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REVISIÓN BIBLIOGRÁFICA ABRIL 2022: Selección de artículos

REVISTAS FARMACÉUTICAS

AJHP American Journal of Health System Pharmacist

Barriers and facilitators to implementing pharmacist-provided comprehensive medication management in primary care transformation

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Abstract

Disclaimer

In an effort to expedite the publication of articles related to the COVID-19 pandemic, AJHP is posting these manuscripts online as soon as possible after acceptance. Accepted manuscripts have been peer-reviewed and copyedited, but are posted online before technical formatting and author proofing. These manuscripts are not the final version of record and will be replaced with the final article (formatted per AJHP style and proofed by the authors) at a later time.

Purpose

How to effectively integrate pharmacists into team-based models of care to maximize the benefit they bring to patients and care teams, especially during times of primary care transformation (PCT), remains unknown. The objective of this study was to identify barriers and facilitators when integrating pharmacist-provided comprehensive medication management (CMM) services into a health system's team-based PCT using the Consolidated Framework for Implementation Research (CFIR).

Methods

Semistructured qualitative interviews were carried out with 22 care team members regarding their perceptions of the implementation of CMM in the PCT. Transcripts were coded to identify CMM implementation barriers and facilitators, and resulting codes were mapped to corresponding CFIR domains and constructs.

Results
Fifteen codes emerged that were labeled as either a barrier or a facilitator to implementing CMM in the PCT. Facilitators were the perception of CMM as an invaluable resource, precharting, tailored appointment lengths, insurance coverage, increased pharmacy presence, enhanced team-based care, location of CMM, and identification of CMM advocates. Barriers included limited clinic leadership involvement, a need for additional resources, CMM pharmacists not always feeling part of the core team, understanding of and training around CMM's role in the PCT, changing mindsets to utilize resources such as CMM more frequently, underutilization of CMM, and CMM scheduling.

Conclusion
Clinical pharmacists providing CMM represent a valuable interdisciplinary care team member who can help improve healthcare quality and access to primary care. Identifying and addressing implementation barriers and facilitators early during PCT rollout is critical to the success of team-based services such as CMM and becoming a learning health system.

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Drug safety

Hydroxyzine Initiation Following Drug Safety Advisories on Cardiac Arrhythmias in the UK and Canada: A Longitudinal Cohort Study

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Abstract
Introduction
Regulatory advisories on hydroxyzine and risk of QT prolongation and Torsade de pointes (TdP) were issued in the UK in April 2015 and Canada in June 2016. We hypothesized patients with risk factors for QT prolongation and TdP, compared with those without risk factors, would be less likely to initiate hydroxyzine in the UK and in British Columbia (BC), Canada, following advisories.

Methods
We conducted a longitudinal study with repeated measures, and evaluated hydroxyzine initiation in a UK cohort and a concurrent BC control cohort (April 2013–March 2016) as well as in a BC advisory cohort (June 2014–May 2017).

Results
This study included 247,665 patients in the UK cohort, 297,147 patients in the BC control cohort, and 303,653 patients in the BC advisory cohort. Over a 12-month post-advisory period, hydroxyzine initiation decreased by 21% in the UK (rate ratio 0.79, 95% confidence interval 0.66–0.96) relative to the expected level of initiation based on the pre-advisory trend.

Hydroxyzine initiation did not change in the BC control cohort or following the Canadian advisory in the BC advisory cohort.
The decrease in hydroxyzine initiation in the UK in the 12 months after the advisories was not significantly different for patients with risk factors compared with those without risk factors.

Conclusion
Hydroxyzine initiation decreased in the UK, but not in BC, in the 12 months following safety advisories. The decrease in hydroxyzine initiation in the UK was not significantly different for patients with versus without risk factors for QT prolongation and TdP.

Disponible en: **https://link.springer.com/content/pdf/10.1007/s40264-022-01175-2.pdf**

Annals of Pharmacotherapy

How measurements affected by medication use are reported and handled in observational research: a literature review

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Abstract
Purpose
In epidemiological research, measurements affected by medication, e.g., blood pressure lowered by antihypertensives, are common. Different ways of handling medication are required depending on the research questions and whether the affected measurement is the exposure, the outcome, or a confounder. This study aimed to review handling of medication use in observational research.

Methods
PubMed was searched for etiological studies published between 2015 to 2019 in fifteen high-ranked journals from cardiology, diabetes, and epidemiology. We selected studies that analyzed blood pressure, glucose, or lipid measurements (whether exposure, outcome or confounder) by linear or logistic regression. Two reviewers independently recorded how medication use was handled and assessed whether the methods used were in accordance with the research aim. We reported the methods used per variable category (exposure, outcome, confounder).

Results
127 articles were included. Most studies did not perform any method to account for medication use (exposure 58%, outcome 53%, confounder 45%). Restriction (exposure 22%, outcome 23%, confounders 10%), or adjusting for medication use using a binary indicator were also used frequently (exposure: 18%, outcome: 19%, confounder: 45%). No advanced methods were applied. In 60% of studies, the methods' validity could not be judged due to ambiguous reporting of the research aim. Invalid approaches were used in 28% of the studies, mostly when the affected variable was the outcome (36%).

