Older Adults’ Response to Analgesic Adverse Drug Reactions: A Pilot Study

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ABSTRACT:
Older adults who take analgesics for chronic pain are at increased risk for adverse drug events (ADEs). The purpose of this descriptive pilot survey was to examine how older adults self-identify analgesic ADEs, and actions they take in response to analgesic ADEs. Twenty-two community dwelling older adults with chronic pain who reported an analgesic ADE associated with their chronic pain management were interviewed and asked to describe their analgesic related ADE. Written responses were content analyzed. Nineteen opioids were reported by 15, 11 NSAIDs were reported by 8, and acetaminophen was reported by 2 older adults as associated with an ADE. Gastrointestinal ADEs were most common with upset stomach (31.8%) most frequent. Neurological ADEs were also common but more varied with dizziness (27.3%) and headache (13.6%) reported most frequently. A total of 54.5% responded to their ADE by contacting their physician. Three (13.6%) went to the emergency department. A total of 36.4% stopped taking their ADE associated analgesic, 22.7% started taking a different analgesic, and 22.7% started prophylaxis. Three (13.6%) continued their ADE related analgesic. A total of 54.5% reported their symptoms subsided, but 13.6% reported their symptoms remained. A significant number of older adults with chronic pain self-manage their analgesic related ADE without contacting their primary care provider. Analgesic related ADE prevention and management should be discussed during primary care visits to reduce ADEs and enhance pain management outcomes for older adults with chronic pain.

Older adults (≥65 y) who take analgesics for chronic pain are at increased risk for an adverse drug reaction (ADR). Adverse drug events are “harms that occur during medical care that are directly caused by a drug including but not limited to medication errors, adverse drug reactions, allergic reactions, and overdoses” (U.S. Department of Health and Human Services, 2014, p. 5). One type of ADR is “harm directly caused by a drug at normal doses” (U.S. Department of Health and Human Services, 2014, p. 5). Analgesics comprise nonsteroidal
anti-inflammatory drugs (NSAIDs), acetaminophen, and opioids and constitute a drug classification frequently associated with ADR in older adults, with 16.7% of ADRs related to analgesics in ambulatory care (Gurwitz et al., 2003). National estimates from data collected from 2007 to 2009 indicate that 4.8% of older adults were hospitalized for an opioid ADR, of which 32.4% were seen in the emergency room (Budnitz, Lovegrove, Shehab, & Richards, 2011). For Canadian older adults, 7.3% and 3.2% of the emergency room visits between 2006 and 2008 were associated with opioids and NSAIDs, respectively (Bayoumi, Dolovich, Hutchison, & Holbrook, 2014). The odds of a hospital admission increase 5.87 from an NSAID-related ADR for older adults (Wierenga et al., 2012).

Analgesic-related ADRs vary by analgesic group. NSAIDs are associated with increased cardiovascular and gastrointestinal ADRs in elders (Aminoshariae, Kulid, & Donaldson, 2016). More specifically, NSAIDs have been associated with heart failure, salt retention, thrombosis, and harmful cardiac remodeling (Kohli et al., 2014). NSAID gastrointestinal ADRs include vomiting, nausea, constipation, diarrhea, and reduced appetite. Duodenal ulcers with perforation and hemorrhage can also result from NSAID use. Hyperkalemia and renal failure can occur as well. Acetaminophen is the most common cause of acute liver failure in the United States (Lee, 2004), and can also result in skin reactions (U.S. Food and Drug Administration, 2015). The most frequently reported opioid-related ADRs in older adults with chronic nonmalignant pain include constipation (30%), nausea (28%), dizziness (22%), and drowsiness (21%) (Papaleontiou et al., 2010). Adults of all ages with chronic pain report being moderately to extremely bothered by the opioid-related ADRs of constipation (31.2%), drowsiness (25.5%), nausea (16.1%), dizziness (14.0%), headache (12.2%), itching (8.3%), and vomiting (7.1%). At least 75% reported one or more adverse drug reactions (Gregorian, Gasik, Kwong, Voeller, & Kavanagh, 2010).

Sixty-six percent of adults with chronic pain self-managed their ADRs: only 19% called and 20% visited their physician to manage their ADR (Gregorian et al., 2010). The majority of older adults therefore are also likely to self-manage their analgesic ADRs. There is a knowledge gap in how older adults identify and self-manage analgesic ADRs and factors that prompt older adults to seek health care for their ADR. Research to address the gap would assist health care practitioners and older adults to communicate better about and further reduce analgesic-related ADRs. The purpose of this pilot research was to describe how older adults recognize and self-manage analgesic-related ADRs and when and how older adults seek health care for their ADRs.

