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REVISIÓN BIBLIOGRÁFICA OCTUBRE Y NOVIEMBRE 2023
Selección de artículos

REVISTAS GERIÁTRICAS

Age and Ageing

New horizons in Parkinson's disease in older populations

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Abstract

Parkinson's disease (PD) is the second most common neurodegenerative disorder after Alzheimer's disease. Ageing is considered to be the greatest risk factor for PD, with a complex interplay between genetics and the environment. With population ageing, the prevalence of PD is expected to escalate worldwide; thus, it is of utmost importance to reduce the burden of PD. To date, there are no therapies to cure the disease, and current treatment strategies focus on the management of symptoms. Older adults often have multiple chronic diseases and geriatric syndromes, which further complicates the management of PD. Healthcare systems and care models necessary to address the broad needs of older PD patients are largely unavailable. In this New Horizon article, we discuss various aspects of PD from an ageing perspective, including disease management. We highlight recent advancements in PD therapies and discuss new care models with the potential to improve patient's quality of life.

Disponible en: https://doi.org/10.1093/ageing/afad186

Carer involvement in medication adherence: carer views and experiences of facilitating medication adherence using pharmacy-filled multi-compartment medication compliance aids and other methods of adherence support—a questionnaire survey

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Abstract

Introduction
Unpaid carers are an increasing proportion of the UK population. One of the many ways in which they help those they care for is assisting with medication adherence. Many older adults have medicines dispensed in pharmacy-filled multi-compartment medication compliance aids (pMCAs). However, evidence suggests that pMCAs may increase medication-related harm, and little is known about the interaction between the user, medication adherence systems and the carer.

Aim

To explore the views of carers supporting older adults to manage their medications with and without a pMCA.

Method

A researcher-administered questionnaire survey of carers supporting older adults to manage their medicines with or without a pMCA. Participants were recruited from inpatient wards, outpatient clinics and community services in central London. Responses were analysed by two independent researchers to identify overarching themes.

Results

Eighty-eight unpaid carers were interviewed and responses were categorised according to the medication adherence method used; 47 supported a user with a pMCA and 41 supported without a pMCA. The main themes were: Time, Responsibility and Mistakes, Waste and Sustainability, and Polypharmacy, with sub-themes of design of multi-compartment medication compliance aids, organisation and reassurance.

Conclusion

Supporting medication adherence puts considerable burden on carers regardless of whether a self- or pharmacy-filled medication compliance aid is used or not. Prescribers could alleviate this burden through regular medication review by considering the prescribing frequency and duration and medication rationalisation. Redesign of both pMCAs and systems surrounding their use could also help reduce carer's burden and environmental burden.

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Archives of Gerontology and Geriatrics

Association of anticholinergic drug use with postoperative mortality among patients with hip fracture. A nationwide cohort study

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Abstract

Purpose

Anticholinergic (AC) drugs are associated with various determinantal outcomes. Data regarding the effect of AC drugs on mortality among geriatric hip fracture patients are limited and inconsistent.

Methods

Using Danish health registries, we identified 31,443 patients aged ≥65 years undergoing hip fracture surgery. AC burden was assessed 90 days before surgery by the Anticholinergic Cognitive Burden (ACB) score and number of AC drugs. Logistic and Cox regression producing odds ratios (OR) and hazard ratios (HR) for 30- and 365- day mortality, adjusting for age, sex, and comorbidities were computed.

Results

AC drugs were redeemed by 42% of patients. The 30-day mortality increased from 7% for patients with ACB score of 0 to 16% for patients with ACB score of ≥5, corresponding to an adjusted OR 2.5 (CI: 2.0–3.1). The equivalent adjusted HR for 365-mortality was 1.9 (CI: 1.6–2.1). Using count of AC drugs as exposure we found a stepwise increase in ORs and HRs with increased number of AC drugs; Compared to non-users, adjusted ORs for 30-days mortality were 1.6 (CI: 1.4–1.7), 1.9 (CI: 1.7–2.1), and 2.3 (CI: 1.9–2.7) for users of 1, 2 and 3+ AC drugs. HRs for 365-day mortality were 1.4 (CI: 1.3–1.5), 1.6 (CI: 1.5–1.7) and 1.8 (CI: 1.7–2.0).

Conclusion

Use of AC drugs was associated with increased 30-day and 365-day mortality among older adults with hip fracture. Simply counting the number of AC drugs may be a clinically relevant and easy AC risk assessment tool. Continued effort to reduce AC drug-use is relevant.

