Long-Term Effects of Analgesics in a Population of Elderly Nursing Home Residents With Persistent Nonmalignant Pain

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Background. Little is known about the long-term effects of analgesics on functional status and well-being of nursing home residents with chronic pain.

Methods. Using the Minimum Data Set, we performed a longitudinal study of nursing home residents \( n = 10,372 \) with persistent pain. Using propensity score adjustment techniques, we compared the effect of different analgesics on changes in physical, cognitive, emotional, and social functioning, and examined rates of adverse events over a 6-month period.

Results. There was no change in the analgesic class for at least 6 months for 35.4\% of residents, including 40\% who received no analgesics during this time. Use of nonopioids was 37.9\%, short-acting opioids was 18.9\%, and long-acting opioids was 3.3\%. We found improvement in functional status (adjusted hazard ratio \( = 1.85 \), 95\% confidence interval \([1.50, 2.28]\)) and social engagement (adjusted hazard ratio \( = 1.58 \), 95\% CI \([1.29, 1.92]\)) with long-acting opioids compared with short-acting opioids. There were no changes in cognitive status or mood status, or increased risk of depression with use of any analgesics, including opioids. There was a trend toward a lower risk of falls with use of any analgesics (adjusted odds ratio \( = 0.87 \), 95\% CI \([0.78, 0.97]\)). Rates of other adverse events (i.e., constipation, delirium, dehydration, pneumonia) were not found to be higher among chronic opioid users compared to those taking no analgesics or nonopioids.

Conclusions. The use of long-acting opioids may be a relatively safe option in the management of persistent nonmalignant pain in the nursing home population, yielding benefits in functional status and social engagement.

The prevalence of persistent pain among institutionalized elderly persons is between 49\% and 84\%, with at least one quarter having daily pain. Furthermore, 41.5\% continue to experience moderate daily pain or excruciating pain 60–180 days later (1–6).

Persistent pain is associated with poorer functional and mood status, and decreased involvement in recreational activities (5,7). Pain is often inadequately treated (5,7,8), perhaps due to fears of addiction and adverse side effects. The extent to which certain analgesics contribute to adverse outcomes or whether they may help reverse problems such as falls, functional decline, depression, and social isolation among frail elderly persons remains unknown.

The main objectives of this study were to (1) examine the effect of analgesic classes on decline or improvement of specific quality-of-life indicators, and (2) determine the risk of adverse events by different analgesic classes.

Methods

Data

Data were obtained from the Systematic Assessment of Geriatric Drug Use via Epidemiology (SAGE) database. This database merged nursing home Resident Assessment Information (RAI) from the Minimum Data Set (MDS, version 2.0), drug utilization data categorized according to the National Drug Code (NDC), Medicare claims data, and organizational data on nursing home providers (9).

Study Sample

The study population consisted of nursing home residents 65 years old or older admitted in 1998 (June through December), 1999, and 2000, from 13 states. We excluded residents with moderate to severe cognitive impairment based on a Cognitive Performance Scale (CPS) score \( \geq 2 \) (equivalent to a Mini-Mental Status Examination score \( < 19 \)) (10). To maintain validity and reliability for the measurement of pain and other psychometric measures, we also excluded residents with moderate to severe communication difficulties (11,12). Those included were able to make simple and concrete requests known (13). Residents with cancer or terminal prognosis were also excluded as these conditions are often associated with pain, depression, and functional decline. The determination of terminal prognosis required documentation in the medical record of the disease diagnosis, deteriorating clinical course, and a doctor’s certification that the resident had 6 months or less to live (13).

Our population was then restricted to states with complete pain and drug data (AL, IL, IN, KS, ME, MS, OH, TX, SD, WV) for five quarterly assessments \( n = 21,380 \). Our target sample consisted of residents with pain recorded in at least two of the three assessments, as we considered these people to be in persistent pain \( n = 10,372 \). Our analysis focused on persons taking the same drug category as a standing dose for three
consecutive quarterly assessments (quarters 3, 4, and 5), \(n = 3669\), and outcomes were determined at 6 months (quarter 5).