Conclusion
Many studies ambiguously stated the research aim and used invalid methods to handle medication use. Researchers should consider a valid methodological approach based on their research question.

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Applying Mixture Cure Survival Modeling to Medication Persistence Analysis

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Abstract
Purpose
Standard survival models are often used in medication persistence analysis.These methods implicitly assume that all patients will experience the event (medication discontinuation), which may bias the estimation of persistence if long-term medication persistent patients rate is expected in the population. We aimed to introduce mixture cure model in medication persistence analysis to describe the characteristics of long-term and short-term persistent patients, and demonstrate its application using a real-world data analysis.

Methods
A cohort of new users of statins was used to demonstrate the differences between the standard survival model and the mixture cure model in medication persistence analysis. The mixture cure model estimated effects of variables, reported as odds ratios (OR) associated with likelihood of being long-term persistent and effects of variables, reported as hazard ratios (HR) associated with time to medication discontinuation among short-term persistent patients.

Results
Long-term persistent rate was estimated as 17% for statin users aged between 45 and 55 vs. 10% for age less than 45 vs. 4% for age greater than 55 via the mixture cure model. The hazard ratios of covariates estimated by the standard survival model (HR = 1.41, 95% CI =[1.35, 1.48]) were higher than those estimated by the mixture cure model (HR = 1.32, 95% CI = [1.25, 1.39]) when comparing patients with age greater than 55 to those between 45 and 55.

Conclusions
Compared with standard survival modeling, a mixture cure model can improve the estimation of medication persistence when long-term persistent patients are expected in the population.

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Risk of myopericarditis following COVID-19 mRNA vaccination in a large integrated health system: A comparison of completeness and timeliness of two methods

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Abstract

Purpose

How completely do hospital discharge diagnoses identify cases of myopericarditis after an mRNA vaccine?

Methods

We assembled a cohort 12–39 year-old patients, insured by Kaiser Permanente Northwest, who received at least one dose of an mRNA vaccine (Pfizer-BioNTech or Moderna) between December 2020 and October 2021. We followed them for up to 30 days after their second dose of an mRNA vaccine to identify encounters for myocarditis, pericarditis or myopericarditis. We compared two identification methods: A method that searched all encounter diagnoses using a brief text description (e.g., ICD-10-CM code I40.9 is defined as 'acute myocarditis, unspecified'). We searched the text description of all inpatient or outpatient encounter diagnoses (in any position) for "myocarditis" or "pericarditis." The other method was developed by the Centers for Disease Control and Prevention's Vaccine Safety Datalink (VSD), which searched for emergency department visits or hospitalizations with a select set of discharge ICD-10-CM diagnosis codes. For both methods, two physicians independently reviewed the identified patient records and classified them as confirmed, probable or not cases using the CDC's case definition.

Results

The encounter methodology identified 14 distinct patients who met the confirmed or probable CDC case definition for acute myocarditis or pericarditis with an onset within 21 days of receipt of COVID-19 vaccination. When we extended the search for relevant diagnoses to 30 days since vaccination, we identified two additional patients (for a total of 16 patients) who met the case definition for acute myocarditis or pericarditis, but those patients had been misdiagnosed at the time of their original presentation. Three of these patients had an ICD-10-CM code of I51.4 "Myocarditis, Unspecified;" that code was omitted by the VSD algorithm (in the late fall of 2021). The VSD methodology identified 11 patients who met the CDC case definition for acute myocarditis or pericarditis. Seven (64%) of the 11 patients had initial care for myopericarditis outside of a KPNW facility and their diagnosis could not be ascertained by the VSD methodology until claims were submitted (median delay of 33 days; range of 12–195 days). Among those who received a second dose of vaccine (n = 146 785), we estimated a risk as 95.4 cases of myopericarditis per million second doses administered (95% CI, 52.1–160.0).

Conclusion
We identified additional valid cases of myopericarditis following an mRNA vaccination that would be missed by the VSD's search algorithm, which depends on select hospital discharge diagnosis codes. The true incidence of myopericarditis is markedly higher than the incidence reported to US advisory committees in the fall of 2021. The VSD should validate its search algorithm to improve its sensitivity for myopericarditis.

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Journal of Clinical Pharmacy and Therapeutics

Use of histamine-2 receptor antagonists and risk of inflammatory bowel diseases: A systematic review and meta-analysis of observational studies

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Abstract
What is known and Objective
The effect of histamine-2 receptor antagonists (H2RAs) use causing inflammatory bowel diseases (IBD) has been reported in few isolated observational studies; however, pooled estimation of IBD risk has not been done. The present study was conducted to estimate the risk of IBD [Crohn's disease (CD), ulcerative colitis (UC) and microscopic colitis (MC)], among H2RAs users.

Methods
Databases such as MEDLINE/PubMed, Scopus and Cochrane Library were searched from inception to January 2021. A bibliographic search of selected articles, random search in Google Scholar and ResearchGate were also performed for any additional studies.