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Guideline concordant prescribing following myocardial infarction in people who are frail: A systematic review

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Abstract

Aims

The risk-to-benefit ratio of cardioprotective medications in frail older adults is uncertain. The objective was to systematically review prescribing of guideline-recommended cardioprotective medications following myocardial infarction (MI) in people who are frail.

Data sources

Ovid Medline, PubMed and Cochrane were searched from inception to October 2022 for studies that reported prescribing of one or more cardioprotective medication classes post-MI or acute coronary syndromes in people with frailty.

Study selection

We included observational studies that reported prescribing of cardioprotective medications post-MI stratified by frailty status.

Results

Overall, 16 cohort studies published from 2013 to 2022 that used seven different frailty scales were included. Prescribing of all cardioprotective medication classes following MI was lower in frail compared to non-frail people, with absolute rates of prescribing varying substantially across studies. Median prescribing in frail and non-frail people, respectively, was 88.9% (IQR 81.5–96.2) and 93.1% (IQR 92.0–98.9) for aspirin; 68.1% (IQR 61.9–91.2) and 86.7% (IQR 79.5–92.8) for P2Y12-inhibitors; 83.1% (IQR 76.9–91.3) and 94.0% (IQR 87.1–95.9) for lipid-lowering therapy; 67.9% (IQR 60.6–74.0) and 74.7% (IQR 71.3–84.5) for angiotensin-converting enzyme inhibitor/angiotensin II receptor blockers; and 74.1% (IQR 69.2–79) and 77.6% (IQR 71.8–85.9) for beta-blockers.

Conclusion

People who were frail were less likely to be prescribed guideline recommended medication classes post-MI than those who were non-frail. Further research is needed into treatment benefits and risks in frail people to avoid unnecessarily withholding treatment in this high-risk population, while also minimising potential for medication related harm.

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Comparison of glomerular filtration rate estimating equations in older adults: A systematic review and meta-analysis

Yao Ma, Xue Shen, Zhenzhu Yong, Lu Wei, Weihong Zhao

Abstract

Background

Debates persist regarding the performance of existing glomerular filtration rate (GFR) estimating equations in older individuals. We performed this meta-analysis to assess the accuracy and bias of six commonly used equations, including the Chronic Kidney Disease Epidemiology Collaboration creatinine equation (CKD-EPICr) and its combination with cystatin C (CKD-EPICr-Cys), with the corresponding pair of the Berlin Initiative Study equations (BIS1 and BIS2) and the Full Age Spectrum equations (FASCr and FASCr-Cys).

Methods

PubMed and the Cochrane Library were searched for studies comparing estimated GFR (eGFR) with measured GFR (mGFR). We analyzed the difference in P30 and bias among the six equations and investigated subgroups based on the area (Asian and non-Asian), mean age (60–74 years and ≥75 years), and levels of mean mGFR (<45 mL/min/1.73m2 and ≥45 mL/min/1.73m2).

Results
27 studies with 18,112 participants were included, all reporting P30 and bias. BIS1 and FASCr exhibited significantly higher P30 than CKD-EPICr. While no significant differences were observed between FASCr and BIS1, or among the three combined equations in terms of either P30 or bias. Subgroup analyses revealed FASCr and FASCr-Cys achieved better results in most situations. However, in the subgroup of mGFR<45 mL/min/1.73m2, CKD-EPICr-Cys had relatively higher P30 and significantly smaller bias.

Conclusions
Overall, BIS and FAS provided relatively more accurate estimates of GFR than CKD-EPI in older adults. FASCr and FASCr-Cys may be better suited for various conditions, while CKD-EPICr-Cys would be a better option for older individuals with impaired renal function.