**Pain Evaluation**

Following MDS procedures, the assessor is instructed to ask the resident simple, direct questions about pain and rely on resident self-report when possible. Daily pain was defined as any type of physical pain or discomfort in any part of the body occurring daily over the 7 days preceding the assessment (14). Pain was also characterized as mild, moderate, or excruciating. Inter-rater reliability for MDS pain items is good \((\kappa > 0.7)\) (15), and correlates with the vertical Visual Analog Scale (VAS) (16). Persistent pain was defined as pain lasting 3 months or longer, or recurring intermittently over 6 months. (i.e., pain recorded in at least two of three quarterly assessments). The baseline assessment used was the third MDS assessment.

**Analgesic Use**

Analgesics given during the week prior to the MDS assessment were recorded. Analgesic classes were categorized as follows:

1. Standing long-acting opioids (LAOs)—persons on one standing order for an LAO. Use of short-acting opioids (SAOs) prescribed “as needed” (prn) were not included. Use of nonopioids (standing or prn) were allowed in this category.
2. Standing SAOs—persons on at least one standing order for an SAO. There were no LAO orders or prn SAO orders. Use of nonopioids (standing or prn) were allowed in this category.
3. Standing Nonopioids—persons on at least one standing order for a nonopioid. Additional use of prn orders for nonopioids was allowed in this category. There were no opioid users in this group.
4. No analgesics used—persons taking no analgesics, opioids, or nonopioids.

Because we were more interested in the impact of the analgesic class on outcomes, we focused only on those residents taking standing doses. We did not ascertain whether residents prescribed analgesics as needed were taking these around-the-clock, nor did we examine the effect of analgesic doses on outcomes.

**Operational Expression of Outcome Variables**

Because quality of life is an important goal in elderly persons, our primary outcomes were improvements in cognitive, functional, mood, and social engagement status.

The MDS CPS (10) was used to evaluate cognition. The CPS score ranges from 0 (intact) to 6 (very severe). Using the Mini-Mental Status Examination as the gold standard, the CPS has high sensitivity \((>90\%)\) and specificity \((>85\%)\), and excellent reproducibility \((\kappa > 0.76)\) (17). We included only residents who scored 0–2 on the CPS. A 1-point reduction on the CPS reflects a clinically significant improvement in cognitive status (17).

Physical function was assessed using a previously developed summary scale for activities of daily living (ADL) in the MDS. This scale is based on six levels of self-performance including dressing, eating, toilet use, bathing, locomotion, and transfer. The reliability of the ADL scores range from 0.86 to 0.94 (18), and are highly correlated (0.89) with the Lawton and Brody Physical Self-Maintenance Scale (12). A 1-point reduction on the MDS ADL scale reflects a clinically significant improvement in functional status.

To evaluate mood problems, we used the MDS Depression Rating Scale, which is based on 12 MDS items (e.g., feelings of worthlessness, pacing, hand wringing, crying, groaning) (13) and is closely correlated with the Hamilton Depression Scale (19). A cut-point score of 3 on the MDS Depression Rating Scale maximizes sensitivity (94\%), with minimal loss of specificity (72\%) when tested against cutoffs for mild to moderate depression on the Hamilton Depression Scale. For baseline scores in the lower part of the MDS Depression Rating Scale, we felt that a 1-point reduction in the score would reflect a clinically significant improvement in mood status.

We also evaluated psychosocial well-being by using the Index of Social Engagement. This index is based on the sum of the following MDS items: (i) at ease interacting with others; (ii) at ease doing planned or structured activities; (iii) at ease doing self-initiated activities; (iv) establishes own goals; (v) pursues involvement in the life of the facility; and (vi) accepts invitations to most group activities. The items have moderately good inter-rater reliability (20) and internal consistency (Cronbach’s \(\alpha = 0.72\)) (21). Scores on the Index of Social Engagement range from 0 (lowest level of social engagement) to 6 (highest level of social engagement). We used a 1-point increase to indicate improvement in social engagement.

Potential adverse events included falls, constipation, pneumonia, gastrointestinal bleed, renal failure, delirium, and depression, which were identified as items on the MDS, as well as by their International Classification of Diseases, Ninth Revision (ICD-9) codes, if these were used. Delirium symptoms were identified by the occurrence of at least one of the six MDS delirium items.

**Analytical Approach**

We first identified baseline characteristics of individuals with persistent pain who took the same analgesic class for 6 months. We recorded pain frequency and intensity, analgesics, and measures of cognitive, functional, emotional status, and social engagement.