The observational studies which assessed the incidence or risk of IBD in H2RA users published in the English language were considered. Modified Downs and Black Checklist was used for quality assessment. Two independent reviewers were involved in study selection, data extraction and quality assessment; any discrepancies were settled through consensus or by consulting a third reviewer.
Results
Four studies out of 2,658 articles were included for this meta-analysis. The meta-analysis of 4 studies with 8939 participants revealed a significantly higher risk of IBD (OR: 2.27; 95% CI: 1.70–3.02; $p < 0.0001$) in H2RA users compared to non-users. Similar significant relationships were observed in the subgroup analysis of adults ($p < 0.0001$) and paediatrics ($p = 0.04$). The quality of included studies was observed to be fair to good.

What is new and Conclusion

Our findings indicate a significantly higher IBD risk among those who used H2RA compared to non-users both in adults and in paediatrics. Further observational studies involving large populations are required to strengthen these results and to generalize these findings.

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High-Dose Clopidogrel versus Ticagrelor in CYP2C19 intermediate or poor metabolizers after percutaneous coronary intervention: A Meta-Analysis of Randomized Trials

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Abstract

What is known and objective

For patients after percutaneous coronary interventions (PCI), clopidogrel combined with aspirin is a conventional dual antiplatelet therapy (DAPT) method. Because the genetic polymorphism of CYP2C19 gene leads to clopidogrel resistance, guidelines for antiplatelet recommendations in CYP2C19 of ultrarapid metabolizers (UM), extended metabolizers (EM) and poor metabolizers (PM) are clear. However, there is no clear recommendation as to whether ticagrelor or double dose clopidogrel is the best antiplatelet regimen for CYP2C19 of intermediate metabolizers (IM). To evaluate the efficacy and safety of ticagrelor (combined with aspirin) and high-dose clopidogrel (combined with aspirin) in patients after PCI with CYP2C19 loss-of-function (LOF) alleles.

Methods

We searched the following databases to select RCTs of comparing ticagrelor with high-dose clopidogrel in patients after PCI with CYP2C19 LOF alleles: CNKI, Wanfang Data, PubMed, Clinical trials, Cochrane, Web of Science and Embase. Major adverse cardiovascular events (MACEs), platelet function and TIMI bleeding event were defined as the outcomes. revman 5.3 software was used to perform meta-analysis.

Results and discussion

A total of 14 RCTs with 2351 patients were enrolled. Meta-analysis showed that compared with high-dose clopidogrel, ticagrelor had reduced incidence of MACEs (OR = 0.32, 95% CI: 0.23–0.44, p < 0.00001), stent thrombosis (OR: 0.24, 95%CI: 0.13–0.44, p < 0.00001), myocardial infarction OR: 0.42, 95%CI: 0.22–0.80, p = 0.008), revascularization (OR: 0.29, 95%CI: 0.10–0.82, p = 0.02) and unstable angina (OR: 0.47, 95%CI: 0.29–0.77, p = 0.003) in patients after PCI with CYP2C19 LOF alleles. A subgroup analysis showed that ticagrelor reduced the risk of MACEs compared with high-dose clopidogrel regardless of the type of metabolizer. Compared with high-dose clopidogrel, ticagrelor significantly reduced the risk of MACE with longer follow-up period (more than 3 months) without increasing the risk of bleeding (OR: 0.89, 95%CI: 0.53–1.49, p = 0.30), while elevated dyspnoea (OR: 5.62, 95%CI: 3.07–10.28, p < 0.00001).

What is new and conclusions
For patients carrying CYP2C19 LOF alleles after PCI, ticagrelor may be better than high-dose clopidogrel in reducing the risk of MACEs, while dyspnoea incidents should be alerted.

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Vitamin D in the Prevention and Treatment of Diabetic Neuropathy

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Abstract
Purpose
Neuropathy is one of the most important complications of diabetes. According to recent advances, vitamin D deficiency might play a role in the development and progression of diabetic neuropathy. Moreover, therapeutic vitamin D supplementation has the potential to improve this condition. The aim of the present review was to summarize new data available in this area.

Methods
The PubMed database was searched for articles written in English and published through September 2021, using combinations of the following key words: *vitamin D, diabetes, diabetes mellitus, diabetic neuropathy, polyneuropathy, peripheral neuropathy, cardiac autonomic neuropathy, supplementation,* and *therapy*.

Findings
A number of studies have suggested that vitamin D deficiency can play a significant role in the development of peripheral neuropathy, diabetic foot ulcers, as well as cardiovascular autonomic neuropathy in patients with type 2 diabetes. Vitamin D supplementation might serve as an effective adjuvant therapy for neuropathic pain and may slow or stop the progression of neural damage.

Implications
Vitamin D therapy for diabetic complications could be a reliable option; however, further studies are needed to confirm this notion.

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Sex Differences in Physical Activity and Incident Stroke: A Systematic Review

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Abstract

Purpose

Physical inactivity, a modifiable risk factor for cardiovascular disease, is independently associated with stroke. Though some prior data have suggested sex differences in levels of physical activity, whether there are sex differences in the role of physical activity in primary stroke prevention is largely unknown. This systematic review identifies and describes recent findings on sex differences in the association between physical activity and incident (first-ever) stroke. This review also describes the current evidence on the strength of the association between physical activity and a reduced stroke risk in women in particular.