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Drugs and Aging

Evaluation and Treatment of Acute Trauma Pain in Older Adults

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Abstract
In the context of an ageing population, the demographic sands of trauma are shifting. Increasingly, trauma units are serving older adults who have sustained injuries in low-energy falls from a standing height. Older age is commonly associated with changes in physiology, as well as an increased prevalence of frailty and multimorbidity, including cardiac, renal and liver disease. These factors can complicate the safe and effective administration of analgesia in the older trauma patient. Trauma services therefore need to adapt to meet this demographic shift and ensure that trauma clinicians are sufficiently skilled in treating pain in complex older people. This article is dedicated to the management of acute trauma pain in older adults. It aims to highlight the notable clinical challenges of managing older trauma patients compared with their younger counterparts. It offers an overview of the evidence and practical opinion on the merits and drawbacks of commonly used analgesics, as well as more novel and emerging analgesic adjuncts. A search of Medline (Ovid, from inception to 7 November 2022) was conducted by a medical librarian to identify relevant articles using keyword and subject heading terms for trauma, pain, older adults and analgesics. Results were limited to articles published in the last 10 years and English language. Relevant articles' references were hand-screened to identify other relevant articles. There is paucity of dedicated high-quality evidence to guide management of trauma-related pain in older adults. Ageing-related changes in physiology, the accumulation of multimorbidity, frailty and the risk of inducing delirium secondary to analgesic medication present a suite of challenges in the older trauma patient. An important nuance of treating pain in older trauma patients is the challenge of balancing iatrogenic adverse effects of analgesia against the harms of undertreated pain, the complications and consequences of which include immobility, pneumonia, sarcopenia,

pressure ulcers, long-term functional decline, increased long-term care needs and mortality.

In this article, the role of non-opioid agents including short-course non-steroidal anti-inflammatory drugs (NSAIDs) is discussed. Opioid selection and dosing are reviewed for older adults suffering from acute trauma pain in the context of kidney and liver disease. The evidence base and limitations of other adjuncts such as topical and intravenous lidocaine, ketamine and regional anaesthesia in acute geriatric trauma are discussed.

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Crushed Tablet Administration for Patients with Dysphagia and Enteral Feeding: Challenges and Considerations

Amie Blaszczyk, Nicole Brandt, Jeremy Ashley, Nancy Tuders, Hannah Doles & Richard G. Stefanacci

Abstract

Dysphagia is increasingly common in older adults; it is especially prevalent in long-term care settings. Patients with dysphagia likely require pharmacologic treatment for multiple comorbidities but may find it difficult or impossible to swallow oral medications. Administering crushed medications mixed with a soft food or liquid vehicle, or via a feeding tube, is a common strategy to circumvent swallowing difficulties in patients with dysphagia. However, inappropriate medication use and improper crushing technique can reduce the medication dose a patient receives, alter medication pharmacokinetics and pharmacodynamics, and compromise treatment efficacy and patient safety. Clinical judgment is needed to identify medications that can and cannot be crushed, select a crushing methodology and vehicle for administering crushed medications, and create a strategy for administering multiple medications. A coordinated effort from the entire care team—including physicians, pharmacists, nurses, advanced practice providers, speech therapists, patients, and caregivers—is necessary to develop and implement an individualized plan for administering medications to patients with dysphagia. This review details the current literature regarding the administration of medications that have been altered, such as by crushing tablets or opening capsules, for patients with dysphagia or who are receiving enteral feeding and provides recommendations on best practices.

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Journal of the American Geriatrics Society

Association of sulfonylureas with the risk of dementia: A population-based cohort study

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Abstract

Background

Sulfonylureas are oral glucose-lowering medications positioned as a second-line therapy for type 2 diabetes. Evidence relating them to cognitive decline has been mixed. The objective was to determine whether sulfonylurea use was associated with a differential risk of dementia compared with dipeptidyl peptidase-4 (DPP4) inhibitor use.

