *U*-test showed a significant difference of the total LAEP-BG scores between patients with idiopathic and symptomatic types of epilepsy ($p < 0.05$). The results suggest that LAEP-BG score shows good discriminative validity between groups with different types of epilepsy.