Methods

Using a prespecified strategy, PubMed/MEDLINE and Cochrane Central were searched to identify observational studies or trials published from 2000 to 2020 and reporting sex differences in physical activity and incident stroke. To be included, among other criteria, studies had to include sex-specific effect estimates from women, men, or both. Titles, abstracts, and full-text articles were screened to identify studies meeting the inclusion criteria, and adjusted sex-specific estimates of the association between physical activity and incident stroke for total stroke (ischemic plus hemorrhagic) or ischemic stroke were abstracted.

Findings

Thirty-seven studies met the inclusion criteria. Of 17 studies that included data on total incident stroke (ischemic and hemorrhagic combined) in both women and men, 7 (41%) showed similar associations between physical activity and incident stroke between women and men, 6 (35%) suggested a significant effect in women but not in men, and 3 (18%) showed a significant effect in men but not in women. Of 10 studies that included data on ischemic stroke in women and men, 5 (50%) suggested similar effects in women and men, 4 (40%) suggested a significant effect in women but not in men, and 1 (10%) showed an effect in men but not women. In women specifically, the majority of included studies demonstrated a reduced risk for incident stroke with physical activity, with relative risk reductions ranging from 11% to 72%, though most estimates fell between 20% and 40%.

Implications

The majority of studies indicated a clear association between physical activity and a reduction in stroke risk. Studies were split as to the potential for sex differences in this association. Future prospective investigations should identify strategies for the use of increased physical activity for primary stroke prevention, with sex-specific considerations as warranted. The data on sex-specific dose–response relationship between physical activity and stroke risk are inconclusive and warrant more research.

Disponible en: https://doi.org/10.1016/j.clinthera.2022.02.006

Efficacy and Safety of SID142 in Patients With Peripheral Arterial Disease: A Multicenter, Randomized, Double-Blind, Active-Controlled, Parallel-Group, Phase III Clinical Trial

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ABSTRACT

Purpose

Renexin® is a combination pill of cilostazol and *Ginkgo biloba* leaf extract that is used for the improvement of ischemic symptoms associated with peripheral arterial disease (PAD). SID142 is a controlled-release tablet of cilostazol (200 mg) and *G biloba* leaf extract (160 mg) that was developed to address the limitation of BID administration with Renexin. This study aimed to verify that SID142 was not inferior to Renexin in the treatment of patients with PAD.

Methods

This was a multicenter, randomized, double-blind, active-controlled, parallel-group, Phase III clinical trial. Study subjects were randomized to receive SID142 once daily or Renexin twice a day for 12 weeks. The primary end point was a change in the patient assessment of lower leg pain intensity with the use of a visual analog scale (VAS) after 12 weeks of treatment. If the lower limit of the two-sided 95% CI was greater than –10, the study drug was declared noninferior to the reference drug. Secondary efficacy end points included cold sensation, ankle-brachial index, ankle systolic pressure, maximum walking distance, pain-free walking distance, and investigator's global assessment. Study group results were compared 4, 8, and 12 weeks after treatment. Adverse events were assessed as a safety end point.

Findings

In total, 344 subjects from 19 medical centers were screened, and a total of 170 subjects were randomly assigned to either the SID142 (n = 86) or the Renexin (n = 84) group. Analysis of the change in lower extremity pain at 12 weeks compared with baseline revealed that SID142 was not inferior to Renexin (21.44 [19.23] vs 22.30 [17.75]; 95% CI, –7.70 to 5.97; $P = 0.5942$). No significant differences were found between groups in any secondary efficacy end point. However, the incidence of adverse reactions was significantly lower in the SID142 group (22.35% vs 39.29%; $P = 0.0171$).

Implications
SID142 once daily was not inferior to Renexin twice a day for efficacy in patients with PAD. SID142 had a favorable safety profile. ClinicalTrials.gov identifier: NCT03318276.

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Melatonin: Translation of Ongoing Studies Into Possible Therapeutic Applications Outside Sleep Disorders

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ABSTRACT
Purpose
Melatonin, a natural hormone mainly synthesized by the pineal gland, is regulated by circadian rhythm. Synthetic melatonin is not approved by the US Food and Drug Administration for any indication. However, melatonin receptor agonists such as ramelteon and tasimelteon are US Food and Drug Administration approved and are considered by the American Academy of Family Physicians for the treatment of insomnia. Due to the availability of over-the-counter products in some countries and the increasing use of melatonin, it is interesting to highlight knowledge regarding the potential benefits of melatonin outside sleep disorders.

Methods
This narrative review included published reports in EMBASE and MEDLINE databases between 1975 and 2021 relating to the therapeutic applications of melatonin.

Findings
Based on the quality of the evidence published to date, the most promising non-insomnia indications are for treating ischemia/reperfusion injury, primary headache disorders, fibromyalgia, glucose control, and blood pressure control.