METHODS

Design

A descriptive pilot survey design was used.

Sample and Setting

The convenience sample comprised English-speaking, community-dwelling adults, aged 65 and older, who had chronic pain lasting 6 months or longer and who reported experiencing a past ADR that they associated with taking an opioid, NSAID, or acetaminophen. Recruitment settings included five elderly congregate housing sites across two states and four senior centers in both urban and suburban settings.

Instruments

Problem Pain Medication Survey. The Problem Pain Medication Survey (PPMS) was Developed for the Current Study and Consists of a Series of five Open-ended Questions Used to Elicit Information on the Process of Self-identifying an Analgesic-associated ADR, Actions Taken after Identifying the ADR, and Outcomes from the ADR and Actions. The Questions Were as Follows:

- Tell me everything that you can recall about how you first identified that you were having a negative response to the pain medication?
- Describe your negative response to the pain medication as completely as possible.
- Tell me the actions that you took in response to your negative pain medication response.
- Tell me what happened as a result of your actions.
- Is there anything else that might be helpful for us to understand about your negative experience with the pain medication?

Demographic and General Health Form. The Demographic and General Health Form Elicited age, Gender, race, Ethnic Group, Marital Status, Education Level, and Self-reported History of Major health Problems, Eyeglass use, and medication Allergies. Participants Were Also Requested to List All Their Current Medications, Vitamins, and Other Supplements.

Procedure

Following university institutional review board approval, participants were recruited from community settings such as senior centers and senior congregate housing. Screening for eligibility was accomplished by asking participants if they were age 65 years or older, if they had continuous or intermittent pain
lasting 6 months or longer, and if they have ever had a problematic response to a self-administered pain medication. Affirmative responses were queried further to ascertain that the medication was an opioid, NSAID, or acetaminophen. Participants were excluded from the study if they were unsure if the medication associated with the ADR was an analgesic. The number of excluded participants and reasons for ineligibility were not documented. Informed consent was secured from eligible participants. All participants were interviewed by trained data collectors. Responses were recorded in writing by the interviewer. After collection of the demographic and health information, the open-ended questions regarding ADRs were posed. Participants who reported ADRs from more than one analgesic type were requested to discuss the most problematic analgesic. Neutral statements such as ‘tell me more’ were used to prompt more complete responses while avoiding directed responses or premature closure of information.

Content Analysis
Content analysis (Krippendorff, 2013) was used to analyze responses to the interview questions. Coding was conducted independently by three trained coders. A priori criteria were identified for the ADR, how the ADR was identified, the response, and the outcome from the ADR. Results were compared, and disagreements were discussed to consensus.

Table 1. Demographic and Comorbidity Frequencies (N = 22)

<table>
<thead>
<tr>
<th>Variable</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>19 (86.4)</td>
</tr>
<tr>
<td>Race</td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>1 (4.5)</td>
</tr>
<tr>
<td>Black</td>
<td>3 (13.6)</td>
</tr>
<tr>
<td>White</td>
<td>18 (81.8)</td>
</tr>
<tr>
<td>Education</td>
<td></td>
</tr>
<tr>
<td>&lt; High school</td>
<td>1 (4.5)</td>
</tr>
<tr>
<td>High school</td>
<td>15 (68.2)</td>
</tr>
<tr>
<td>College</td>
<td>6 (27.2)</td>
</tr>
<tr>
<td>Comorbidities*</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>16 (72.7)</td>
</tr>
<tr>
<td>Other cardiovascular</td>
<td>9 (40.9)</td>
</tr>
<tr>
<td>Renal failure</td>
<td>2 (9.1)</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>15 (68.2)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>9 (40.9)</td>
</tr>
<tr>
<td>Thyroid disease</td>
<td>6 (27.3)</td>
</tr>
<tr>
<td>Arthritis</td>
<td>21 (95.5)</td>
</tr>
<tr>
<td>Depression</td>
<td>5 (22.7)</td>
</tr>
</tbody>
</table>

* A total of 12 additional comorbidities (combined frequency = 46) were reported.

Statistical Analyses
Content analysis results were entered into SPSS and summarized with frequencies. Sample demographic and health information was also summarized with frequencies and means and standard deviations for interval-level data.