A one-unit change in the cognitive, function, emotional status, and social engagement score reflected a clinically significant change of status. Cox proportional hazards models provided estimates of rate ratios for decline or improvement of these outcomes. We adjusted for sociodemographic variables, psychotropic medications, pain severity and intensity, and cognitive and physical functioning (except for when these variables were the outcome of interest). We also developed propensity scores predicting treatment and included the predicted probability of treatment as a covariate in the Cox proportional hazards models. We used a similar approach for adverse events, but in the absence of the exact date of event, used logistic regression models. We estimated adjusted odds ratios (ORs) from the models, and interpreted the OR as an estimate of the relative risk. Because analgesics could potentially lower quality of life, we also examined rates of decline in cognitive, functional, mood status, and social engagement status over 6 months. We performed all analyses using SAS software (version 6.8; SAS Institute, Cary, NC).

**RESULTS**

**Prevalence of Analgesic Use**

For 35.4% \((n = 3669)\) of residents, there was no change in the analgesic class for at least 6 months. Forty percent \((n = 1467)\) of these received no analgesics during this time. Use of standing
dose nonopioids was 37.9%, standing SAOs was 18.9%, and standing LAOs was 3.3%. At baseline, among residents on LAOs there were greater proportions of persons with daily pain (70.0%) and severe pain (20.7%), as well as the highest proportion of persons with severe ADL impairment (4.2%) and a diagnosis of depression (64.2%) (Table 1).

Quality-of-Life Measures
There was a significantly higher rate of improvement in ADL status observed in persons taking LAOs compared to those taking nonopioids (propensity adjusted rate ratio 1.84; 95% confidence interval [CI], 1.07–3.14), and those taking LAOs compared to those taking SAOs (propensity adjusted rate ratio 1.85; 95% CI, 1.05–3.23) (Table 2).

We also observed significantly greater improvement in social engagement with use of LAOs compared to use of nonopioids (propensity adjusted rate ratio 1.60; 95% CI, 1.02–2.48), and a trend toward improvement with use of LAOs compared to SAOs (propensity adjusted rate ratio 1.58; 95% CI, 0.99–2.50). No significant improvement was seen for any other analgesic classes (Table 2). There were no significant declines in cognitive function, ADL status, mood status, or social engagement over 6 months with use of any analgesics.

Risk of Adverse Events
Overall, there was a trend toward a decreased risk for falls over 6 months with use of any analgesics (236 falls/2200 persons), compared to use of no analgesics (212 falls/1467 people), with adjusted OR = 0.87 (95% CI, 0.70–1.06; data not shown). Long-term use of opioids did not significantly increase the risk of falls. There were no increased risks for the development of other adverse events such as constipation, pneumonia, gastrointestinal bleeding, dehydration, renal failure, delirium, or depression with long-term opioid use (short- or long-acting). However, there was a lower rate of gastrointestinal bleeding with use of SAOs (OR = 0.53; 95% CI, 0.28–0.98) (Table 3).

Discussion
These data raise concerns that pain is not adequately monitored or addressed in the nursing home. Despite the
Table 2. Effect of Pain Medications on Rates of Improvement of Specific Quality-of-Life Indicators

<table>
<thead>
<tr>
<th>Improvement in CPS</th>
<th>No. of Persons Improving Person-Years</th>
<th>Rates per 1000 Person-Years</th>
<th>Propensity-Adjusted Crude RR</th>
<th>Propensity-Adjusted Adjusted RR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>LAOs vs no analgesics</td>
<td>n &lt; 11 vs 71 10.4 vs 8.5</td>
<td>1.21</td>
<td>1.41</td>
<td>0.60–3.31</td>
<td></td>
</tr>
<tr>
<td>LAOs vs nonopioids</td>
<td>n &lt; 11 vs 59 8.2 vs 7.5</td>
<td>1.38</td>
<td>1.60</td>
<td>0.70–3.61</td>
<td></td>
</tr>
<tr>
<td>LAOs vs SAOs</td>
<td>n &lt; 11 vs 32 10.4 vs 8.2</td>
<td>1.27</td>
<td>1.26</td>
<td>0.54–2.90</td>
<td></td>
</tr>
</tbody>
</table>

