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Author(s): Wissam K. Kabbara, Hani Dimassi and Marwan Sheikh-Taha

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Title: Patterns of pain medication use in older individuals with cardiovascular disease

Authors

1. Wissam Kabbara, Pharm.D., BCPS-AQ ID

Clinical Associate Professor

Lebanese American University, Department of Pharmacy Practice

Byblos, Lebanon

Email: wissam.kabbara@lau.edu.lb

2. Hani Dimassi, MPH, PhD Biostatistics

Associate Professor

Lebanese American University, Department of Pharmaceutical Sciences

Byblos, Lebanon

Email: hani.dimassi@lau.edu.lb

Corresponding author

3. Marwan Sheikh-Taha, Pharm.D., BCPS-AQ Cardiology

Clinical Associate Professor

Lebanese American University, Department of Pharmacy Practice

Byblos, Lebanon

Tel: +9613586965

Email: marwantaha@yahoo.com

Abstract

Background

Pain is common in older adults and clinicians are often faced by many challenges when selecting appropriate treatment due to age-related changes in pharmacokinetics, pharmacodynamics, increased comorbidities, and polypharmacy.

Methods

We assessed the patterns of pain medications used at home among older adults admitted to the cardiology service in a tertiary care teaching center in USA from March to May 2016. A retrospective chart review was conducted where adults, 65 years of age or older, with cardiovascular diseases admitted to the cardiology service and taking at least one pain medication at home were studied.

Results

Out of 404 patients who were admitted to the cardiology service, 228 (56.4%) were on at least one pain medication. Among the admitted patients, 64.2% of the females received at least one pain medication as compared to 49% of the males ($p= 0.002$). Participants had a mean age of 76.34 ± 7.43 years, and received a mean of 1.81 ± 0.83 pain medications. Neuropathic pain was the most common indication (33.4%), followed by unknown indications (18.9%), arthritis

(17.5%), and cancer (15.8%). The most commonly used pain medications were gabapentin/pregabalin 79 (34.6%), acetaminophen plus an opiate 78 (34.2%), opiates 56 (24.6%), tramadol 36 (15.8%), followed by non-selective NSAIDs 21 (9.2%). Twelve (5.3%) patients received duplication of pain medications, while 14 (5.7%) received inappropriate combination of pain medications. Twenty three patients (10.1%) received muscle relaxants in conjunction with pain medications, 20 of which are considered poorly tolerated by older adults.

Conclusion

We described the patterns of use of pain medications among older adults with cardiovascular disease. Careful selection of appropriate pain medications based on different clinical parameters is very essential to avoid prescribing inappropriate therapy that can lead to patient harm.

Keywords: Pain, cardiovascular disease, geriatrics.

Introduction

Pain is a common complaint in older adults. Data from the National Health and Aging Trends Study showed that the prevalence of bothersome pain in adults aging 65 years and above was about 53% (1). If remain untreated, pain can lead to social isolation, depression, sleep disturbances, and immobility (2). When treating pain, clinicians' main goal is to maximize function and quality of life while minimizing adverse effects that may be associated with drug therapy. Age-related changes in pharmacokinetics and pharmacodynamics should be taken into consideration when recommending pain medications to older adults. In addition, polypharmacy and multiple chronic illnesses make this process more challenging in this group of patients.

The American Geriatrics Society (AGS) recommends acetaminophen as the first-line treatment of mild persistent pain because of its greater safety compared to other analgesics (3). However, since it lacks significant anti-inflammatory properties, acetaminophen is less effective in the management of chronic inflammatory pain than non-steroidal anti-inflammatory drugs (NSAIDs). On the other hand, NSAIDs should only be used for a short period of time due to their associated adverse effects including gastrointestinal (GI), renal, and cardiovascular toxicity which increase in severity and frequency with age (4).

The use of opioids in older patients with persistent non-cancer pain is based on comparing the potential efficacy and risks, keeping in mind the potential harm of unrelieved pain. The most common indication for opioid use in non-cancer pain is musculoskeletal pain, including

degenerative joint disease, fibromyalgia, back pain, and headache. Many physicians are often reluctant to use opioids because of their abuse potential which can deprive patients with severe pain from receiving those agents (5).

