

Delirium, in 405 articles of medical (non-surgical or ICU) inpatients: unproven speed of onset and recovery

Paul Jay Regal

Regal Elderly Medicine, Kanwal
Medical Centre, Kanwal, NSW,
Australia

Purpose: There is agreement in the medical literature that delirium is of sudden or rapid onset. Although the speed of recovery cannot be used for initial diagnosis, recovery speed provides a test of diagnostic criteria. The aim of this study was to determine whether articles on delirium among medical inpatients proved sudden onset and rapid recovery.

Methods: The literature was searched for studies with at least 50 patients on medical or geriatric wards. Excluded were postoperative, critical care, and nursing home studies. Speed of onset was extracted as either the interval between symptom onset and diagnosis or between hospital admission and diagnosis of incident delirium. Mean or median days to recovery from delirium and the scale used to measure recovery were identified.

Results: Four-hundred and five articles were analyzed with 789,709 patients. The median article had 220 patients. Onset could only be extracted in 11 articles (2.7%): mean onset was 3.09 ± 2.38 days. Median onset was 3.0 days, which conforms to *Diagnostic and Statistical Manual of Mental Disorders (DSM-V)*. Only 56 of 405 articles (13.8%) reported timing of recovery but mean or median recovery was available in 25 of 405 (6.2%): 6.56 ± 4.80 days.

Conclusion: Medical delirium articles have failed to establish rapid onset and rapid recovery.

Keywords: delirium, dementia, cognitive decline

Introduction

There is consensus that delirium is of sudden or rapid onset although a few authors contend delirium is a chronic condition with exacerbations.¹ The *Diagnostic and Statistical Manual of Mental Disorders (DSM-V)* lists onset as hours to several days.² The delay between onset and diagnosis is a crucial variable because if patients enter a delirium study late in the course of their illness study results will be skewed toward lower rates of reversibility and lower mortality because of deaths before study entry, especially in nursing home residents.

Delirium is related to dementia in a manner similar to how asthma is related to chronic obstructive pulmonary disease (COPD). Both delirium and asthma are of rapid onset and generally rapid recovery. Every diagnostic formulation for delirium agrees the key feature is rapid onset of inattention and disorientation and is generally reversible, unlike dementia which is of gradual onset and rarely reversible.

Does delirium in the medical literature reflect the gold standard of rapid high amplitude onset and relatively rapid recovery?

Correspondence: Paul Jay Regal
Suite A6 Kanwal Medical Centre 654
Pacific Highway, Hamlyn Terrace, Kanwal,
NSW 2259, Australia
Tel +61 448 675 993
Email regalelderlymedicine@gmail.com

Methods

Every issue of the 14 medical journals with the most delirium articles since 1990 was reviewed. The table of contents was searched for each of these journals for “delirium” references were tracked from the articles uncovered. After gathering these articles, PubMed was searched for “Delirium” which generated 13,200 articles.

A total of 1,586 articles on delirium were critically analyzed, and studies that were 1) postoperative, 2) in critical care units, 3) reviews or letters to the editor not reporting new studies, and 4) clinical reports on medical (non-surgical and non-critical care) with less than 50 subjects were excluded. Studies with less than 50 subjects were often case series or retrospective and tended to be lower quality than larger studies, as evidenced by retrospective chart reviews. The final sample contained 339 journals published in the year a mean of 2006.8 ± 7.3 years (range 1982–2016). With this number of articles, it was impossible to contact the study authors for personal comments. In part, unpublished comments are irrelevant because the rate of onset and recovery of delirium is crucial and worthy of mention in all studies.