Improvement in ADL

<table>
<thead>
<tr>
<th>Improvement in mood</th>
<th>No. of Persons vs</th>
<th>Rates per 1000 Person-Years</th>
<th>Propensity-Adjusted Crude RR</th>
<th>Propensity-Adjusted Adjusted RR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>LAOs vs no analgesics</td>
<td>17 vs 141</td>
<td>26.2 vs 17.2</td>
<td>1.52</td>
<td>1.70</td>
<td>0.96–2.98</td>
</tr>
<tr>
<td>LAOs vs nonopioids</td>
<td>17 vs 108</td>
<td>26.2 vs 13.8</td>
<td>1.89</td>
<td>1.84</td>
<td>1.07–3.14</td>
</tr>
<tr>
<td>LAOs vs SAOs</td>
<td>17 vs 53</td>
<td>26.2 vs 13.7</td>
<td>1.91</td>
<td>1.85</td>
<td>1.05–3.23</td>
</tr>
</tbody>
</table>

Improvement in functional and psychological wellbeing

<table>
<thead>
<tr>
<th>Improvement in social engagement</th>
<th>No. of Persons vs</th>
<th>Rates per 1000 Person-Years</th>
<th>Propensity-Adjusted Crude RR</th>
<th>Propensity-Adjusted Adjusted RR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>LAOs vs no analgesics</td>
<td>24 vs 237</td>
<td>37.3 vs 29.6</td>
<td>1.26</td>
<td>1.18</td>
<td>0.73–1.88</td>
</tr>
<tr>
<td>LAOs vs nonopioids</td>
<td>24 vs 197</td>
<td>37.3 vs 29.9</td>
<td>1.44</td>
<td>1.60</td>
<td>1.02–2.48</td>
</tr>
<tr>
<td>LAOs vs SAOs</td>
<td>24 vs 89</td>
<td>37.3 vs 27.5</td>
<td>1.59</td>
<td>1.58</td>
<td>0.99–2.50</td>
</tr>
</tbody>
</table>

Note: Due to the current policy regarding disclosure of Medicare Beneficiary Data and concerns about confidentiality, data for patients with n < 11 are not specified.

RR = rate ratio; CI = confidence interval; LAO = long-acting opioid; SAO = short-acting opioid; CPS = cognitive performance scale; ADL = activities of daily living.

documentation of daily or severe pain, almost 40% of residents remained without analgesics for 6 months.

We also found that long-term use of analgesics was associated with a trend toward fewer falls, particularly among SAOs (OR = 0.81; 95% CI, 0.60–1.08). In the Women’s Health and Aging Study (WHAS), researchers also found that the risk for falls among community-dwelling elderly women was lower for those using daily analgesics (adjusted OR = 0.79; 95% CI, 0.63–0.98) (5,22–24). It is possible that we did not detect statistical differences among LAO users because of insufficient power. The decreased risk of falls may be explained by a few hypotheses: (i) Pain may contribute to joint instability and loss of balance from unconscious attempts to guard painful joints, (ii) Pain itself can cause muscle weakness by a centrally mediated mechanism (25,26), or (iii) residents having less pain may exercise more and be less deconditioned, therefore less prone to falls.

This study also demonstrates that functional and psychological improvement in the frailest residents with chronic pain is possible with adequate treatment. Our findings corroborate those from another study of nursing home residents (n = 92) which found that residents receiving analgesics were more physically active and verbally interactive (27). In addition, because improvements were seen when LAO use was compared with use of nonopioids or SAOs, we hypothesize that steady drug levels or higher doses may be providing better pain relief and therefore improved functioning. Future studies should focus on these points.

With regard to adverse effects, confounding by indication may explain our (nonsignificant) findings of increased renal failure with LAOs. Even so, rates of gastrointestinal bleeding for SAO users were almost half the rate of those of nonopioid users. There are many studies of long-term adverse effects of nonsteroidal anti-inflammatory drugs and COX-2 inhibitors (28). However, there are few studies of long-term adverse opioid side effects. Higher rates of adverse effects are observed with initiation of opioids, but data also suggest that these may be preventable if monitored closely (29–31). We found no long-term adverse events in our study. Thus, it appears that although short-term risks may be higher with opioids, long-term toxicity appears to be low.

This study has several limitations. To achieve internal validity of the study, it was necessary to restrict the sample severely (persons taking analgesics in only one class for 6 months). The study design also contributed to low rates of adverse events. Not only could resident risk factors influence initial choice of drugs, those persons with adverse events may have switched classes soon after initiation, and thus were screened out of the study. We should emphasize, however, that the study was not designed to examine short-term adverse effects. In addition, because the number of persons on SAOs and LAOs was so small, we also included in these categories persons who used nonopioids. This inclusion may have diluted any differences in adverse events. Subset analysis of specific analgesics (e.g., nonsteroidal anti-inflammatory drugs, COX-2 inhibitors) could have helped clarify this, but was not possible because of the small number of events. The identification of adverse events was also limited to the list of common diagnoses.