RESULTS
A total of 22 older adults participated in the survey. The majority were White non-Hispanic women with a high school education. The mean age was 77.3 (SD = 9.04), and the mean number of comorbidities was 5.6 (SD = 2.46). All but one reported arthritis. Table 1 summarizes the demographics and comorbidities.

Opioids were associated with the most ADRs, whereas acetaminophen was associated with the least ADRs. Fifteen participants reported an opioid-related ADR, eight reported an NSAID-related ADR, and two reported an acetaminophen-related ADR. Three of the opioid-related analgesics were opioid/acetaminophen combinations. Six participants reported multiple analgesics associated with their ADR, which included three opioids (n = 1); two opioids (n = 2); one opioid, two NSAIDs, and acetaminophen (n = 1); one opioid and one NSAID (n = 1); and two NSAIDs (n = 1).

Participants responded to the question about how they identified their analgesic-related ADR by generally describing the timing of their ADR identification. In response to the analgesic, three (13.6%) described immediate identification of the ADR, two (9.1%) identified the ADR within hours, five (22.7%) identified the ADR days later, and one (4.5%) identified the ADR months afterward. Another person identified the ADR for three participants (13.6%).

A total of 51 ADRs were reported, with gastrointestinal-related ADRs the most frequently reported type of ADR. ADRs ranged from feeling dizzy to life-threatening hemorrhage. Perceptual disturbances included confusion, hallucinations, decreased feeling of reality, and not feeling like oneself. Withdrawal symptoms included irritability, shakiness, and feeling hyperactive. Table 2 contains frequencies for the ADR symptoms specific to opioids, NSAIDs, and acetaminophen, and for the total of all the analgesics.

Older adults responded to their ADR symptoms in several different ways. Slightly more than half (13, 59.1%) contacted their physician. Eight (36.4%) stopped the analgesic. Five (22.7%) started a different analgesic. Table 3 contains frequencies for actions that older adults took in response to their ADR. Twelve (54.5%) reported that their symptoms subsided. Three
(13.6%) reported their symptoms remained. Three (13.6%) reported that their pain continued. Eight older adults (36.4%) reported no health care consultation for their analgesic ADR (did not contact a physician or visit the emergency department). Symptoms for these individuals are summarized in Table 4 and range from constipation to confusion. All were opioid-related ADRs.

### DISCUSSION

Adverse drug reactions reported by the older adults ranged from fatigue to life-threatening internal hemorrhage. Opioid analgesics were most frequently associated with ADRs, with 15 older adults reporting 19 symptoms. The percentage of reported opioid-associated ADRs for constipation, nausea, and dizziness were similar to previously reported percentages (Papaleontiou et al., 2010). No drowsiness was reported by the older adults taking opioids, perhaps because tolerance to symptoms such as drowsiness develops after taking opioids for 2 to 3 days (British Geriatrics Society, 2013).

Although some participants identified their ADR immediately, just as many identified their ADRs days or longer after initiating their analgesic. More troubling was lack of self-awareness of the ADR until another person identified the ADR for 13.6% of the older adults. Timely identification of an analgesic-related ADR is important to reduce serious complications and ensure safe and full recovery. Older adults should be taught to consider new symptoms as medication-related symptoms until the medication can be ruled out and to consult with their primary care practitioner for expert assistance in determining the cause of symptoms.

Twenty percent more older adults in the current study contacted their practitioner about their analgesic ADRs than reported by Gregorian et al. (2010), which is encouraging. However, 36.4% of the older adults in the current study did not contact their practitioner

### Table 2.

Analgesic ADR Symptom Frequencies (N = 22)