Implications
Most of the studies were preclinical and in *in vivo* and *in vitro* phases. More clinical trials are needed before recommending melatonin as a treatment in clinical practice.
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REVISTAS GERIÁTRICAS

Age and Ageing

New national osteoporosis guidance—implications for geriatricians

Abstract

Fragility fractures are painful, debilitating, often life-changing and accounted for an estimated 2.4% of pre-pandemic health care spending in the UK. Those who are older, frail and multimorbid have the highest fracture risk and therefore the most to gain from anti-osteoporosis treatments to reduce this risk. Currently, an unacceptable treatment gap exists between those eligible for and those who receive treatment. This commentary discusses the major changes to the new, National Institute for Health and Care Excellence accredited, UK National Osteoporosis Guideline Group (NOGG) guidance (published March 2022) most relevant to the management of older people's bone health. Changes include intervention thresholds; using fracture probabilities from FRAX; for patients too frail to undergo DXA; greater emphasis on vertebral fracture detection and the use of intravenous zoledronate as a first-line anti-osteoporosis therapy; the new concept of 'very high fracture risk' which should prompt consideration of use of parenteral anti-osteoporosis therapy; new guidance regarding anabolic treatment options; concerns regarding denosumab cessation; and the urgent need to get patients with a fragility fracture onto treatment to reduce re-fracture risk with follow-up to check tolerance and ensure adherence.

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BMC Geriatrics

Sarcopenia and associated factors according to the EWGSOP2 criteria in older people living in nursing homes: a cross-sectional study

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Abstract

Background

In 2018, the European Working Group on Sarcopenia in Older People (EWGSOP2) updated the original definition of sarcopenia, establishing new criteria to be used globally. Early diagnosis of sarcopenia in nursing home residents and the identification of contributing factors would target interventions to reduce the incidence of malnutrition, social isolation, functional decline, hospitalization and mortality.

Aim

Verify the prevalence and the degree of severity of sarcopenia according to the new EWSGOP2 criteria and to analyse its associated factors in residents living in nursing homes in Central Catalonia (Spain).

Design

A cross-sectional multicenter study was conducted in 4 nursing homes. SARC-F test was applied as the initial screening, muscle strength was measured by a dynamometer, skeletal muscle mass by bioimpedance analysis and physical performance by Gait Speed. Four categories were used: total probable sarcopenia, probable sarcopenia, confirmed sarcopenia and severe sarcopenia.

Results

Among the total sample of 104 nursing home residents (mean age 84.6, ± 7.8; median 86, IQR 110), 84.6% were women and 85 (81.7%) (95% confidence interval [CI] 73.0-88.0) had total probable sarcopenia, 63 (60.5%) had probable sarcopenia, 19 (18.3%) had confirmed sarcopenia and 7 (6.7%) had severe sarcopenia. In the bivariate analysis, obesity was negatively associated and total time in sedentary behavior positively associated with all sarcopenia categories. In addition, malnutrition and urinary continence were positively associated with total and probable sarcopenia. Urinary incontinence was a positive associated factor of total and probable sarcopenia. In the multivariate analysis, obesity represented a negative associated factor: OR = 0.13 (0.03 - 0.57), p = 0.007 and OR = 0.14 (0.03 - 0.60), p = 0.008 with total and probable sarcopenia, respectively, adjusted by urinary incontinence status. For confirmed sarcopenia, obesity also represented a negative associated factor OR = 0.06 (0.01 - 0.99), p = 0.049 and the total time in sedentary behavior a positive associated factor OR = 1.10 (1.00- 1.20), p = 0.040.

Conclusions

According the EWGSOP2 criteria, high prevalence of sarcopenia was found in institutionalized older people, ranging from 6.7 to 81.7% depending on the category. Malnutrition, urinary incontinence and total time in sedentary behavior were associated with sarcopenia, whilst obesity represented a protective factor in this population.

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Subclinical cardiovascular disease and frailty risk: the atherosclerosis risk in communities study

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Background

Cardiovascular disease (CVD) is associated with a greater frailty risk, but it remains unknown if pathways that contribute to CVD are associated with the frailty risk. Thus, we aimed to investigate whether elevations in high-sensitivity cardiac troponin T (hs-cTnT) and N-terminal pro-B-type natriuretic peptide (NT-proBNP) for those without known CVD at baseline are associated with a higher frailty risk.

Methods

This study used data from the Atherosclerosis Risk in Communities study. Cardiac biomarkers were measured from stored plasma samples collected at Visit 2 (1991–1993). Frailty was recorded at Visit 5 (2011–2013). Cox regression models were used to determine the association of cardiac biomarkers with frailty risk.

Results

Overall, 360/5199 (6.9%) participants aged 55.1 ± 5.1 years developed frailty during a median follow-up of 21.7 years. The incidence of frailty was significantly higher in participants with hs-cTnT ≥14 ng/L (vs. < 14 ng/L: 17.9% vs. 6.7%) or NT-proBNP ≥300 pg/ml (vs. < 300 pg/ml: 19.7% vs. 6.8%) (all P < 0.001). Comparing higher vs. lower cut-off levels of either hs-cTnT (14 ng/l) or NT-proBNP (300 pg/ml) demonstrated a greater than two-fold higher frailty risk, with hazard ratios (HRs) of 2.13 (95% confidence interval (CI): 1.130–4.01, P = 0.020) and 2.61 (95% CI: 1.28–5.33, P = 0.008), respectively. Individuals with both elevated hs-cTnT and NT-proBNP had a higher frailty risk than those without it (HR: 4.15; 95% CI: 1.50–11.48, P = 0.006).