The journals with the highest number of delirium articles in medical/geriatric inpatients with at least 50 subjects were *Journal of the American Geriatrics Society* (55 articles), *Age and Ageing* (29), *International Psychogeriatrics* (25), *International Journal of Geriatric Psychiatry* (23), *Psychosomatics* (15), *American Journal of Geriatric Psychiatry* (14), *Archives of Internal Medicine/JAMA Internal Medicine* (13), *Journal of Gerontology Medical Sciences* (13), *Journal of Geriatric Psychiatry and Neurology* (9), *Dementia and Geriatric Cognitive Disorders* and *Dementia and Geriatric Cognitive Disorders Extra* (7), and *Journal of the American Medical Directors Association* (7).

The speed of onset of delirium was defined as the interval in days between the last normal cognitive day and symptom/sign onset, or symptom and sign onset to diagnosis. Articles that did not report either were deemed to have no documented speed of onset. The rate of recovery was defined by the days between onset/diagnosis for incident delirium or hospital admission for prevalent delirium and recovery by either a delirium instrument such as the Delirium Rating Scale Revised-98 (DRS-R98),³ Confusion Assessment Method (CAM),⁴ Memorial Delirium Assessment Scale (MDAS),⁵ Delirium Index (DI),⁶ or by global assessment. Either a mean or median number of days to recovery was accepted. A report stating 25% improved by day 2 would not be sufficient to estimate mean or median recovery. Length of stay was not used to estimate recovery because each study site would have a different policy on

discharge of delirious patients to subacute care or nursing homes. Authors of studies with missing data for onset and recovery were not contacted, because it was anticipated less than 5% would have this information and of that 10% of the latter group would disclose the information.

Results

These 405 articles on delirium in non-surgical, non-intensive care unit (ICU) patients contained 789,709 subjects ([Supplementary materials](#)). This high number came from 13 large studies, most retrospective. The median of 405 articles contained 220 subjects. Only 12/405 articles (2.96%) screened hearing. This is of grave concern because many elderly in the emergency department or medical wards have severe hearing loss and are not wearing hearing aids. Only 17/405 articles (4.2%) quantified onset in days, but 6/17 provided too little information to estimate mean or median onset. Onset could be extracted in 11 articles (2.7%) containing a median of 136 subjects per article: mean onset was 3.09 ± 2.38 days. Median onset was 3.0 days, which conforms with *DSM-IV*. This is comparable to claiming diagnosis of lobar pneumonia when only 3% of chest radiographs showed lobar consolidation.

Only 56/405 articles (13.8%) reported the timing of recovery but mean or median recovery was available in 25/405 (6.2%): 6.56 ± 4.80 days. These 25 articles contained a median of 191 subjects per article. This figure must be viewed with caution because of the different instruments for measuring recovery: unspecified methods in 42/56 studies, DRS or DRS-R98 in five studies, CAM in four studies, MDAS in three studies, DI in one study, and Montreal Cognitive Assessment in one study. Using the CAM to measure recovery is less than ideal because it is a diagnostic scale and not a severity instrument.

Discussion

Results of this study strongly endorse the conclusion that physicians are content to diagnose delirium without documentation of its onset in 95.8% of delirium studies. It is almost certain that in clinical practice, which is less rigorous than delirium research, more than 98% of delirium cases will be of unspecified acuity, making it more likely the patient has behavioral and psychological symptoms of dementia (BPSD). There are many reasons for relaxed diagnostic standards such as: DRG funding favors diagnosis of delirium over BPSD; referring physicians can justify admissions for delirium whereas they would be denied admission for BPSD which is managed in the community or nursing home; and physicians disregard delirium diagnostic scales in clinical practice.

It is of great concern that only 6.2% of 405 delirium articles reported recovery in days. Many clinicians care for delirious patients without using Delirium scales on a daily basis to assess recovery; they rely on global impression, which is often misleading.

