Archives of Psychiatric Nursing 28 (2014) 187–192

Contents lists available at ScienceDirect

Archives of Psychiatric Nursing

journal homepage: www.elsevier.com/locate/apnu

Gender Differences in Factors Associated With Delirium Severity in Older Adults With Dementia

Ann M. Kolanowski [a,*], Nikki L. Hill [a,1], Esra Kurum [b,2], Donna M. Fick [a,3], Andrea M. Yevchak [c,4], Paula Mulhall [a,5], Linda Clare [d,6], Michael Valenzuela [e,7,8]

[a] The Pennsylvania State University, College of Nursing, University Park, PA
[b] Istanbul Medeniyet University, Istanbul, Turkey
[c] Duquesne University, School of Nursing, Pittsburgh, PA
[d] Bangor University, School of Psychology, Gwynedd, UK
[e] Regenerative Neuroscience Group, Brain and Mind Research Institute, University of Sydney, Sydney, Australia

A B S T R A C T

The purpose of this descriptive correlational study was to explore potential gender differences in the relationship of dementia severity, age, APOE status, cognitive reserve and co-morbidity (two potentially modifiable factors), to delirium severity in older adults. Baseline data from an ongoing clinical trial and a Poisson regression procedure were used in the analyses. Participants were 148 elderly individuals with dementia and delirium admitted to post-acute care. In women, delirium severity was related to dementia severity ($p = 0.002$) and co-morbidity moderated that effect ($p = 0.03$). In men, education was marginally associated with delirium severity ($p = 0.06$). Implications for research are discussed.

Older adults with dementia have the highest risk for delirium, a neurobehavioral syndrome caused by acute physiological and/or psychological insults and characterized by an abrupt decline in cognitive function (Inouye, 2006). Delirium is prevalent in older adults with dementia: up to 89% experience delirium when hospitalized (Fick, Agostini, & Inouye, 2002). Delirium also carries a high rate of mortality: between 24 and 76% die within 1 year of the index episode (McCusker, Cole, Dendukuri, Han, & Belzile, 2003).

Beyond increased mortality, delirium has a major impact on other clinical and cost outcomes because it often persists beyond the acute phase of an illness. For example, two thirds of older adults admitted to post-acute (rehabilitation) care have delirium symptoms on admission (Kiely et al., 2003). Unresolved delirium in the post-acute phase of an illness prolongs rehabilitation because the associated cognitive decline interferes with the ability to fully engage in restorative therapies and increases the risk for permanent institutionalization (Fong et al., 2009). In addition to these poor health outcomes, delirium costs the U.S. healthcare system a staggering $152 billion annually (Leslie, Marcantonio, Zhang, Leo-Summers, & Inouye, 2008).

It may be difficult to prevent delirium in older adults with dementia due to their underlying brain vulnerability (Marcantonio, Flacker, Wright, & Resnick, 2001). The need for evidence based treatment strategies that reduce the severity of delirium in people with dementia is critical and rests on a more informed understanding of etiology and associated risk factors.

Currently we do not know what biological and environmental factors increase delirium severity in people with dementia. Data indicate that delirium and dementia share many clinical, metabolic and cellular manifestations that indicate heightened brain vulnerability (Inouye & Ferrucci, 2006). Other data demonstrate gender differences in the clinical manifestation and outcome of dementia (Barnes et al., 2005). Additionally, males may have had a historical advantage with respect to building cognitive reserve against brain vulnerability, i.e., greater education and occupational achievement (Valenzuela et al., 2013). Given the close relationship of delirium and dementia and the gender differences in dementia manifestation and outcome, we anticipated that there may be important gender differences in risk factors for greater delirium severity. The Institute of Medicine has argued for examination of gender differences in clinical research (National Research Council, 2001). Thus, the purpose of this descriptive correlational study was to explore a gap in

* Corresponding Author: Ann M. Kolanowski, PhD, RN, FAAN, The Pennsylvania State University, College of Nursing, Nursing 106 Health & Human Development, University Park, PA 16802.
E-mail addresses: amk20@psu.edu (A.M. Kolanowski), Nln101@psu.edu (N.L. Hill), esrakurum@gmail.com (E. Kurum), dmf21@psu.edu (D.M. Fick), yevchaka@duq.edu (A.M. Yevchak), pmk9@psu.edu (P. Mulhall), l.clare@bangor.ac.uk (L. Clare), michael.valenzuela@sydney.edu.au (M. Valenzuela).
[1] Tel.: +1 814 867 3265.
[2] Tel.: +90 216 280 33 33.
[3] Tel.: +1 814 865 9325.
[4] Tel.: +1 412 396 6543.
[5] Tel.: +1 814 867 4656.
[6] Tel.: +44 1248 388178.
[7] Tel.: +61 2 9114 4135.
[8] Michael Valenzuela was supported by a National Health & Medical Research Council of Australia Clinical Career Development Fellowship (1004156).

http://dx.doi.org/10.1016/j.apnu.2014.01.004
0883-9417/

knowledge about the potential gender differences in the relationship of dementia severity, age, apolipoprotein E (APOE) status, as well as cognitive reserve and co-morbidity, (two potentially modifiable factors), to delirium severity in older adults.

REVIEW OF THE LITERATURE

Non-modifiable Factors Related to Delirium

There are likely multiple neurobiological mechanisms contributing to delirium, and currently the neurotransmitter imbalance and the inflammatory hypotheses are the most prominent (Maldonado, 2013). The apolipoprotein E (APOE) gene, located on chromosome 19, has been associated with cognitive decline (Ertekin-Taner, 2007). A recent review of biomarkers for delirium found that most, but not all, of the six studies evaluated supported a role for APOE in the development of delirium (Khan, Zawahiri, Campbell, & Boustani, 2011). Though findings have not always been consistent (van Munster, Korevaar, de Rooij, Levi, & Zwinderman, 2007), the weight of the evidence indicates that having at least one copy of the e4 allele is associated with an increased risk of delirium in young and older adults as well as a more protracted course, independent of demographic and clinical covariates or premorbid cognitive impairments (Adamis et al., 2007).

