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Research paper

Associations between pain and depression in nursing home patients at different stages of dementia

Ane Erdal[a,*], Elisabeth Flo[a,b], Geir Selbaek[c,d,e], Dag Aarsland[f,g], Sverre Bergh[c,d], Dagrun D. Slettebo[a], Bettina S. Husebo[a,h]

[a] Department of Global Public Health and Primary Care, Centre for Elderly and Nursing Home Medicine, University of Bergen, Bergen, Norway
[b] Department of Clinical Psychology, University of Bergen, Bergen, Norway
[c] Centre for Old Age Psychiatric Research, Innlandet Hospital Trust, Ottestad, Norway
[d] National Advisory Unit on Ageing and Health, Tønsberg, Norway
[e] Institute of Health and Society, Faculty of Medicine, University of Oslo, Oslo, Norway
[f] Department of Old Age Psychiatry, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, UK
[g] Centre for Age-related Medicine, Stavanger University Hospital, Stavanger, Norway
[h] Municipality of Bergen, Bergen, Norway

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ABSTRACT

Background: Pain is associated with depression in nursing home patients with dementia. It is, however, unclear whether pain increases depression. Therefore we evaluated the prospective associations between pain and depressive symptoms in nursing home patients at different stages of cognitive impairment.

Methods: Two longitudinal studies were combined, including 931 patients (≥65 years) from 65 nursing homes. One study assessed patients at admission, with 6-month follow-up (2012–2014). The other study assessed residents with varying lengths of stay, with 4-month follow-up (2014–2015). Patients were assessed with the Mini-Mental State Examination, the Mobilisation-Observation-Behaviour-Intensity-Dementia-2 Pain Scale, and the Cornell Scale for Depression in Dementia.

Results: At baseline, 343 patients (40% of 858 assessed) had moderate to severe pain, and 347 (38% of 924) had depression. Pain increased the risk of depression (OR 2.35, 95% CI 1.76–3.12). Using mixed model analyses, we found that a 1-point increase in pain was associated with a .48 increase in depression ($p < .001$). This association persisted in mild, moderate, and severe cognitive impairment. In those recently admitted, depressive symptoms decreased over time, and having less pain at follow-up was associated with a decrease in depressive symptoms (within-subject effect; $p = .042$).

Limitations: The two cohorts had different inclusion criteria, which may reduce generalisability. The study design does not allow conclusions on causality.

Conclusions: Pain and depressive symptoms are associated in patients with dementia. Because reduced pain is associated with less depressive symptoms, these patients should be assessed regularly for untreated pain. The benefit of analgesic treatment should be weighed carefully against the potential for adverse effects.

1. Introduction

In Norway, over 80% of nursing home patients have dementia (Helvik et al., 2015). Symptoms of depression affect up to 50% of people with dementia, causing increased suffering, reduced quality of life, and possibly shortened life expectancy (Enache et al., 2011; Gonzalez-Salvador et al., 2000; Janzing et al., 1999; Todd et al., 2013). Depression in people with dementia may also accelerate the decline in daily functioning and cognition, and contribute to the loss of independence and earlier nursing home placement (Luppa et al., 2008; Potter and Steffens, 2007; Rapp et al., 2011). Over time, depression often persists and re-occurs in these individuals (Selbaek and Engedal, 2012; Selbaek et al., 2013), and may be associated with worse outcomes of medical treatment (Bellelli et al., 2008; Lenze et al., 2007; Smith et al., 2015).

To manage mild to moderate depression in people with dementia, nonpharmacological interventions such as psychotherapy, reminiscence therapy, and personalized pleasant activities are recommended as first-line treatment (Kales et al., 2015; Orgeta et al., 2015; Testad et al., 2014). In severe depression, pharmacological treatment with antide-

* Corresponding author.
E-mail address: Ane.Erdal@uib.no (A. Erdal).

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pressants is recommended, although updated systematic reviews of the use of antidepressants for depression in people with dementia did not find conclusive evidence for efficacy in this population (Leong, 2014; Nelson and Devanand, 2011).

Thus far, little attention has been paid to potential modifiable causal factors of depression such as untreated chronic pain. Approximately 40–60% of nursing home patients are suggested to be in daily moderate to severe pain (Achterberg et al., 2010; Husebo et al., 2011). People with dementia are at particular risk of untreated pain because their ability to understand, evaluate, and verbally communicate symptom severity gradually decreases (Flo et al., 2014). This may trigger symptoms such as depression, agitation, and sleep problems (Ballard et al., 2009). The interrelationship between pain and depression, known as the "pain-depression dyad", is well documented in people *without* dementia (Bair et al., 2003; Goldenberg, 2010). Although no clear aetiology has been established, the conditions are known to commonly coexist, mutually exacerbate each other, share common signal pathways and neurotransmitters, and respond to similar treatments (Chopra and Arora, 2014).