<table>
<thead>
<tr>
<th>ADR</th>
<th>Opioid</th>
<th>NSAID</th>
<th>Acetaminophen</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upset stomach</td>
<td>2 (15.4)</td>
<td>3 (50.0)</td>
<td>0 (0.0)</td>
<td>7 (31.8)</td>
</tr>
<tr>
<td>Constipation</td>
<td>4 (26.7)</td>
<td>2 (33.3)</td>
<td>0 (0.0)</td>
<td>6 (27.3)</td>
</tr>
<tr>
<td>Nausea or vomiting</td>
<td>3 (23.1)</td>
<td>2 (33.3)</td>
<td>0 (0.0)</td>
<td>6 (27.3)</td>
</tr>
<tr>
<td>Anorexia or weight loss</td>
<td>0 (0.0)</td>
<td>3 (50.0)</td>
<td>0 (0.0)</td>
<td>3 (13.6)</td>
</tr>
<tr>
<td>Cramps</td>
<td>1 (7.7)</td>
<td>1 (16.7)</td>
<td>0 (0.0)</td>
<td>2 (9.1)</td>
</tr>
<tr>
<td>Epistaxis</td>
<td>0 (0.0)</td>
<td>1 (16.7)</td>
<td>0 (0.0)</td>
<td>1 (4.5)</td>
</tr>
<tr>
<td>Internal hemorrhage</td>
<td>1 (7.7)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>1 (4.5)</td>
</tr>
<tr>
<td>Cardiac dysrhythmia</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>1 (4.5)</td>
</tr>
<tr>
<td>Difficulty breathing</td>
<td>1 (7.7)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>1 (4.5)</td>
</tr>
<tr>
<td>Dizzy</td>
<td>4 (30.8)</td>
<td>1 (16.7)</td>
<td>0 (0.0)</td>
<td>6 (27.3)</td>
</tr>
<tr>
<td>Feeling faint</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>1 (4.5)</td>
</tr>
<tr>
<td>Headache</td>
<td>2 (15.4)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>3 (13.6)</td>
</tr>
<tr>
<td>Sleep disorder</td>
<td>1 (7.7)</td>
<td>0 (0.0)</td>
<td>1 (100)</td>
<td>2 (9.1)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>2 (15.4)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>2 (9.1)</td>
</tr>
<tr>
<td>Perceptual disturbance</td>
<td>2 (15.4)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>4 (18.2)</td>
</tr>
<tr>
<td>Depressed</td>
<td>1 (7.7)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>1 (4.5)</td>
</tr>
<tr>
<td>Withdrawal symptoms</td>
<td>3 (23.1)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>4 (18.2)</td>
</tr>
</tbody>
</table>

ADR = adverse drug reaction; NSAID = nonsteroidal anti-inflammatory drug.
or go to an emergency department for treatment of their ADR. All of these older adults experienced an opioid-related ADR. Older adults who chose not to contact their physician or visit the emergency department might have experienced mild, easily managed ADRs. One older adult reported confusion, which should be assessed and treated by a practitioner. The individual might not have been capable of identifying the need to seek health care while confused. A second individual reported possible withdrawal symptoms from one or both of the opioids he was taking and would likely have benefitted from a health care consultation. Although some of the ADR symptoms such as mild constipation might be safely self-managed, older adults should seek health care consultation for more complete assessment when analgesic-related ADR symptoms occur. Some older adults might hesitate to reveal their opioid-related ADR to their practitioner for fear of discontinuation of the opioid and being left with no effective analgesic for their pain. Results from the current study provide tentative evidence that opioid-related ADRs might be underreported by older adults.

If opioid-associated ADRs are being left unidentified and/or untreated by some older adults, a significant portion of older adults may be experiencing ADRs for extended periods. Prolonged experience of ADRs may deteriorate health or result in the development of other health issues. Gastrointestinal-related ADRs, including constipation, were reported most frequently in the present study. Although constipation may seem relatively harmless and easy to self-manage, a long-term repercussion is increased risk of colorectal cancer, a life-threatening condition for all ages (Guerin et al., 2014). Additionally, chronic constipation has been reported to increase the risk of hemorrhoids, rectal prolapse, fecal incontinence, volvulus, and anal fissures (Arora, Mannalithara, Mithal, Triadafilopoulous, & Singh, 2012). Health conditions that develop from chronic constipation may further exacerbate pain. Although some opioid-related ADRs seem to lack severity and urgency to resolve, studies examining the long-term consequences of ADRs enforce how vital early discovery and intervention are.

Results from this study must be interpreted with caution because of several limitations. The major limitation was the small sample size. Recruitment took place in five elderly congregate housing sites in two different states and four senior centers in both urban and suburban settings. Despite face-to-face recruitment, few older adults were identified as eligible for the study, usually because of no self-identified analgesic ADR. Previous research indicates that 16.7% of older adults report analgesic-related ADRs during ambulatory care visits (Gurwitz et al., 2003). Many older adults might experience an analgesic-related ADR, but not report the ADR or simply not associate the symptom with the analgesic. Research is needed to more accurately measure the frequency and severity of analgesic-related ADRs among older adults. The national repository for adverse drug events, the U.S. Food and Drug Administration (FDA) Adverse Events Reporting System, cannot be used to estimate ADR prevalence because of the voluntary nature and varied sources of the ADR reports. The relatively small percentage of older adults who recognize and report analgesic ADRs greatly limited the current sample size.