Dementia is arguably the strongest risk factor for delirium (Cole, 2004; Miller & Ely, 2006). For example, in their observational study of 330 older adults admitted to a medical unit of a general hospital, Margiotta, Bianchetti, Ranieri, and Trabucchi (2006) found that patients with pre-existing dementia were vulnerable to delirium at low levels of medical acuity than dementia-free patients. Moreover, the risk for delirium becomes greater as dementia severity increases (Voyer, McCusker, Cole, & Khomenko, 2006). Voyer, Richard, Doucet, and Carmichael (2009) also found that advancing age increased risk for delirium in persons with dementia.

It may be difficult to prevent delirium in older adults with dementia due to their underlying brain vulnerability and risk profile (Marcantonio et al., 2001), so the identification of modifiable factors that influence delirium severity would be advantageous for this population. This knowledge could be used to inform the development of strategies, tailored to gender, that reduce the severity of delirium as well as the high cost and poor health outcomes that are associated with it.

Modifiable Factors and Relationship to Gender

Cognitive reserve is a theoretical concept used to explain why some people cope better than others with brain pathology (Tucker & Stern, 2011). An active cognitive lifestyle, involving lifelong participation in mentally stimulating educational, occupational and leisure activities, is thought to be a key contributor to building up such reserve (Bennett et al., 2003; Stern, 2012; Tucker & Stern, 2011). Much of the evidence in support of the cognitive reserve hypothesis has been in the area of risk for age-associated cognitive decline and dementia (Valenzuela & Sachdev, 2006). Older adults who engaged in mentally stimulating activities showed less than half the hippocampal volume decline over a 3 year period compared to those who engaged in fewer activities (Valenzuela, Sachdev, Wen, Chen, & Brodaty, 2008).

There is some evidence that cognitive reserve may also play a role in delirium. Jones et al. (2006) reported that level of education was significantly lower in patients who developed delirium during hospitalization compared to those who did not develop it. Further, leisure activity participation prior to hospitalization mediated the effect of education on delirium incidence, with physical activity exerting the greatest effect (Yang et al., 2008).

The cognitive benefits of mentally stimulating activities are evident when participation in mentally stimulating activities is a lifetime pattern as well as when they are initiated for the first time in late life (Leung et al., 2011). While educational level has been associated with incidence of delirium, the contribution of late-life cognitive lifestyle to delirium severity has not been studied in older adults with dementia. Because women tend to have a more active late life cognitive lifestyle than men (Valenzuela et al., 2013), but men in this historical cohort enjoyed greater educational opportunities than women, we explored gender differences in the effects of cognitive reserve on delirium severity.

Multiple co-morbidities have the potential to initiate a cascade of negative health outcomes. The loss of physiological reserves brought on by multiple diseases predicts vulnerability to diminished homeostatic capacity (Quinlan et al., 2011). The existing evidence indicates that comorbidity and frailty are distinct but related entities that manifest complex interactions which signal a state of vulnerability to physical and cognitive stressors, and thus, increase the risk of delirium during acute illnesses. Because men with dementia carry a higher burden of co-morbidity than women (Buchanan, Wang, Ju, & Graber, 2004) we explored gender differences in the association of co-morbidity with delirium severity.

METHODS

Data from the baseline period of an ongoing clinical trial were used to address the aim of this project. In the parent study, cognitively stimulating activities are being tested for their efficacy in resolving delirium in older adults with dementia. The protocol has been published and received approval from the university institutional review board (blinded for review).

In the trial, subjects are recruited at admission to post-acute care following a hospitalization. Eight community-based skilled nursing facilities in central and northeast Pennsylvania serve as recruitment sites. All subjects have a diagnosis of dementia and delirium. Dementia is established based on a score of three or greater on the Modified Blessed Dementia Rating Scale (MBDRS) with symptoms evident for at least 6 months duration (Blessed, Tomlinson, & Roth, 1968), and a Clinical Dementia Rating (CDR) score from 0.5 to 2.0, indicating mild to moderate stage dementia (Hughes, Berg, Danziger, Coben, & Martin, 1982). Presence of delirium is established by positive findings on the Confusion Assessment Method (CAM; Inouye et al., 1990), a standardized diagnostic algorithm for delirium allowing persons without formal psychiatric training to quickly and accurately identify delirium. The CAM has been validated in persons with dementia, but because of the risk of feature overlap with dementia, we take a conservative approach and include only subjects with full (three or more features) or sub-syndromal (two features) delirium. A panel of three experts in dementia (neuropsychologist, neurologist and geriatrician) adjudicates all dementia and delirium diagnoses.

Other inclusion criteria include: age 65 years or older; English speaking; community-residing prior to most recent hospitalization; and having a legally authorized representative (usually a spouse or adult child) who provides medical history, education, occupation and leisure data. These individuals meet criteria specified by Ritchie and Fuhrer (1996) for knowledgeable informants, i.e., monthly contact with the subject for 10 years during the subject's adult life prior to the dementia diagnosis. Subject exclusion criteria include: having any neurological condition associated with cognitive impairment other than dementia, including Parkinson's disease with Lewy Body dementia, Huntington's disease, normal pressure hydrocephalus, seizure disorder, subdural hematoma, head trauma, or known structural brain abnormalities; nonverbal; having a life expectancy of 6 months or less; acute major depression; acute psychiatric condition; stroke; and severe hearing and vision impairment. Individuals who meet enrollment criteria are invited to participate in the trial.