Antidepressants, including tricyclic antidepressants (TCAs), selective serotonin reuptake inhibitors (SSRIs), and selective noradrenaline reuptake inhibitors (SNRIs) can be used in patients with chronic neuropathic pain. TCAs are highly anticholinergic, and can cause sedation and orthostatic hypotension while SSRIs and SNRIs have fewer anticholinergic and cardiovascular adverse effects (6). Anticonvulsants, mainly gabapentin, and pregabalin are also effective in the treatment of neuropathic pain and have a safer side effect profile as compared to TCAs.

Examining the prescription pattern of analgesics in older individuals with cardiac diseases is rare. The main objective of this study was to assess the patterns of pain medications used at home among older patients with cardiovascular diseases admitted to the cardiology service in a tertiary care teaching center in USA.

Methods

We conducted a retrospective chart review where all patients with cardiovascular diseases admitted to the cardiology service at a tertiary care hospital in Alabama, USA, from March to May 2016 were assessed. Inclusion criteria were patient age of 65 years and above, taking at

least one pain medication at home, history of cardiovascular disease, and admission to the cardiology service. Data collected from medical records were recorded on a spreadsheet and analyzed using SPSS version v23 (BM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp). Descriptive statistics was expressed as mean and standard deviations for numerical data, and frequencies and percentages for categorical data. **Hani, please feel free to make changes/add statements related to statistics.** We assessed correlation between pain medications , sex and age (test?).

Results

A total of 404 patients were admitted to the cardiology service during the study period, out of which 228 (56.4%) were on at least one pain medication and were included in the study. Among the admitted female patients, 64.2% received at least one pain medication as compared to 49% of the admitted male patients ($p= 0.002$). No difference in the use of pain medications was seen in patients older than 80 years as compared to those younger than 80 years or among those between 65-69, 70-74, 75-79, 80-84, 85-89, and > 90 years of age (data not shown). Table 1 describes patient characteristics. Participants had a mean age of 76.34 ± 7.43 years, suffered from a mean of 6.35 ± 2.41 comorbidities, and received a mean of 13.27 ± 4.24 medications at home (mean of 1.81 ± 0.83 pain medication) . One hundred and twenty five (54.8%) of study participants were females. Several comorbidities were documented in patients, of which hypertension was the most common (72.8%), followed by dyslipidemia (48.2%), coronary artery disease (46.5%), heart failure (42.5%), diabetes mellitus (38.6%), and atrial fibrillation or flutter (34.6%).

Table 2 indicates indications for pain medications. Neuropathic pain was the most common indication (33.4%), followed by unknown indications (18.9%), arthritis (17.5%), and cancer (15.8%). The most commonly used pain medications were gabapentin/pregabalin 79 (34.6%), acetaminophen plus an opiate 78 (34.2%), opiates 56 (24.6%), tramadol 36 (15.8%), followed by non-selective NSAIDs 21 (9.2%). Table 3

Twelve (5.3%) patients received duplication of pain medications, while 14 (5.7%) received inappropriate combination of pain medications (Table 4) and 23 patients (10.1%) received muscle relaxants in conjunction with pain medications, 20 of which are considered poorly tolerated by older adults.

Discussion

We conducted a retrospective chart review to assess the prescribing patterns of pain medications in older patients with cardiovascular disease. The studied patients had a mean of 6 comorbidities and received an average of 13 medications at home. Suffering from high number of comorbidities and receiving poly-pharmacy makes prescribing appropriate pain medications while avoiding side effects, drug-drug interaction, and drug-disease interaction a very challenging task.

Around 6 out of 10 patients were receiving pain medications; 40% of which received one, 42% received two, and 14% received three medications, translating to an average of almost two pain

medications per patient. In our study, females were more likely to receive pain medications as compared to males. This sex difference is consistent with other studies (7, 8). Females have greater pain sensitivity and report higher pain intensity as compared to males. Studies investigating mechanistic and physiological causes of gender-related differences in pain are needed.

