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Combined detection of depression and anxiety in epilepsy patients using the Neurological Disorders Depression Inventory for Epilepsy and the World Health Organization well-being index

Christian Pilebæk Hansen *, Moshgan Amiri

Copenhagen University Hospital of North Zealand, Department of Neurology, Dyrehavevej 29, DK-3400 Hillerød, Denmark

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ABSTRACT

Purpose: To validate the Danish version of the Neurological Disorders Depression Inventory for Epilepsy (NDDI-E), and compare it with the World Health Organization index for psychological well-being (WHO-5) as screening tests for depression and anxiety in epilepsy patients.
Methods: Epilepsy outpatients filled out NDDI-E and WHO-5. A Mini International Neuropsychiatric Interview (MINI) as gold standard for psychiatric diagnoses was carried out with every patient.
Results: We included 124 epilepsy patients. According to MINI, 5% had depression without anxiety, 6% anxiety without depression, and 6% had both. For the detection of depression, NDDI-E was slightly better than WHO-5. With a score of more than 13, NDDI-E as a screening tool for depression had a sensitivity of 0.92, a specificity of 0.84, a positive predictive value (PPV) of 0.40, and a negative predictive value (NPV) of 0.99. In the detection of anxiety WHO-5 was better than NDDI-E. With a score below 50, WHO-5 as screening for anxiety had a sensitivity of 0.80, a specificity of 0.92, PPV 0.57, and NPV 0.97. When combining NDDI-E $>$ 13 and WHO-5 $<$ 50, 95% of patients with depression and/or anxiety are identified, and in addition there are 17% false positives.
Conclusion: NDDI-E in Danish is valid and slightly better than WHO-5 in the detection of depression in epilepsy patients. WHO-5 is valid for the detection of anxiety disorders. Combined use of NDDI-E and WHO-5 is recommended, since 95% of all epilepsy patients with depression and/or anxiety disorder are identified with only a modest number of false positives.

1. Introduction

In the treatment of epilepsy patients the relatively frequent occurrence of depression and anxiety often go unnoticed and therefore untreated [1–3]. In order to discover depression in epilepsy patients, the Neurological Disorder Depression Inventory for Epilepsy (NDDI-E) has been developed [4]. NDDI-E has been translated from English to other languages and validated as a screening tool for depression in epilepsy patients [5–15]. Recently, we published a Danish translation of NDDI-E [16]. The first purpose of the present study was to validate the Danish NDDI-E.

WHO-5 is a questionnaire with five positive statements, which measure mental well-being in the past two weeks [17]. WHO-5 has a value between 0 and 100. In a population study WHO-5 was in average 70, whereas depressive patients had a mean score of about 30 [17]. The second purpose of the present study was to examine WHO-5 as a screening test for depression and compare it with NDDI-E in epilepsy patients.

Anxiety, like depression, is also a relatively frequent companion of epilepsy [3], but detection of anxiety may be more difficult in epilepsy patients because no epilepsy specific inventory for anxiety exists. Furthermore, there are several different anxiety disorders including panic disorder, agoraphobia, social phobia, and generalized anxiety. The third purpose of our study was to investigate whether WHO-5 or NDDI-E could be used in the detection of anxiety disorders in patients with epilepsy.

The fourth and final purpose of the study was to investigate if a combination of NDDI-E and WHO-5 would be better than either test alone in the identification of both depression and anxiety disorders in epilepsy patients.

* Corresponding author. Tel.: +45 23 10 55 83.
E-mail address: Christian.pilebaek.hansen.01@regionh.dk (C.P. Hansen).

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2. Methods

2.1. Subjects

Adult patients with epilepsy treated at the epilepsy outpatient clinic, Department of Neurology, University Hospital of North Zealand, Hillerød, were included from October 1st 2013 to April 30th 2015. The inclusion criteria were as follows: age 18 years or above, diagnosis of epilepsy according to criteria by the International League Against Epilepsy, MRI or CT scan of the brain, EEG, treatment with at least one antiepileptic drug in a constant dose in the previous month, and the ability to read and speak Danish. Exclusion criteria were severe medical or psychiatric comorbidity and inability to read and/or speak Danish.