A second limitation was the selection effect of analgesic ADR recall. Older adults might recall more severe ADRs and omit less severe ADRs. In the current study older adults were instructed to report the most problematic analgesic-related ADR when more than one ADR was experienced. Therefore, ADRs reported in the current study might not be representative of analgesic ADRs typically experienced by older adults. It is important to describe all analgesic ADRs, but particularly important to describe more serious analgesic-related ADRs.

A third limitation was that the open-ended interview questions allowed older adults to describe the analgesic ADR in their own words, but the initial question that asked how they first identified their ADR generally resulted in information about the timing of ADR identification. It remains unclear if other important information such as a cumulative effect from additional analgesic doses, taking more analgesic than

### Table 4.
**Analgesic ADRs of Participants Who Did Not Seek Health Care (n = 8)**

<table>
<thead>
<tr>
<th>Case No.</th>
<th>ADR Symptom</th>
<th>Analgesic</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>Withdrawal</td>
<td>Opioid</td>
</tr>
<tr>
<td></td>
<td>Irritable</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Insomnia</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Constipation</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Headache</td>
<td>Opioid</td>
</tr>
<tr>
<td>7</td>
<td>Upset stomach</td>
<td>Opioid</td>
</tr>
<tr>
<td></td>
<td>Cramps</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Nausea</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>Constipation</td>
<td>Opioid</td>
</tr>
<tr>
<td>11</td>
<td>Confusion</td>
<td>Opioid</td>
</tr>
<tr>
<td>13</td>
<td>Constipation</td>
<td>Opioid</td>
</tr>
<tr>
<td>18</td>
<td>Dizziness</td>
<td>Opioid</td>
</tr>
<tr>
<td></td>
<td>Headache</td>
<td></td>
</tr>
<tr>
<td>20</td>
<td>Fatigue</td>
<td>Opioid</td>
</tr>
<tr>
<td></td>
<td>Fatigue</td>
<td></td>
</tr>
</tbody>
</table>

ADR = adverse drug reaction.
prescribed, co-administration of other medications, or other factors might have helped precipitate the analgesic ADR and been associated with ADR self-identification. Future research should include additional questions to clarify if additional factors contribute to ADR identification.

Additional limitations include that the sample was composed of only English-speaking older adults. Non-English speakers might be at even greater risk for analgesic-related ADRs because of additional communication barriers. The majority of the older adults were women. Men might differ in the ADRs experienced and the response to ADRs.

Analgesic-related ADR monitoring by older adults and their practitioners is essential for ADR reduction. Written patient education about medications side effects provided when medications are dispensed remains an important part of ADR prevention efforts. The significant number of older adults that continue to experience analgesic-related ADRs indicates patient education alone is insufficient, however. Medication reconciliation during ambulatory and inpatient encounters provides an opportunity to ask older adults if they have experienced any ADRs or unpleasant symptoms while taking their analgesics. Affirmative responses could be immediately followed up by a practitioner to assess symptoms and treatment needs and ensure continued pain management with reduced risk of ADRs. The Joint Commission goals specific to medication reconciliation currently do not include ADR assessment (Joint Commission, 2017). Identification of current medications is a vital part of ADR prevention. For example, almost 50% of over-the-counter NSAIDs were not included in the medication list provided by older adults during geriatric ambulatory care visits (Vejar, Makic, & Kotthoff-Burrell, 2015).

Early identification of ADRs is even more important, however, to prevent more serious, life-threatening analgesic-related ADRs. Research is needed to test patient safety outcomes from an ADR-specific question during medication reconciliation and the feasibility of routinely including a question about ADRs in ambulatory care and inpatient settings. Routine text messages to query older adults about new symptoms or problems from newly prescribed analgesics might also assist in early identification, treatment, and reduction of analgesic-related ADRs. Analgesic ADR text queries could be tested in a randomized clinical trial.

Results suggest that analgesic-related ADRs may be underrecognized and underreported by older adults with chronic pain and that some older adults might not seek health care when they experience ADRs, particularly opioid-related ADRs. Practitioners can reduce analgesic-related ADRs by routinely asking about unpleasant symptoms associated with taking an analgesic. To increase patient safety, health care system-wide change beyond simple medication reconciliation is needed to increase timely identification of analgesic-related ADRs.

REFERENCES


