New screening tool for identifying major depression in patients with epilepsy

Original article Gilliam FG *et al.* (2006) Rapid detection of major depression in epilepsy: a multicentre study. *Lancet Neurol* **5:** 399–405

SYNOPSIS

KEYWORDS antiepileptic drugs, epilepsy, major depression

BACKGROUND

Major depression is relatively common among patients with epilepsy, but there is currently no easy-to-use screening tool that can pick up symptoms of major depression while reliably excluding other factors such as adverse effects of antiepileptic drugs or memory problems due to temporal lobe epilepsy.

OBJECTIVE

To develop and validate a brief and accurate screening instrument for major depression in epilepsy.

DESIGN AND INTERVENTION

This study included a screen-development phase and a screen-validation phase. During the development phase, investigators at five outpatient epilepsy clinics in the US compiled a list of 46 symptoms that could help to identify major depression in patients with epilepsy. This preliminary screen was applied to 205 adults with epilepsy who were treated at a participating outpatient clinic; 35 of these patients had major depression according to the Mini International Neuropsychiatric Interview (MINI). Using discriminant function analysis, the investigators narrowed the preliminary list of symptoms down to the most essential items that correctly identified patients who had MINI-diagnosed major depression. The resultant screen was termed the Neurological Disorders Depression Inventory for Epilepsy (NDDI-E). The investigators used logistic regression analysis to determine whether adverse effects of antiepileptic drugs had a confounding influence on the assessment of depression with the NDDI-E. In addition, the NDDI-E was validated in an independent cohort of 229 adults with epilepsy; 71 of these patients fulfilled the MINI criteria for major depression.

OUTCOME MEASURES

The outcome measures were the internal consistency and test–retest reliability of the NDDI-E, and its sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) for identifying major depression in patients with epilepsy.

RESULTS

The NDDI-E consisted of the following items: "everything is a struggle", "nothing I do is right", "feel guilty", "I'd be better off dead", "frustrated" and "difficulty finding pleasure". Each item was rated on a five-point Likert scale. The screen had sufficient internal consistency (Cronbach's alpha coefficient 0.85) and test–retest reliability (Spearman correlation coefficient 0.78 for two NDDI-E assessments done 2 weeks apart). At a cutoff score >15, the NDDI-E had a sensitivity of 81%, a specificity of 90%, a PPV of 62% and an NPV of 96% for predicting MINI-diagnosed major depression. A patient's adverse-event profile did not influence the screening result. Validation of the NDDI-E in the independent sample of epilepsy patients confirmed that optimum results are obtained at an NDDI-E cutoff score >15, with a sensitivity of 73%, a specificity of 72%, a PPV of 53% and an NPV of 86% for predicting major depression.

CONCLUSION

The NDDI-E can help to identify symptoms of major depression in epilepsy patients; these symptoms can be differentiated from adverse events of antiepileptic treatment.

COMMENTARY

Andrew J Cole

Major depression is a common comorbidity with epilepsy, with an estimated prevalence of 20–55% in those with chronic epilepsy.[1] Although depression is often treatable, it is underdiagnosed by neurologists and primary-care physicians in the setting of chronic neurological disease.[2] Depression is an important contributor to decline in perceived health status, causes significant functional and psychosocial disability, and might lead to suicide or self-injury. Recognition of depression in patients with epilepsy can be especially difficult because of the effect of the primary illness on mood, cognition and memory function,[3] and because of the adverse effects of anticonvulsant drugs, some of which can mimic symptoms of depression.

Clinical diagnosis is a hypothesis-driven iterative process that involves the consideration of a specific diagnosis, data gathering and analysis to support or refute the hypothesis, refinement of the hypothesis, reanalysis of available data and a directed search for additional data, and ultimately confirmation of a specific diagnosis. Diagnostic errors can arise from misinterpretation of data, omission of critical tests, or unusual features of an individual's clinical presentation, but perhaps the most serious errors arise from a failure to even consider the correct diagnosis in the process of hypothesis generation. Robust diagnostic screening tools are particularly useful in reducing the frequency of the last of these errors. An ideal screening tool should be sensitive, specific, easy to use, inexpensive, and validated in a sample of the population to be screened. The trade-off between sensitivity and specificity must be negotiated in the context of the 'cost' of false negatives and false positives.

Gilliam and colleagues used rigorous methods to develop and test a screening tool for major depression in patients with epilepsy. Beginning with an inventory of 46 items selected to identify symptoms of depression that were unlikely to be influenced by cognitive deficits and drug-related adverse events, they applied a discriminant function analysis to identify six items that together efficiently identified patients with depression. They defined appropriate statistical boundaries to maximize sensitivity (81%) and specificity (90%), documented internal consistency and test–retest reliability, and validated the screen in a larger independent sample of patients with epilepsy. The resultant NDDI-E screen is brief, simple to administer and score, and costs nothing.

An important strength of this work derives from the authors' broad experience in assessing mood disorders in the context of neurological disease, and their sensitivity to the problem of potential false positives that could result from the disease itself or from its treatment, but that do not reflect genuine depression. These potential false positives are important to avoid, because it is unlikely that targeted antidepressant treatment would help improve secondary symptoms.

A limitation of the study is that all patients—those in the initial screen-development study and those in the validation study—were drawn from tertiary-care epilepsy centers, and this population is not fully representative of the broader population of patients with epilepsy. Patients with refractory epilepsy in particular might have a higher incidence of depression than those with good seizure control, and the sensitivity and specificity of a screening test are likely to be altered by the prior probability of having the condition detected by the screen. The utility of the NDDI-E should, therefore, be monitored in a community-based population. Ultimately, however, the value of the tool depends not only on its accuracy and ease of use, but also on the availability of effective treatments and a clear management plan for the specific type of major depression that affects patients with epilepsy.

References

1 Ettinger A *et al.* (2004) Depression and comorbidity in community-based patients with epilepsy or asthma. *Neurology* **63:** 1008–1014
2 Gilliam FG *et al.* (2004) Depression in epilepsy: ignoring clinical expression of neuronal network dysfunction? *Epilepsia* **45 (Suppl 2):** S28–S33
3 Getz K *et al.* (2002) Negative symptoms in temporal lobe epilepsy. *Am J Psychiatry* **159:** 644–651

AJ Cole is Director of the Epilepsy Service and Chief of the Epilepsy Research Laboratory at Massachusetts General Hospital, Boston, MA, USA.

Acknowledgments
The synopsis was written by Martina Habeck, Associate Editor, Nature Clinical Practice.

Competing interests
The author declared associations with the following companies: Abbott Laboratories, GlaxoSmithKline, Ortho-McNeil and Pfizer.

Correspondence
MGH Epilepsy Service
Massachusetts General Hospital
Fruit Street
Boston
MA 02114
USA
cole.andrew@mgh.harvard.edu

Received 26 May 2006
Accepted 11 September 2006
www.nature.com/clinicalpractice
doi:10.1038/ncpneuro0346

PRACTICE POINT
The NDDI-E—a simple and robust screening tool for major depression in patients with epilepsy—should be offered to all epilepsy patients; positive screens should be confirmed with more-detailed assessment