The Central Coast Australia Delirium Intervention Study (CADIS) a prospective randomized clinical trial was compared.⁷ The 116 subjects recruited from July 2012 to May 2014 were of mean age 83.6 years with prevalent delirium by CAM plus three additional criteria to make CAM more specific: 1) at least a 25% decline in attention by forward or reverse imputation, 2) not counting impaired level of consciousness toward diagnosis if this followed sedatives or antipsychotics, and 3) rigorous exclusion of BPSD. The 116 subjects had a mean onset of 1.31 ± 1.36 days compared to 3.09 ± 2.38 in the medical literature. Digit span forward (DSF) and DI were measured 365 days per year, which permits exact measurement of recovery. The mean recovery days by 5-DSF was 2.00 ± 3.79 ; mean recovery days for 6-DSF was 5.61 ± 6.06 ; mean recovery days for DI was 8.00 ± 4.45 .

Adamis et al explain the challenges of measuring delirium recovery.⁸ The author concurs that some scales capture certain features such as hallucinations better than other scales and that two studies using the same scale may employ different cutoffs. However, sharing raw data can overcome some of these problems.

Teale and Young⁹ outlined difficulties in diagnosing delirium, highlighting subjectivity of many criteria. The author believes that explicit criteria such as a 25% of greater decline in attention may overcome subjectivity.

Delirium articles (N=1,695) were reviewed, of all subtypes: medical, surgical, hip fracture, critical care, and prevention to determine the significance of the collection of 405 medical delirium studies. Sixteen meta-analyses or systematic reviews were found, containing only 256 studies compared to the single review of 405 studies. The mean number of studies in each of the 16 articles^{10–25} was 16.0 ± 11.7 and the largest contained only 42 studies.

Conclusion

It is recommended that all delirium studies measure and report: 1) interval between last normal cognitive state and start of symptoms and signs, 2) interval between symptoms and signs and hospital admission or diagnosis, and 3) daily neurocognitive scores to assess reversibility and speed of recovery. Daily measurement of neurocognitive tests such as DI, MDAS and DRS-R98 should use material that cannot

be learned such as a different number sequences for 5-DSF and 6-DSF, different word list for immediate and delayed verbal memory and different baseline number for serial subtraction task.

Disclosure

The author reports no conflicts of interest in this work.

References

1. Cole MG, McCusker J. Delirium in older adults: a chronic disorder? *Int Psychogeriatr*. 2016;28:1229–1233.
2. American Psychiatric Association. *Diagnostic and Statistical Manual for Mental Disorders*. 5th ed. Washington DC: American Psychological Association; 2013.
3. Trzepacz PT, Mittal D, Torres R, Kanary K, Norton J, Jimerson N. Validation of the delirium rating scale revised-98 (DRS-R-98). *J Neuropsychiatry Clin Neurosci*. 2001;13:229–242.
4. Inouye SK, van Dyck CH, Alessi CA, Balkin S, Siegel AP, Horwitz RI. Clarifying confusion: the confusion assessment method. A new model for detection of delirium. *Ann Intern Med*. 1990;113:941–948.
5. Breitbart W, Rosenfeld B, Roth A, Smith MJ, Cohen K, Passik S. The Memorial Delirium Assessment Scale. *J Pain Symptom Management*. 1997;13:128–137.
6. McCusker J, Cole M, Bellavance F, Primeau F. Reliability and validity of a new measure of severity of delirium. *Int Psychogeriatr*. 1998;10:421–433.
7. Regal PJ. A new delirium phenotype with rapid high amplitude onset and nearly as rapid reversal: Central Coast Australia Delirium Intervention Study (CADIS). *Clin Interv Aging*. 2015;10(2):473–480.
8. Adamis D, Devaney A, Shanahan E, McCarthy G, Meagher D. Defining 'recovery' for delirium research: a systematic review. *Age Ageing*. 2015;44:318–321.
9. Teale E, Young J. Multicomponent delirium prevention: not as effective as NICE suggest? *Age Ageing*. 2015;44:915–917.
10. Ahmed S, Leurent B, Sampson EL. Risk factors for incident delirium among older people in acute hospital medical units: a systematic review and meta-analysis. *Age Ageing*. 2014;43:326–333.
11. Fok MC, Sepehry AA, Frisch L, et al. Do antipsychotics prevent postoperative delirium? A systematic review and meta-analysis. *Int J Geriatr Psychiatry*. 2015;30:333–344.
12. Fox MT, Persaud M, Maimets I, et al. Effectiveness of acute geriatric unit care using acute care for elders components: a systematic review and meta-analysis. *J Am Geriatr Soc*. 2012;60:2237–2245.
13. Gilmore ML, Wolfe DJ. Antipsychotic prophylaxis in surgical patients modestly decreases delirium incidence but not duration in high-incidence samples: a meta-analysis. *General Hosp Psychiatry*. 2013;35:370–375.
14. Hsieh TT, Yue J, Oh E, et al. Effectiveness of multicomponent non-pharmacological delirium interventions: a meta-analysis. *JAMA Intern Med*. 2015;135:512–520.
15. Kempton MJ, Bonoldi I, Vafmaggia L, McGuire P, Fusar-Poli P. Speed of psychosis progression in people at ultra-high clinical risk: a complementary meta-analysis. *JAMA Psychiatry*. 2015;72:622–623.
16. Martinez F, Tobar C, Hill N. Preventing delirium: should non-pharmacological, multicomponent interventions be used? A systematic review and meta-analysis of the literature. *Age Ageing*. 2015;44:196–204.
17. Mayo-Smith MF, Beecher LH, Fischer TL, et al. Management of alcohol withdrawal delirium. An evidence-based practice guideline. *Arch Intern Med*. 2004;164:1405–1412.
18. Neto AS, Nassar AP, Cardoso SO, et al. Delirium screening in critically ill patients: a systematic review and meta-analysis. *Crit Care Med*. 2012;40:1946–1951.

