MEASUREMENT OF MANIA AND DEPRESSION

AKADEMISK AVHANDLING
som för avläggande av medicine doktorsexamen vid Karolinska Institutet offentligen försvaras i Sal H3, Alfred Nobels Alle 23, KI Campus Huddinge

Fredagen den 21 oktober, 2011, kl 09.15

av
Mats Adler
MD

Huvudhandledare:
Docent Göran Isacsson
Karolinska Institutet
Institutionen för klinisk neurovetenskap

Bihandledare:
Professor Jerker Hetta
Karolinska Institutet
Institutionen för klinisk neurovetenskap

Fakultetsopponent:
Docent Eva Lindström
Uppsala Universitet
Institutionen för neurovetenskap

Betygsnämnd:
Professor Lisa Ekselius
Uppsala Universitet
Institutionen för neurovetenskap

Professor Mikael Landén
Göteborgs Universitet
Institutionen för neurovetenskap och fysiologi

Professor Bo Runeson
Karolinska Institutet
Institutionen för klinisk neurovetenskap

Stockholm 2011
ABSTRACT

**Background:** In psychiatry, the assessment of symptom severity is being increasingly assisted by rating scales, in clinical practice as well as in research and quality control. Transforming the subjective symptoms of psychiatric disorders into valid numerical measures is subjected to numerous confounding factors. Careful evaluation of rating scales is therefore essential. This doctoral project arose from a clinical need for a useful self-rating scale for affective symptoms at an outpatient clinic for affective disorders. No existing rating scales fulfilling the clinical need were found in the literature.

**Aims:** The aims of the doctoral project were to develop and evaluate a self rating scale for measurement of severity in depressive, manic and mixed affective states and to explore if Item Response Theory (IRT) is useful for evaluation and improvement of rating scales for mania and depression. A further aim was to investigate if Randomized Controlled Studies of Antidepressants (RCT-ADs) might be biased due to measurement properties of the most commonly used rating scale, the Hamilton Depression Rating Scale (HDRS).

**Methods:** A self rating scale consisting of 18 items was developed and named the Affective Self-Rating Scale (AS-18) with separate subscales for depression and mania/hypomania. It was evaluated in two samples of patients (N=61 and N=231) and was compared to the Patient Health Questionnaire (PHQ9) and the Montgomery Åsberg Depression Rating Scale (MADRS). Data from five RCT-ADs included in a recently published meta-analysis were analyzed (N=516). Statistical methods from Classical Test Theory (CTT) and IRT were used.

**Results:** The AS-18 showed good estimates of reliability with Cronbachs alpha (CTT) of 0.89 and 0.91 for the depression and mania subscales. The ratings on the AS-18 showed strong correlation to reference scales. A factor analysis largely confirmed the predicted factor structure. Items for irritability, risk-taking and increased sleep did not, however, behave as predicted. The IRT analysis showed that the AS-18 and PHQ9 had strong capacities to rank respondents according to their scores, while the MADRS had weak such properties. Several items in the rating scales contributed little information to the measurement. There was a shortage of items covering lower levels of the depression and mania dimensions making measurement of lower levels of symptoms imprecise.

In the analysis of five RCTs it was found that the HDRS yielded decreasing amounts of information at declining levels of depression severity. In addition it was found that the items of HDRS were understood differently by the study persons of the different RCT-ADs. The conclusion of the meta-analysis, that antidepressants had negligible effect in low to moderate depression severity, was therefore found to be unsupported by data.

**Conclusions:** The AS-18 has demonstrated reliability and validity in two studies. In outpatient settings for affective disorder patients, it can be used as a time-efficient aid for clinicians in identifying patients with different affective states as well as rating their severity. IRT-methods were demonstrated to be useful for analyzing rating scales concerning the amount of information that individual items contribute to the measurement, how the precision of measurement varies over the severity spectrum and for investigating whether different study populations perceive items differently. Studies of antidepressant efficacy can be biased due to shortcomings of measurement.