Neuropathy (mainly diabetic neuropathy) was the most common indication for a pain medication in our study (33.4%) and most patients were treated with gabapentin or pregabalin. Although considered first-line agents for the treatment of neuropathic pain, they can cause sedation, dizziness, and cognitive difficulties which should be closely monitored in older patients receiving other drugs that can affect the central nervous system (9). In addition, recent concerns about the misuse or abuse of gabapentinoids have arisen, especially among patients with current or previous use of opioids or benzodiazepines (10). Six patients (2.6%) received TCAs which should be avoided in older patients because of their anticholinergic and sedating properties, according to the AGS 2015 updated Beers Criteria (11). TCAs can also cause cognitive decline and orthostatic hypotension which can be especially harmful in the older patient population with cardiovascular disease receiving multiple medications (12, 13).

Chronic oral NSAID therapy was used by 24 (10.5%) patients in our study. The AGS updated Beers Criteria does not recommend the chronic use of these agents unless no other drugs are effective (11). These medications should be particularly avoided in patients older than 75 years taking oral or injectable corticosteroids, anticoagulants, or antiplatelet agents due to the increased

risk of peptic ulcer disease and gastrointestinal bleeding (14). A significant percentage of the patients in our study had coronary artery disease and/or atrial fibrillation which necessitates the use of antiplatelet agents and/or anticoagulants. Although the addition of a proton pump inhibitor or misoprostol can decrease the risk of upper gastrointestinal ulcers, it does not eliminate it completely. Furthermore, NSAIDs should also be avoided in older patients with heart failure due to fluid retention and the increased risk for heart failure exacerbation and in older patients with a creatinine clearance of less than 30 ml/minute (Stage IV and V chronic kidney disease) due to the increased risk of acute kidney injury and further decline of renal function (11,15) . Around 42.5% and 28.5% of the patients in our study had heart failure and chronic renal disease respectively.

A big percentage of patients (around 75%) in our study received tramadol or an opioid analgesic alone or in combination with acetaminophen. According to Centers for Disease Control and Prevention (CDC), opioid prescribing remains high and drugs prescribed tend to be given at higher doses and for longer periods of time which increases the risk of addiction, overdose, and death (16). The severity of pain and the potential risk of drug adverse effects and misuse/abuse should be considered before prescribing an opioid for pain relief in older patients and health care professionals can identify patients at high risk of opioid overdose through the state prescription drug monitoring program (PDMP). Furthermore, all opioids should be avoided in older patients with a history of falls or fractures (11).

Around 1 in 10 patients in our study received a duplication of pain medication and/or an inappropriate combination treatment regimen. Seventy five percent of the incorrect regimens included a duplication or inappropriate treatment with an opioid with or without acetaminophen or tramadol. Khodneva et al assessed prescription opioid use and the risk of cardiovascular disease among older adults. Ten percent of patients in the study received more than two opioids simultaneously and prescription opioid use was associated with increased cardiovascular mortality even after controlling for cardiovascular disease risk factors (17).

Twenty (8.8%) patients received muscle relaxants that are considered poorly tolerated by older adults and should be avoided since they have anticholinergic adverse effects and cause sedation which increases the risk of fractures (11). A detailed assessment of pain medications upon hospital admission can help in stopping unnecessary medications and avoiding side effects or possible drug interactions.

We were not able to identify the reason behind taking pain medications in around 19% of the studied patients. This could be due to several reasons including forgetfulness, which can be common in older individuals, poor education about prescribed drugs, taking a large number of medications, which leads to confusion and improper chart documentation by healthcare professionals.

To our knowledge, this is the first study that describes the patterns of pain medication use in older individuals with cardiovascular disease. Nevertheless, there are several limitations. The study is retrospective and was conducted in a single medical center in the United States. Data were collected from patients' electronic records with potential for missing information. Assessment of the doses and the duration of therapy of specific medications could have provided more information about individual patient benefits and risks.

Conclusion

We described the patterns of use of pain medications among older adults with cardiovascular disease. Future studies can identify, implement, and evaluate policies and procedures that can improve pain medication prescribing in older patients with cardiovascular disease.

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