Methods

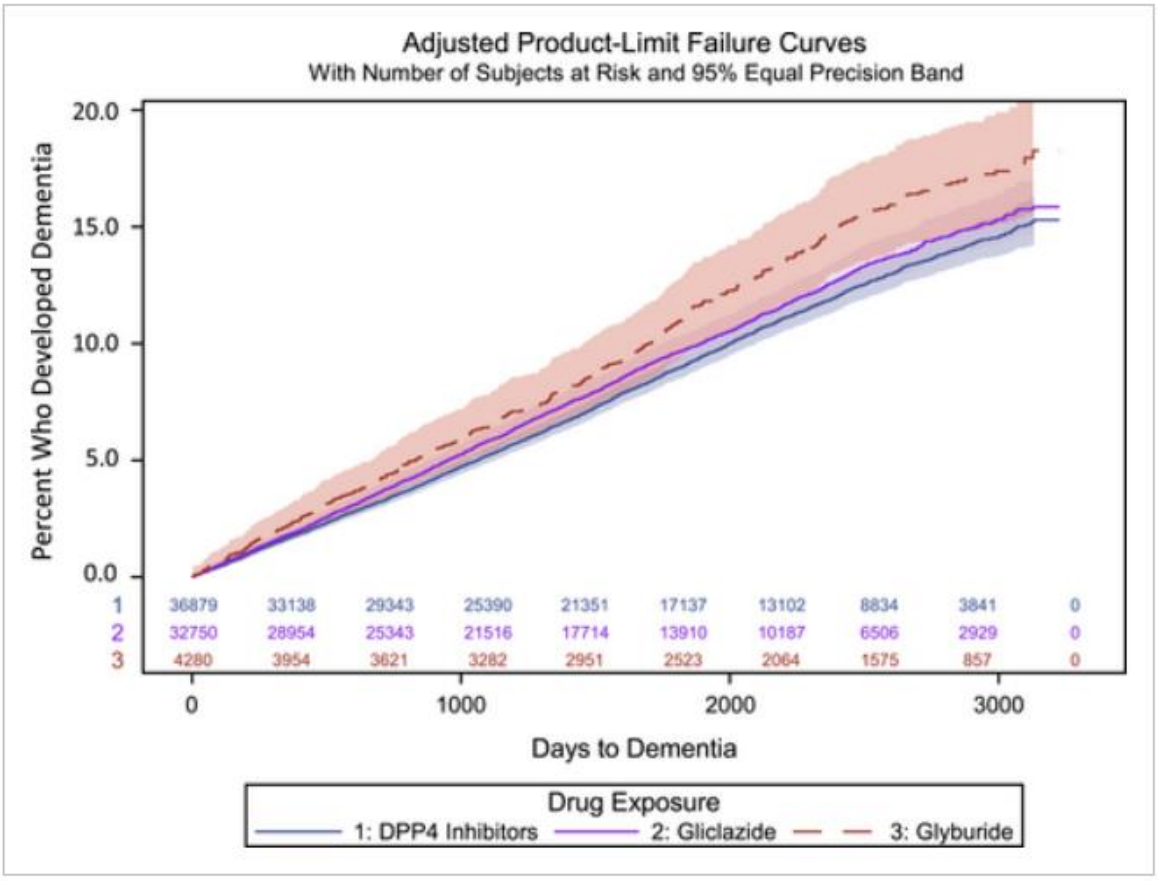
Using administrative data from residents in Ontario, Canada, adults aged ≥66 years who were new users of a sulfonylurea or a DPP4 inhibitor from June 14, 2011, to March 31, 2021 entered this population-based retrospective cohort study. Dementia was ascertained using a validated algorithm for Alzheimer's disease and related dementias. Propensity-score weighted Cox proportional hazards models were used to obtain adjusted hazard ratios (aHR) and confidence intervals (CI) for time to incident dementia. The observation window started at 1 year after cohort entry to mitigate protopathic bias due to delayed diagnosis. The primary analysis used an intention-to-treat exposure definition. A separate propensity-score weighted analysis was conducted to explore within-class differences in dementia risk among sulfonylurea new users selected from the primary cohort.

Results

Among 107,806 DPP4 inhibitor new users and 37,030 sulfonylurea new users, sulfonylureas compared with DPP4 inhibitors were associated with a higher risk of dementia (18.4/1000 person-years; aHR [95% CI] = 1.09 [1.04–1.15]) over a mean follow-up of 4.82 years from cohort entry. Glyburide compared to gliclazide exhibited a higher dementia risk (aHR [95% CI] = 1.17 [1.03–1.32]).

Conclusion

New use of a sulfonylurea especially glyburide was associated with a higher dementia risk compared with new use of a DPP4 inhibitor in older adults with diabetes.



Weighted Kaplan–Meier curves for glyburide, gliclazide and DPP4 inhibitor users. The figure illustrates the cumulative proportions of individuals who developed dementia from the beginning of the observation window (i.e., 1-year lag-time after cohort entry).

Disponible en: https://doi.org/10.1111/jgs.18397

Comparative safety of adding serotonin and norepinephrine reuptake inhibitors (SNRIs) versus nonsteroidal anti-inflammatory drugs (NSAIDs) to short-acting opioids for non-malignant pain in nursing homes

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Abstract

Background

The comparative safety of serotonin and norepinephrine reuptake inhibitors (SNRIs) as adjuvants to short-acting opioids in older adults is unknown even though SNRIs are commonly used. We compared the effects of SNRIs versus nonsteroidal anti-Inflammatory drugs (NSAIDs) on delirium among nursing home residents when SNRIs or NSAIDs were added to stable regimens of short-acting opioids.