Table 3. Risk of Adverse Events Over 6 Months

<table>
<thead>
<tr>
<th>Adverse Events</th>
<th>No Analgesics N = 1467</th>
<th>Nonopioids N = 1387</th>
<th>LAOs N = 120</th>
<th>SAOs N = 693</th>
</tr>
</thead>
<tbody>
<tr>
<td>Falls</td>
<td>212</td>
<td>185</td>
<td>17</td>
<td>83</td>
</tr>
<tr>
<td>Constipation</td>
<td>117</td>
<td>94</td>
<td>n &lt; 11</td>
<td>62</td>
</tr>
<tr>
<td></td>
<td>0.89</td>
<td>0.89</td>
<td>0.89</td>
<td>1.24</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>28</td>
<td>26</td>
<td>n &lt; 11</td>
<td>15</td>
</tr>
<tr>
<td></td>
<td>1.01</td>
<td>0.57</td>
<td>0.85</td>
<td>0.53</td>
</tr>
<tr>
<td>GI bleeding</td>
<td>54</td>
<td>42</td>
<td>n &lt; 11</td>
<td>15</td>
</tr>
<tr>
<td></td>
<td>0.79</td>
<td>0.51</td>
<td>0.85</td>
<td>0.53</td>
</tr>
<tr>
<td>Renal failure</td>
<td>13</td>
<td>n &lt; 11</td>
<td>n &lt; 11</td>
<td>15</td>
</tr>
<tr>
<td></td>
<td>0.50</td>
<td>0.18</td>
<td>2.16</td>
<td>1.05</td>
</tr>
<tr>
<td>Delirium</td>
<td>129</td>
<td>109</td>
<td>12</td>
<td>51</td>
</tr>
<tr>
<td></td>
<td>0.87</td>
<td>0.65</td>
<td>1.09</td>
<td>0.79</td>
</tr>
<tr>
<td>Depression</td>
<td>63</td>
<td>50</td>
<td>n &lt; 11</td>
<td>32</td>
</tr>
<tr>
<td></td>
<td>0.87</td>
<td>0.58</td>
<td>0.88</td>
<td>1.20</td>
</tr>
</tbody>
</table>

Notes: All drug categories are for standing doses of each category. The reference group is no analgesics, and adverse events are adjusted for concomitant medications (steroids, diuretics, antidepressants, anxiolytics, and antipsychotics) and comorbidities (age, sex, race, activities of daily living [ADL] scale score, cognitive performance score [CPS] score, pain frequency, and pain intensity). Data for dehydration not shown because n < 11. Due to the current policy regarding disclosure of Medicare Beneficiary Data and concerns about confidentiality, data for patients with n < 11 are not specified.

LAO = long-acting opioid; SAO = short-acting opioid; OR = odds ratio; CI = confidence interval; GI = gastrointestinal.
in the MDS database. More accurate identification of adverse events would require extensive chart reviews; these reviews were not feasible.

With regard to the analysis of quality-of-life outcomes, we believe that confounding by indication is not likely. Although one might expect persons with severe, persistent pain, and poor functional and mood status at baseline to have poorer outcomes, these residents (who tend to take LAOs) appear to do better with regard to function and social engagement.

Randomized clinical trials provide the closest estimate of causal treatment effects. Yet, such trials are unlikely to occur in frail nursing home populations. The use of propensity scores can provide tighter control of confounding in observational studies of treatment effects. Although confounding can never be completely ruled out as an alternative explanation of treatment effects, we have derived adjusted estimates of effect using methods thought to provide the most unbiased estimates.

With regard to generalizability, our restricted sample had baseline characteristics similar to the general nursing home population with persistent pain. Our results are applicable only to persons with persistent pain on a stable analgesic regimen.

Conclusion
Although all these limitations are recognized, to our knowledge no other studies examining quality-of-life outcomes of chronic analgesic use in frail elderly persons has ever been done. This study demonstrates that chronic use of opioids may indeed be a relatively safe option in the management of persistent nonmalignant pain in the nursing home population, yielding benefits in functional improvement and social engagement.

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References

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