The pain-depression dyad is not sufficiently investigated in people *with* dementia (Bair et al., 2003; Goldenberg, 2010). Thus far, four cross-sectional studies have found a significant association between pain and depression in nursing home patients with moderate to severe dementia (Cipher and Clifford, 2004; Leong and Nuo, 2007; Malara et al., 2016; Williams et al., 2005), including one study which also reported the prevalence of pain and depression stratified by cognitive status (Leong and Nuo, 2007). The most recent study by Malara et al. (2016) included 233 patients at different stages of dementia and found a significant association between pain and depression as evaluated by a physician. Although these studies provide important insights, some had a low sample size, did not assess pain and/or depression with validated proxy-rated instruments, and all studies lack prospective data to evaluate whether pain is associated with future worsening of depression. In the current study, we investigate the prospective associations between pain and depression in nursing home patients with advanced dementia to explore whether pain may be an exacerbating factor for depression, or vice versa. We addressed the following research questions: i) Is the intensity of pain associated with the severity of depression? ii) Is change in pain over time associated with change in depression? iii) How are these associations affected by cognitive function and use of analgesic or antidepressant drugs?

2. Methods

2.1. Sample

We analysed prospective data from two independent multicentre studies in 6 counties of Norway. The REDIC (*RE*source Use and *DI*sease *C*ourse in Dementia) study included all patients aged ≥65 years (or younger, if established dementia diagnosis) at admission to nursing home care with an expected stay of > 4 weeks, and life expectancy > 6 weeks, from January 2012 to June 2014 (Sandvik et al., 2016a). In total, 696 patients were included from 47 nursing homes. The current analyses use data collected at month 0 and 6, excluding 12 patients aged < 65 years (Fig. 1). The other study, COSMOS (*CO*mmunication, *S*ystematic pain treatment, *M*edication review, *O*rganized activities and *S*afety), included all patients aged ≥65 years in long-term nursing home care, excluding patients with diagnosis of schizophrenia or life expectancy < 6 months, from April 2014 to June 2015 (Husebo et al., 2015). In total, 545 patients were included from 67 units (clusters) in 31 nursing homes. Clusters were randomised to receive either a complex intervention or care as usual (Husebo et al., 2015). The current analyses use data from the control group, comprising 247 patients from 26 units, collected at month 0 and 4 (Fig. 1).

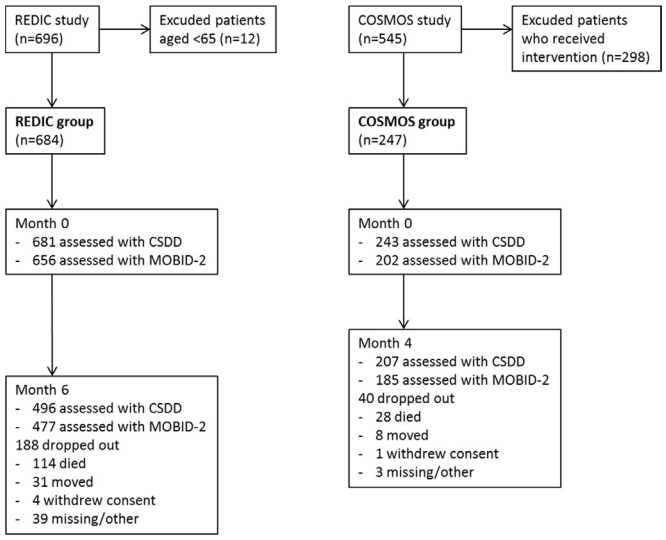

Fig. 1. Patients included in the final analyses.

2.2. Data collection

Data collection in both studies was completed in close collaboration with a staff member who had been familiar with the patients for a minimum of 4 weeks prior to data collection. The staff received training in the appropriate use of each outcome measure (Table 1), and had assistance from the researchers as needed. Demographic information and scheduled drug prescriptions (excluding prescriptions given "as needed") were extracted from the patients' medical records. Analgesic use at baseline and follow-up was assessed by counting the number of prescriptions for drugs classified as systemic analgesics (Anatomical Therapeutic Chemical (ATC) code N02 or M01A) at each time point. Similarly, antidepressant use was assessed by counting the number of prescriptions for drugs classified as antidepressants (ATC code N06A) at baseline and follow-up. We did not assess the appropriateness of dose; i.e. a dose adjustment from baseline to follow-up was not registered.

Cognitive function was assessed using the Mini-Mental State Examination (MMSE), with scores from 26 to 30 defined as no/questionable, 21–25 as mild, 11–20 as moderate and 0–10 as severe cognitive impairment (Folstein et al., 1975; Perneczky et al., 2006). Pain was assessed using the Mobilisation-Observation-Behaviour-Intensity-Dementia-2 (MOBID-2) Pain Scale, with moderate to severe pain defined as a score of ≥3 (Husebo et al., 2014). Depressive symptoms were assessed using the Cornell Scale for Depression in Dementia (CSDD), and depression defined as a score of ≥8 (Alexopoulos et al., 1988; Burns et al., 2004). The Neuropsychiatric Inventory – Nursing Home version (NPI-NH) was used to assess neuropsychiatric symptoms (Cummings et al., 1994; Selbaek et al., 2008), and the NPI-depression subscale was used as a secondary outcome measure.

2.3. Statistical analysis

Baseline characteristics were described with mean and standard deviation (SD) for continuous variables and with number of patients and percentages of sample size for categorical variables. Differences at baseline between the studies were tested with independent samples *t*-tests for normally distributed continuous variables, Mann-Whitney *U*-test for non-normal distributed continuous variables and Pearson χ^2 tests for categorical variables. The unadjusted odds ratio (OR) for depression among patients with moderate to severe pain was calculated at baseline. Linear regression models were fitted to analyse the prospective association between pain at baseline and depression at follow-up, and vice versa, adjusted for depression, pain, age, sex, and cognitive function at baseline. To account for intra-cluster correlation