Methods

Using 2011–2016 national Minimum Data Set (MDS) 3.0 and Medicare claims data to implement a new-user design, we identified a cohort of nursing home residents receiving short-acting opioids who initiated either an SNRI or an NSAID. Delirium was defined from the Confusion Assessment Method in MDS 3.0 assessments and ICD9/10 codes using Medicare hospitalization claims. Propensity score matching balanced underlying differences for initiating treatments on 39 demographic and clinical characteristics (nSNRIs = 5350; nNSAIDs = 5350). Fine and Gray models provided hazard ratios (HRs) and 95% confidence intervals (CIs) adjusting for the competing risk of death.

Results

Hydrocodone was the most commonly used short-acting opioid (48%). Residents received ~23 mg daily oral morphine equivalent at the time of SNRIs/NSAIDs initiation. The majority were women, non-Hispanic White, and aged ≥75 years. There were no differences in any of the confounders after propensity matching. Over 1 year, 10.8% of SNRIs initiators and 8.9% of NSAIDs initiators developed delirium. The rate of delirium onset was similar in SNRIs and NSAID initiators (HR(delirium in nursing home or hospitalization for delirium):1.10; 95% CI: 0.97–1.24; HR(hospitalization for delirium): 1.06; 95% CI: 0.89–1.25), and were similar regardless of baseline opioid daily dosage.

Conclusions

Among nursing home residents, adding SNRIs to short-acting opioids does not appear to increase risk of delirium relative to initiating NSAIDs. Understanding the comparative safety of pain regimens is needed to inform clinical decisions in a medically complex population often excluded from clinical research.

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Journal of Clinical Interventions In Aging

Future Perspectives to Improve CHA2DS2VASc Score: The Role of Left Atrium Remodelling, Inflammation and Genetics in Anticoagulation of Atrial Fibrillation

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Abstract

In 10% of ischemic strokes, non-valvular atrial fibrillation (NVAF) is detected retroactively. Milder, or even asymptomatic forms of NVAF have shown high mortality, thrombotic risk, and deterioration of cognitive function. The current guidelines for the diagnosis and treatment of AF contain “grey areas”, such as the one related to anticoagulant treatment in men with CHA2DS2-VASc score 1 and women with score 2.

Moreover, parameters such as renal function, patient weight or left atrium remodelling are missing from the recommended guidelines scores. Vulnerable categories of patients including the elderly population, high hemorrhagic risk patients or patients with newly diagnosed paroxysmal episodes of atrial high rate at device interrogation are at risk of underestimation of the thrombotic risk. This review presents a systematic exposure of the most important gaps in evaluation of thrombotic and hemorrhagic risk in patients with NVAF. The authors propose new algorithms and risk factors that should be taken into consideration for an accurate thrombotic and hemorrhagic risk estimation, especially in vulnerable categories of patients.

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Management of Glucose-Lowering Therapy in Older Adults with Type 2 Diabetes: Challenges and Opportunities

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Abstract
The population of older adults (≥ 65 years) with type 2 diabetes mellitus (T2DM) is diverse, encompassing individuals with varying functional capabilities, living arrangements, concomitant medical conditions, and life expectancies. Hence, their categorization into different patient profiles (ie, good health, intermediate health, poor health) may aid in clinical decision-making when establishing glycemic goals and pharmacological treatment strategies. Further granularity in assessing each patient profile through interdisciplinary collaboration may also add precision to therapeutic and monitoring decisions. In this review, we discuss with a multidisciplinary approach how to deliver the best benefit from advanced diabetes therapies and technologies to older adults with T2DM according to each patient profile. There remain however several areas that deserve further research in older adults with T2DM, including the efficacy and safety of continuous glucose monitoring and automated insulin delivery systems, the switch to once-weekly insulin, the effectiveness of multidisciplinary care models, and the use of supported telemedicine and remote blood glucose monitoring in the oldest-old (≥ 85 years) who particularly require the assistance of others.

Disponible en: https://doi.org/10.2147/CIA.S423122

Prevalence and Associated Predictors of Inappropriate and Omitted Medications Prescribing in Older Patients with Advanced Cancer: A Cross-Sectional Study

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Abstract

Aims of the Study

This study aimed to identify the prevalence and significant predictors of both potentially inappropriate medications (PIMs) and potentially omitted medications (POMs) events among geriatric patients with advanced cancer using the STOPP (Screening Tool of Older Persons' Prescriptions) and START (Screening Tool to Alert to Right Treatment) criteria.