19. Neufeld KJ, Yue J, Robinson TN, Inouye SK, Needham DM. Antipsychotic medication for prevention and treatment of delirium in hospitalized adults: a systematic review and meta-analysis. *J Am Geriatr Soc.* 2016;64:705–714.
20. Salluh JE, Schneider EB, Nagaraja N, et al. Outcome of delirium in critically ill patients: systematic review and meta-analysis. *BMJ.* 2015;350:h2538.
21. Shi Q, Presutti R, Selchen D, Saposnik G. Delirium in acute stroke: a systematic review and meta-analysis. *Stroke.* 2012;43:645–649.
22. Teslyar P, Stock VM, Wilk CM, Camsari U, Ehrenreich MJ, Himelhoch S. Prophylaxis and antipsychotic medication reduces the risk of postoperative delirium in elderly patients: a meta-analysis. *Psychosomatics.* 2013;54:124–131.
23. Van Meenen LCC, Van Meenen DMP, de Rooij SE, ter Riet G. Risk prediction models for postoperative delirium: a systematic review and meta-analysis. *J Am Geriatr Soc.* 2014;62:2383–2390.
24. Weber JB, Coverdale JH, Kunik ME. Delirium: current trends in prevention and treatment. *Intern Med J.* 2004;34:115–121.
25. Zhang H, Lu Y, Liu M, et al. Strategies for prevention of postoperative delirium: a systematic review and meta-analysis of randomized trials. *Crit Care.* 2013;13:47. doi:10.1186/cc12566.

Clinical Interventions in Aging

Publish your work in this journal

Clinical Interventions in Aging is an international, peer-reviewed journal focusing on evidence-based reports on the value or lack thereof of treatments intended to prevent or delay the onset of maladaptive correlates of aging in human beings. This journal is indexed on PubMed Central, MedLine,

CAS, Scopus and the Elsevier Bibliographic databases. The manuscript management system is completely online and includes a very quick and fair peer-review system, which is all easy to use. Visit <http://www.dovepress.com/testimonials.php> to read real quotes from published authors.

Submit your manuscript here: <http://www.dovepress.com/clinical-interventions-in-aging-journal>

Dovepress