Conclusions

High hs-cTnT and NT-proBNP levels are strongly associated with incident frailty in the community-dwelling population without known CVD. Subclinical cardiac damage (hs-cTnT) and/or wall strain (NT-proBNP) may be the key pathway of CVD patients developing frailty. Detection of hs-cTnT and NT-proBNP may help for early screening of high-risk frailty and providing individualised intervention.

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Drugs and Aging

Benefit–Risk Assessment of Psychotropic Drugs in Older Patients with Chronic Obstructive Pulmonary Disease

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Abstract

Depression, anxiety, and other mental health disorders, including bipolar disorder and schizophrenia, occur commonly in older adults with chronic obstructive pulmonary disease (COPD), and they are often inadequately treated. We review the available evidence for benefits and risks of pharmacologic treatments (e.g. selective serotonin reuptake inhibitors [SSRIs], serotonin-noradrenaline reuptake inhibitors [SNRIs], tricyclic antidepressants [TCAs], antipsychotic drugs, and benzodiazepines) for common mental illnesses in older persons with COPD. Evidence to use both SSRIs/SNRIs and TCAs from randomized controlled trials is uncertain for treating major depression in patients with COPD. However, population-based findings indicate that they are widely used, and this valuable intervention (preferably SSRIs/SNRIs) should not be denied for selected patients after evaluating potential risks and benefits, especially patients presenting with major depression and suicidal ideation, when a collaborative-care approach is being used. Although there is some evidence for the short-term use of benzodiazepines for treating insomnia, breathlessness, and anxiety in patients with COPD, their long-term use should be closely monitored or avoided to reduce the increased rate of major adverse events. Currently, there are only limited data on the use of antipsychotic drugs for managing schizophrenia or bipolar disorder in older patients with COPD. Hence, clinicians should use extra caution when prescribing antipsychotic agents and be vigilant for symptoms of acute respiratory failure and other adverse effects.

Psychotropic medications are clearly beneficial for younger, healthy persons with depression and anxiety; however, the risk–benefit calculation is not so clear for treating psychological problems, schizophrenia, and bipolar disorder in older adults with COPD, given older-adult sensitivity to medications and the mixed findings of relatively few controlled trials.

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Journal of Geriatric Oncology

The association of age with acute toxicities in NRG oncology combined modality lower GI cancer trials

Abstract

Purpose

Expected toxicity from chemoradiation (CRT) is an important factor in treatment decisions but is poorly understood in older adults with lower gastrointestinal (GI) malignancies. Our objective was to compare acute adverse events (AAEs) of older and younger adults with lower GI malignancies treated on NRG studies.

Methods

Data from 6 NRG trials, testing combined modality therapy in patients with anal or rectal cancer, were used to test the hypothesis that older age was associated with increased AAEs. AAEs and compliance with protocol-directed therapy were compared between patients aged ≥70 and < 70. Categorical variables were compared across age groups using the chi-square test. The association of age on AAEs was evaluated using a covariate-adjusted logistic regression model, with odds ratio (OR) reported. To adjust for multiple comparisons, a p-value <0.01 was considered statistically significant.

Results

There were 2525 patients, including 380 patients ≥70 years old (15%) evaluable. Older patients were more likely to have worse baseline performance status (PS 1 or 2) (23% vs. 16%, p = 0.001), but otherwise baseline characteristics were similar. Older patients were less likely to complete their chemotherapy (78% vs. 87%, p < 0.001), but had similar RT duration.

On univariate analysis, older patients were more likely to experience grade ≥ 3 GI AAEs (36% vs. 23%, p < 0.001), and less likely to experience grade ≥ 3 skin AAEs (8% vs. 14%, p = 0.002). On multivariable analysis, older age was associated with grade ≥ 3 GI AAE (OR 1.93, 95% CI: 1.52, 2.47, p < 0.001) after adjusting for sex, race, PS, and disease site.

Conclusions

Older patients with lower GI cancers who underwent CRT were less likely to complete chemotherapy and had higher rates of grade 3+ GI AAEs. These results can be used to counsel older adults prior to treatment and manage expected toxicities throughout pelvic CRT

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Patterns of first-line targeted therapy utilization and adherence among older adults diagnosed with metastatic renal cell carcinoma

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Background

Despite the rapid approval of targeted therapies for metastatic renal cell carcinoma (mRCC) evidence on real world treatment patterns remains limited. This study evaluated patterns of first-line targeted therapy utilization and adherence in older adults, a population with a high burden of RCC.