Methods

This retrospective cross-sectional study included patients aged ≥ 65 years who were diagnosed and treated for advanced stage of cancer. Patients' medical charts were evaluated to identify polypharmacy (≥ 5 medications) prevalence as well as potential PIMs and POMs incidents and their associated predictors. SPSS software was used to perform the analysis. Multivariate logistic regression models were used to identify factors associated with dependent variables including PIMs use and POMs.

Results

Electronic medication charts of 510 patients were evaluated. The average age of the patients was 73.25 years, and 264 (51.8%) patients were males. The average number of medications prescribed per patient was 10.3 (range– 2– 26). Polypharmacy was present in 85.9% of patients, while excessive polypharmacy prevalence was 52.2%. At least one PIM was encountered in 253 patients (49.6%), while at least one POM was encountered in all patients owing to the omission of pneumococcal vaccines. The most common PIMs were opioid analgesics, followed by benzodiazepines, and hypnotics. Additionally, the most omitted medications, excluding vaccinations, were cardiovascular agents and laxatives in patients on regular opioid analgesics. Polypharmacy and diagnosis with solid cancer compared to hematological cancer were associated with increased odds for PIMs occurrence (ORs = 1.293 ($p < 0.001$) and 3.022 ($p = 0.03$), respectively), while coexistence of hypertension diagnosis in cancer patients was associated with increased the odds for

POMs events (OR = 2.286 ($p = 0.007$)).

Conclusion

Polypharmacy, PIMs, and POMs were highly prevalent among older cancer patients based on the polypharmacy definition and STOPP/START Criteria.

Disponible en: https://doi.org/10.2147/CIA.S430208

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Journal of Aging and Health

Association Between Frailty, 30-day Unplanned Readmission and Mortality After Hospitalization for Heart Failure: Results From the Nationwide Readmissions Database

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Abstract

Objectives

This study examined how frailty in traditional risk-adjusted models could improve the predictability of unplanned 30-day readmission and mortality among heart failure patients.

Methods

This study was a retrospective analysis of Nationwide Readmissions Database data collected during the years 2010–2018. All patients ≥65 years who had a principal diagnosis of heart failure were included in the analysis. The Johns Hopkins Adjusted Clinical Groups frailty-defining diagnosis indicator was used to identify frail patients.

Results

There was a total of 819,854 patients admitted for heart failure during the study period. Among them, 63,302 (7.7%) were frail. In the regression analysis, the risk of all-cause 30-day readmission (OR, 1.18; 95% CI, 1.14–1.22) and in-hospital mortality (OR, 1.52; 95% CI, 1.40–1.66) were higher in patients with frailty.

Discussion

Inclusion of frailty in comorbidity-based risk-prediction models significantly improved the predictability of unplanned 30-day readmission and in-hospital mortality.

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International Journal of Geriatric Psychiatry

Discontinuation of benzodiazepines and Z-drugs in hospitalised population at the age of 60 and above. An open-label randomized controlled trial

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Abstract

Background

Treating insomnia with hypnotic drugs in elderly patients has many adverse effects. This study aims to assess the effect of two discontinuation methods of hypnotic drugs during acute hospitalization.

Methods

We conducted an open-label randomized controlled trial that included participants aged 60 and above taking benzodiazepines or Z-Drugs for at least 3 months as a treatment for insomnia and were admitted to the hospital. In the prospective arm, patients were randomly assigned into two intervention groups. In the Minimal Intervention (MI) group, patients received an explanation of the dangers of long-term treatment and a recommendation to stop the treatment. In the Tapering Down Intervention (TDI) group, in addition to the explanation, patients received a tapering down table. In the retrospective arm (control group), we examined the use of hypnotic drugs among hospitalized patients 3 months after hospitalization, similar to the patients in the prospective arm.

Results

46 patients were enrolled in the MI group, 55 patients in the TDI group, and 114 patients in the control group. The mean age in the three groups was 75.0 ± 8.2, 75.9 ± 9.0, and 75.0 ± 7.9 years respectively (p = 0.85). After 3 months, seven (15.2%) of the patients in the MI group, 15 (27.3%) in the TD group, and 2 (1.8%) in the control group (p = 0.00003) were weaned from the hypnotic drugs treatment, without a significant difference between the intervention groups (p = 0.221).

Conclusions

A short intervention during hospitalization results in a significant decrease in hypnotic drug use.

