

Diagnosing Subtypes of Neuroleptic Malignant Syndrome: An Introduction to the Lee-Carroll Scale

BRENDAN T. CARROLL, MD

University of Cincinnati, Ohio, USA

JOSEPH W.Y. LEE, MBBS, MRCPsych, FRANZCP

University of Western Australia, Perth, Australia

KEVIN T. GRAHAM, MD

Good Samaritan Medical Center, Phoenix, AZ, USA

ARTHUR THALASSINOS, MD

New Horizons Mental Health Center, Lancaster, Ohio, USA

CHRISTOPHER THOMAS, PHARM D

University of Cincinnati, Cincinnati, Ohio, USA

ROB KIRKHART, PH.D., PA-C

Marietta College, Department of Veterans Affairs Medical Center, Chillicothe, Ohio, USA

Background. Neuroleptic malignant syndrome (NMS) shares common features with catatonia and serotonin syndrome (SS). For instance, catatonia is a risk factor for the development of NMS.

Methods. We performed a pilot study to examine if the Lee-Carroll Scale is able to differentiate the proposed NMS subtypes and explore possible relationship between NMS and SS. A consecutive series of cases reported to the Neuroleptic Malignant Syndrome Information Service (NMSIS) were reviewed with 29 cases of “definite NMS.” The Hynes-Vickar Scale (an NMS scale), Hegerl Scale (a SS scale), and Lee-Carroll Scale (an NMS subtype scale) were applied to these case report forms.

Conclusions. Although the groups were too small for statistical analysis, the 2 catatonic NMS subtypes appear to have higher NMS scores on the Hynes-Vickar Scale, and lower SS scores on the Hegerl Scale than the non-catatonic NMS subtype. The scores on the Lee-Carroll Scale were highest for non-catatonic NMS subtype. This pilot study suggests that the Lee-Carroll scale may help differentiate the subtypes of NMS, and provides some support that non-catatonic NMS may be a form of SS. NMS subtypes may be important in the early detection and treatment of NMS.

Keywords Catatonia, Neuroleptic malignant syndrome, Antipsychotics, Serotonin syndrome, Delirium

An analysis of 14 episodes in patients as having neuroleptic malignant syndrome (NMS) yielded three different subtypes: 2 catatonic and 1 non-catatonic (1). It is important to identify subtypes of NMS so that NMS may be detected earlier and its

incidence reduced. Newer antipsychotics may not lead to the development of rigidity but might lead to intermediate states of drug toxicity or the Serotonin Syndrome (SS) (2–4).

A nosological relationship between catatonia and NMS has been proposed based upon observations of patients with NMS and scores on rating scales developed for NMS (5,6). Moreover, Catatonia is a risk factor for NMS (3). The non-catatonic subtype of NMS (NC-NMS) is important because its distinctive

Address correspondence to Brendan T. Carroll, The Neuroscience Alliance, 330 Taylor Blair Road, West Jefferson, OH 43162, USA. E-mail: BTCARROLL1@cs.com

presentation and its possible association with newer neuroleptics (second generation antipsychotics-SGAs. These clinical observations suggest that there may be different encephalopathic processes underlying the development of NMS (3).

We selected a consecutive series of cases reported to the Neuroleptic Malignant Syndrome Information Service (NMSIS) over a 2 year period. An NMS scale (Hynes-Vickar Scale (9)), a serotonin syndrome scale (Hegerl Scale (10)) and an NMS subtype scale (Lee-Carroll Scale) were used to rate the severity of NMS and SS in patients receiving an atypical antipsychotic. In each case, the consultant collects clinical information and enters it into a computer database. This database includes ratings of behavioral signs including: agitation, mutism, delirium, confusion, stupor, catalepsy, coma, negativism, automatic obedience, echophenomena and "other." It also includes a narrative section when catatonic signs can also be listed. Vital signs, neurologic signs (i.e., rigidity, and myoclonus) and autonomic signs (i.e., diaphoresis, and incontinence), laboratory, imaging and treatment information sections are also included.

The Serotonin Syndrome Scale required modification (3). It has 10 items rated on scales of 0 to 3 yielding a total score of 0 to 30. The cutoff score for possible serotonin syndrome was set at ≥ 7 . We then chose to have three reviewers (AT, BTC, KTG) apply the scales and make determinations regarding NMS and SS based upon the NMS Hotline Case Report Form in each case. Only cases of definite NMS were included.

In order to address the subtypes of NMS we developed the Lee-Carroll Scale. The Lee-Carroll Scale is a 7-item assessment tool that can be applied to medical records and case reports of patients with a signs of NMS. Its score ranges from 0 to 14 with items to address 7 features of these subtypes identified by Lee (1,2). It differs from other scales because it requires:

1. a determination regarding the presences of catatonia or catatonic signs, and
2. if present, whether the catatonia preceded or followed the development of NMS.

The cases were called into the Neuroleptic Malignant Syndrome Information Service (NMSIS) between January 1, 2000 and January 1, 2002. In each case, clinical information was gathered, entered into a computer database, and subjected to descriptive analysis. This database included ratings of behavioral signs and other signs from NMS Hotline Case Report Form. Only those cases with complete database information were used. Only cases in which the NMSIS consultant determined "definite NMS" were used.

There were 96 reports from the NMSIS hotline during the time specified. Of these, 29 were determined by the NMSIS consultants to be definite NMS cases. Of these, 12 were considered C-NMS, 10 were NMSwC, and 7 were NC-NMS. Scores on the Hines-Vicar Scale, for each type of NMS were as follows: C-NMS = 11.0 (± 2.9), NMSwC = 9.3 (± 4.0), and NC-NMS = 3.9 (± 1.2).

Scores on the Serotonin Syndrome Scale for each type of NMS are as follows: C-NMS = 5.5 (± 1.2), NMSwC = 4.9 (± 1.2), and NC-NMS = 9.3 (± 2.6). Finally, when the Lee-Carroll Scale was applied to each case, separation occurred between the subtypes of NMS. Scores for each type of NMS were as follows: C-NMS = 3.3 (± 1.6), NMSwC = 2.4 (± 0.8), and NC-NMS = 6.3 (± 2.7).

Although the groups were too small for statistical analysis, the two catatonic NMS subtypes appear to have higher NMS scores on the Hynes-Vickar Scale, and lower Serotonin Syndrome Scale scores than the non-catatonic NMS subtype. The Lee-Carroll Scale was highest for NC-NMS and identified this subtype more clearly than the other scales and the presence of myoclonus and hyperreflexia in SS (1,5).

This pilot study suggests that the Lee-Carroll scale may help differentiate the subtypes of NMS. NMS subtypes may be important in the early detection and treatment of NMS. We propose that the Lee-Carroll Scale be applied with other rating scales to larger databases to help identify subtypes of NMS.

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