Methods

2093 patients aged ≥66 years with a primary diagnosis of mRCC were identified from United States (US)-based cancer registry and administrative claims data (2007–2015). We included only patients with de novo disease. We assessed the initiation of first-line targeted therapy within four months of diagnosis and persistence and adherence to targeted therapy, using the proportion of days covered (PDC). Multivariable logistic regression yielded adjusted odds ratios (ORs) and 95% confidence intervals (CIs) to describe characteristics associated with targeted therapy versus no targeted therapy initiation and for high (≥80% PDC) versus low adherence.

Results

28.8% of patients received first-line targeted therapy within four months of diagnosis, with the proportion of patients receiving targeted therapy increasing over time. Older age (one-year increment OR:0.95 95%CI 0.93, 0.97), high comorbidity burden (OR:0.65 95%CI0.46, 0.93) and clear cell histology (OR:1.54 95%CI 1.19, 2.00) were associated with targeted therapy initiation. 48.2% of patients exhibited a high PDC to oral targeted therapy at 120 days, which was attenuated with inclusion of patients who died during the time period (34.2% PDC ≥80%).

Conclusion

Increasing age, high comorbidity burden and non-clear cell histology were associated with decreased targeted therapy initiation among patients with de novo mRCC. Our findings suggest adherence to oral therapies was low; future research exploring the mechanisms and impact of low adherence in this older patient population is warranted.

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International Journal of Geriatric Psychiatry

Blood pressure and heart rate responses to orthostatic challenge and Valsalva manoeuvre in mild cognitive impairment with Lewy bodies

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Abstract

Objectives

Orthostatic hypotension is a common feature of normal ageing, and age-related neurodegenerative diseases, in particular the synucleinopathies including dementia with Lewy bodies. Orthostatic hypotension and other abnormal cardiovascular responses may be early markers of Lewy body disease.

We aimed to assess whether abnormal blood pressure and heart rate responses to orthostatic challenge and Valsalva manoeuvre would be more common in mild cognitive impairment with Lewy bodies (MCI-LB) than MCI due to Alzheimer's disease (MCI-AD).

Methods

MCI patients (n = 89) underwent longitudinal clinical assessment with differential classification of probable MCI-LB, possible MCI-LB, or MCI-AD, with objective autonomic function testing at baseline. Blood pressure and heart rate responses to active stand and Valsalva manoeuvre were calculated from beat-to-beat cardiovascular data, with abnormalities defined by current criteria, and age-adjusted group differences estimated with logistic models.

Results

Orthostatic hypotension and abnormal heart rate response to orthostatic challenge were not more common in probable MCI-LB than MCI-AD. Heart rate abnormalities were likewise not more common in response to Valsalva manoeuvre in probable MCI-LB. An abnormal blood pressure response to Valsalva (delayed return to baseline/absence of overshoot after release of strain) was more common in probable MCI-LB than MCI-AD. In secondary analyses, magnitude of blood pressure drop after active stand and 10-s after release of Valsalva strain were weakly correlated with cardiac sympathetic denervation.

Conclusions

Probable MCI-LB may feature abnormal blood pressure response to Valsalva, but orthostatic hypotension is not a clear distinguishing feature from MCI-AD.

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Journal of gerontology A biol sci med sci

Predictors of Receipt of Comprehensive Medication Reviews in Older Adults

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Abstract

Background

Polypharmacy is highly prevalent among older adults. This study's purpose was to provide nationally representative estimates of self-reported comprehensive medication review (CMR) receipt among older adults and describe factors associated with their receipt, as CMRs are available through the Medicare Part D program.

Methods

This cross-sectional study used data from the National Poll on Healthy Aging (NPHA), a nationally representative online survey of community-dwelling adults aged 50-80, administered in December 2019. Participants included older adults aged 65-80 with any health insurance (n = 960). Outcomes were self-reported CMR receipt, awareness of CMR insurance coverage, and interest in a future CMR with a pharmacist. Sociodemographic and health-related variables were included. Descriptive statistics and multivariable logistic regression with NPHA population sampling weights were used.

Results

Among older adults on two or more prescription medications, only 20.8% had received a CMR while 34.3% were interested in a future CMR. Among individuals who had not received a CMR, most (83.4%) were unaware their insurance might cover a CMR. Factors associated with higher odds of receiving a CMR included taking five or more prescription medications (AOR=2.6, 95% CI: 1.59-4.38) and reporting food insecurity (AOR=2.9, 95% CI: 1.07-7.93). Having fair or poor self-reported physical health was associated with lower odds of receiving a CMR (AOR=0.49, 95% CI: 0.25-0.97).

Conclusions

Most older adults on two or more prescription medications with health insurance had not received a CMR and many were interested in one. Targeted strategies to increase older adults' awareness and receipt of CMRs are warranted.

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REVISTAS MÉDICAS

JAMDA: Journal of the American Medical Directors Association

Tolerance of Fentanyl Pectin Nasal Spray for Procedural Pain in Geriatric Patients

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Abstract

Objectives

We aimed to assess the tolerance of fentanyl pectin nasal spray (FPNS) when used to treat procedural pain caused by wound dressing or physiotherapy in patients older than 75 years with or without opioid background treatment.

Design

This is a prospective monocentric, noncontrolled, nonrandomized study conducted from December 2014 to October 2017 in 2 geriatric wards (rehabilitation and acute medicine).