2.2. Flow of patients

All patients received oral and written information. After informed consent to participate in the study, patients were given the following self-report inventories:

- Neurological Disorder Depression Inventory for Epilepsy (NDDI-E)
- World Health Organization Well-being Index (WHO-5)
- Major Depression Inventory (MDI)
- Anxiety Symptom Scale (ASS)

2.3. The Mini International Neuropsychiatric Interview version 5.0.0 (MINI)

The patients included in the study returned to the outpatient clinic for a focused neuropsychiatric interview. A Danish version of the Mini International Neuropsychiatric Interview version 5.0.0 (MINI) was used. MINI is a validated interviewer-administered, structured, diagnostic psychiatric interview for DSM-IV [18]. We used MINI as the gold standard for current psychiatric diagnosis. MINI was carried out before examining the self-report inventories which the patients filled out at home and brought to the interview. Patients, who were diagnosed with a psychiatric disorder, were offered treatment according to local practice.

2.4. The Neurological Disorder Depression Inventory for Epilepsy (NDDI-E)

This screening tool for depression was developed for use specifically in patients with epilepsy [4]. It consists of six statements about the past two weeks that are scored between 1 (never) and 4 (always/often), with a minimum score of 6 and maximum of 24. In the original version, a score above 15 has been shown to have high predictive value for major depression [4]. Recently, we have published a translation of NDDI-E to Danish [16].

2.5. The World Health Organization Well-being Index (WHO-5)

The WHO-5 consists of five items. Each item is rated on a 6-point scale from 0 to 5. The score ranges from 0 to 25. The percentage value is calculated by multiplying the score by 4 and thus obtaining a scale from 0 (worst) to 100 (best). A percentage score below 50 is interpreted as indicating risk of depression and anxiety [17,19].

2.6. The Major Depression Inventory (MDI)

This scale contains the items that cover the ICD-10 symptoms of depression. We used the MDI as a diagnostic tool requiring core symptoms of depression to be present most of the time for the past two weeks [17].

2.7. The Anxiety Symptom Scale (ASS)

The ASS consists of 10 items. The presence of the items on levels 0–5 in the previous 14 days is assessed. The ASS was considered positive when item 10, the impact on daily activities, had a score of three or more, and there was a score on the top three symptoms which are the actual anxiety symptoms [17].

2.8. Statistics

We used SAS 9.3. Continuous data were compared using unpaired *t*-tests. The Chi-square test was used for categorical data and Fisher's exact test if the cells had a frequency of five or less. $P < 0.05$ was considered statistically significant. Excel was used to calculate sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), receiver operating characteristic (ROC) curves and area under the curve (AUC).

2.9. Ethics

The study was approved by the Ethical Committee of the Capital Region of Denmark (H-3-2012-086, anm. no. 39222). All patients gave their written informed consent prior to inclusion in the study.

3. Results

3.1. Basic characteristics

A total of 124 patients were included in this study. Of these 21 patients (17%) were diagnosed with depression ($n = 6$), anxiety ($n = 8$) or both in combination ($n = 7$). The group of patients with an anxiety disorder included 3 patients with generalized anxiety and 12 patients with one or two of the disorders panic disorder, agoraphobia, and social phobia. Other MINI-verified diagnosis found were dysthymia ($n = 5$), alcoholism ($n = 9$), dissocial personality disorder ($n = 1$), obsessive compulsive disorder ($n = 1$) and current mania ($n = 1$). In Table 1 the basic data are shown.

3.2. Screening for depression

Fig. 1 shows ROC curves for NDDI-E (A) and WHO-5 (B) as screening tests for depression in epilepsy patients. The ROC curves are based on 124 epilepsy patients including 13 patients (10.5%) with depression. The AUC for the two curves are almost identical ($AUC_{NDDI\text{-}E} = 0.932$, $AUC_{WHO\text{-}5} = 0.916$). The ideal test has a sensitivity of 1 and specificity of 1, which means that the point on the ROC curve closest to the top left corner is the best possible combination of sensitivity and specificity. In the original English version of NDDI-E [4], a threshold of 15 was found to be optimal. In the present study 18 patients scored above 15.

However, the best combination of sensitivity, specificity, PPV and NPV was found with a cut-off value of >13 for NDDI-E and <50 for WHO-5. 29 patients had a score below 50 in WHO-5. With a cut-off value > 13, the NDDI-E outweighs the WHO-5 (<50) with higher sensitivity and slightly higher PPV and NPV, see Table 2. The NDDI-E cut-off value > 13 was also used in the subsequent tables.

Table 2 also shows the sensitivity, specificity, PPV and NPV for MDI. The sensitivity of MDI as a screening tool for depression in epilepsy patients is low (0.308). Depression was indicated by MDI in 7 patients, but only 4 of these were true positive.