Disponible en: https://doi.org/10.1002/gps.6012

REVISTAS FARMACÉUTICAS

American Journal of Health System Pharmacist

Evaluation of a novel blood volume–based enoxaparin dosing guideline for venous thromboembolism prophylaxis in trauma patients

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Abstract

Purpose

Fixed-dose and body mass index (BMI)–based enoxaparin regimens provide inadequate venous thromboembolism (VTE) prophylaxis for many trauma patients. The purpose of this study was to evaluate the effectiveness of a novel blood volume (BV)–based enoxaparin guideline vs a historical BMI-based guideline for VTE prophylaxis in trauma patients.

Methods

This was a retrospective pre/post study completed at a large academic level 1 trauma center. All adult trauma patients admitted from October through December 2019 and August through October 2020 who received prophylactic enoxaparin per guideline were included. The BV dosing was as follows: patients with a BV of 3 to 4.9 L received enoxaparin 30 mg every 12 hours, those with a BV of 5 to 6.9 L received 40 mg every 12 hours, and those with a BV of ≥7 L received 60 mg every 12 hours. The primary outcome was the percentage of patients who attained a target anti–factor Xa (anti-Xa) postdosing level at the first steady-state assessment (0.2 to 0.5 IU/mL).

Results

A total of 241 patients (99 for the BMI group and 142 for the BV group) were included. The study groups had a median age of 38 vs 42 years, a mean BMI of 27.4 vs 27.7 kg/m2, and a mean BV of 5.1 vs 5.1 L, respectively. A total of 63 patients (62.6%) in the BMI group attained target anti-Xa levels compared to 115 patients (81%) in the BV group (P = 0.008). In multivariate regression, the BV-based guideline was the only variable associated with attainment of target anti-Xa levels (adjusted odds ratio, 2.02; P = 0.01). Clinically relevant bleeding and VTE rates were similar between the groups.

Conclusion

Dosing prophylactic enoxaparin using a BV-based dosing guideline significantly increased attainment of target anti-Xa levels.

Disponible en: https://doi.org/10.1093/ajhp/zxad119

Comparison of effectiveness and safety of sodium polystyrene sulfonate and sodium zirconium cyclosilicate for treatment of hyperkalemia in hospitalized patients

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Abstract

Purpose

Potassium binders are frequently utilized for the treatment of hyperkalemia in hospitalized patients; however, there is limited data directly comparing individual agents. The purpose of this study was to compare the effectiveness and safety of sodium polystyrene sulfonate (SPS) and sodium zirconium cyclosilicate (SZC) for hyperkalemia treatment in hospitalized patients.

Methods

This retrospective cohort study evaluated adult patients who were admitted within a 7-hospital health system and received SPS or SZC for a serum potassium level greater than 5.0 mEq/L. Patients receiving dialysis prior to SPS/SZC administration, those receiving other potassium-lowering medications within 6 hours prior to blood sampling for a repeat potassium level, and those started on kidney replacement therapy prior to sampling for a repeat potassium level were excluded.

Results

Following evaluation of 3,903 patients, the mean reduction in serum potassium 4 to 24 hours after binder administration was 0.96 mEq/L with SPS and 0.78 mEq/L with SZC ($P < 0.0001$). The median dose of SPS was 30 g (interquartile range [IQR], 15-30 g) while the median (IQR) dose of SZC was 10 g (10-10 g). Resolution of hyperkalemia within 24 hours was achieved in a higher percentage of patients with use of SPS (74.9%) versus SZC (68.8%) ($P < 0.001$).

Conclusion

One of the largest comparisons of SPS and SZC conducted to date, this study demonstrated the effectiveness and safety of both agents. While a statistically greater reduction in serum potassium was observed with use of SPS, there was significant dosing variability among agents that limited the ability to directly compare specific doses. Further investigation is needed to determine the optimal dose of each agent for acute hyperkalemia management. This data will inform clinical decisions about the choice of potassium binder for acute hyperkalemia.

Disponible en: https://doi.org/10.1093/ajhp/zxad137

British Journal of Clinical Pharmacology

Deprescribing interventions for gabapentinoids in adults: A scoping review

Prue A. Anderson, Andrew J. McLachlan, Christina Abdel Shaheed, Danijela Gnjidic, Rowena Ivers, Stephanie Mathieson