Setting and Participants

Fifty-seven patients were included and 314 procedures were monitored.

Methods

For each patient, 6 procedures were monitored: the first 2 without specific treatment, then fentanyl was started at 100 µg with a titration over a few procedures up to 800 µg in non–opioid-naïve patients and 400 µg in opioid-naïve. Sedation and respiratory scale were monitored during the procedures. All adverse drug events occurring from inclusion to 5 days after the intervention were collected and their imputability was assessed separately by 2 pharmacovigilance experts.

Results

Overall, 14.4% of the sessions with FPNS administration resulted in adverse drug events. Main adverse drug events were nausea and vomiting, somnolence, and confusion. Most of them were of mild to moderate severity. Four severe adverse events were due to accidental overdoses. No unexpected adverse event occurred. Tolerance was similar for opioid-naïve and non–opioid-naïve patients (*P* value = .93).

Conclusion and implications

FPNS was overall well tolerated in geriatric patients. Given its interesting pharmacokinetics, fentanyl is a promising lead for procedural pain treatment in geriatric patients, even those who are opioid naïve.

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Annals of Internal Medicine

Adverse Events Associated With Coprescription of Phosphodiesterase Type 5 Inhibitors and Oral Organic Nitrates in Male Patients With Ischemic Heart Disease

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Background:
Concomitant use of oral organic nitrates (nitrates) and phosphodiesterase type 5 (PDE5) inhibitors is contraindicated.

Objective:
To measure temporal trends in the coprescription of nitrates and PDE5 inhibitors and to measure the association between cardiovascular outcomes and the coprescription of nitrates with PDE5 inhibitors.

Results:

From 2000 to 2018, 249 541 male patients with IHD were identified. Of these, 42 073 patients had continuing prescriptions for nitrates. During this period, the prescription rate for PDE5 inhibitors in patients with IHD who were taking nitrates increased from an average of 0.9 prescriptions (95% CI, 0.5 to 1.2 prescriptions) per 100 persons per year in 2000 to 19.5 prescriptions (CI, 18.0 to 21.1 prescriptions) in 2018. No statistically significant association was found between the coprescription of nitrates with PDE5 inhibitors and the risk for either composite outcome (odds ratio [OR], 0.58 [CI, 0.28 to 1.13] for the first outcome and OR, 0.73 [CI, 0.40 to 1.32] for the second outcome).

Limitation:
An assumption was made that concurrently filled prescriptions for nitrates and PDE5 inhibitors equaled concomitant use.

Conclusion:
From 2000 to 2018, the use of PDE5 inhibitors increased 20-fold among Danish patients with IHD who were taking nitrates. A statistically significant association between concomitant use of these medications and cardiovascular adverse events could not be identified.

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BMJ: British Medical Journal

Efficacy of interventions to reduce long term opioid treatment for chronic non-cancer pain: systematic review and meta-analysis

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Abstract

Objective

To review interventions to reduce long term opioid treatment in people with chronic non-cancer pain, considering efficacy on dose reduction and discontinuation, pain, function, quality of life, withdrawal symptoms, substance use, and adverse events.

Design

Systematic review and meta-analysis of randomised controlled trials and non-randomised studies of interventions.

Data sources

Medline, Embase, PsycINFO, CINAHL, and the Cochrane Library searched from inception to July 2021. Reference lists and previous reviews were also searched and experts were contacted.

Eligibility criteria for study selection

Original research in English. Case reports and cross sectional studies were excluded.

Data extraction and synthesis

Two authors independently selected studies, extracted data, and used the Cochrane risk-of-bias tools for randomised and non-randomised studies (RoB 2 and ROBINS-I). Authors grouped interventions into five categories (pain self-management, complementary and alternative medicine, pharmacological and biomedical devices and interventions, opioid replacement treatment, and deprescription methods), estimated pooled effects using random effects meta-analytical models, and appraised the certainty of evidence using GRADE (grading of recommendations, assessment, development, and evaluation).

Results

Of 166 studies meeting inclusion criteria, 130 (78%) were considered at critical risk of bias and were excluded from the evidence synthesis. Of the 36 included studies, few had comparable treatment arms and sample sizes were generally small. Consequently, the certainty of the evidence was low or very low for more than 90% (41/44) of GRADE outcomes, including for all non-opioid patient outcomes.

Despite these limitations, evidence of moderate certainty indicated that interventions to support prescribers' adherence to guidelines increased the likelihood of patients discontinuing opioid treatment (adjusted odds ratio 1.5, 95% confidence interval 1.0 to 2.1), and that these prescriber interventions as well as pain self-management programmes reduced opioid dose more than controls (intervention *v* control, mean difference –6.8 mg (standard error 1.6) daily oral morphine equivalent, P<0.001; pain programme *v* control, −14.31 mg daily oral morphine equivalent, 95% confidence interval −21.57 to −7.05).

Conclusions

Evidence on the reduction of long term opioid treatment for chronic pain continues to be constrained by poor study methodology. Of particular concern is the lack of evidence relating to possible harms. Agreed standards for designing and reporting studies on the reduction of opioid treatment are urgently needed.

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