Abstract

The emerging issue of rising gabapentinoid misuse is being recognized alongside the lack of current evidence supporting the safe and effective deprescribing of gabapentinoids. This scoping review aimed to assess the extent and nature of gabapentinoid deprescribing interventions in adults, either in reducing dosages, or prescribing of, gabapentinoids. Electronic databases were searched on 23 February 2022 without restrictions. Eligible studies included randomized, non-randomized and observational studies that assessed an intervention aimed at reducing/ceasing the prescription/use of a gabapentinoid in adults for any indication in a clinical setting. The research outcomes investigated the type of intervention, prescribing rates, cessations, patient outcomes and adverse events. Extracted outcome data were categorized as either short (≤3 months), intermediate (>3 but <12 months) or long (≥12 months) term. A narrative synthesis was conducted. The four included studies were conducted in primary and acute care settings. Interventions were of dose-reducing protocols, education and/or pharmacological-based approaches. In the randomized trials, gabapentinoid use could be ceased in at least one third of participants. In the two observational trials, gabapentinoid prescribing rates decreased by 9%. Serious adverse events and adverse events specifically related to gabapentinoids were reported in one trial. No study included patient-focused psychological interventions in the deprescribing process, nor provided any long-term follow-up. This review highlights the lack of existing evidence in this area. Due to limited available data, our review was unable to make any firm judgements on the most effective gabapentinoid deprescribing interventions in adults, highlighting the need for more research in this area.

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Short-term efficacy and safety of personalized antiplatelet therapy for patients with acute ischaemic stroke or transient ischaemic attack: A randomized clinical trial

Mengqi Han, Weijie Jia, Yifan Wu, Jie Kuang, Jianglong Tu, Shujuan Yin, Jibiao Chen, Xiaolin Zhang, Jingyi Li, Yongsen Chen, Bin Wu, Yingping Yi

Abstract

Aims

The aim of this study was to determine whether the testing strategy for clopidogrel and/or aspirin resistance using CYP2C19 genotyping or urinary 11-dhTxB2 testing has an impact on clinical outcomes.

Methods

A multicentre, randomized, controlled trial was conducted at 14 centres in China from 2019 to 2021. For the intervention group, a specific antiplatelet strategy was assigned based on the CYP2C19 genotype and 11-dhTxB2, a urinary metabolite of aspirin, and the control group received nonguided (ie, standard of care) treatment. 11-dhTXB2 is a thromboxane A2 metabolite that can help quantify the effects of resistance to aspirin in individuals after ingestion. The primary efficacy outcome was new stroke, the secondary efficacy outcome was a poor functional prognosis (a modified Rankin scale score ≥3), and the primary safety outcome was bleeding, all within the 90-day follow-up period.

Results

A total of 2815 patients were screened and 2663 patients were enrolled in the trial, with 1344 subjects assigned to the intervention group and 1319 subjects assigned to the control group. A total of 60.1% were carriers of the CYP2C19 loss-of-function allele (*2, *3) and 8.71% tested positive for urinary 11-dhTxB2- indicating aspirin resistance in the intervention group. The primary outcome was not different between the intervention and control groups (P = .842). A total of 200 patients (14.88%) in the intervention group and 240 patients (18.20%) in the control group had a poor functional prognosis (hazard ratio 0.77, 95% confidence interval [CI] 0.63 to 0.95, P = .012). Bleeding events occurred in 49 patients (3.65%) in the intervention group and 72 patients (5.46%) in the control group (hazard ratio 0.66, 95% CI 0.45 to 0.95, P = .025).

Conclusions

Personalized antiplatelet therapy based on the CYP2C19 genotype and 11-dhTxB2 levels was associated with favourable neurological function and reduced bleeding risk in acute ischaemic stroke and transient ischaemic attack patients. The results may help support the role of CYP2C19 genotyping and urinary 11-dhTxB2 testing in the provision of precise clinical treatment.

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Sodium-glucose cotransporter 2 inhibitors and the risk of venous thromboembolism: A population-based cohort study

Stephanie Aloe, Christopher Filliter, Shahrzad Salmasi, Samuel Igweokpala, Oriana H. Y. Yu, Vicky Tagalakis, Kristian B. Filion

Abstract

Aims

The cardiovascular benefits of sodium-glucose cotransporter 2 inhibitors (SGLT2Is) result from their complex impact on coronary and arterial vessels. However, their effect on veins and the risk of venous thromboembolism (VTE) remains unclear. Meta-analysis of trials has suggested no significant change in risk, but observational studies on the topic are scarce. Our objective was to determine if the use of SGLT2Is, compared to the use of dipeptidyl peptidase 4 inhibitors (DPP-4Is), is associated with the risk of VTE among patients with type 2 diabetes.

Methods

Using the Clinical Practice Research Datalink linked to hospitalization and vital statistics databases, we conducted a retrospective cohort study using a prevalent new-user design. SGLT2Is were matched to DPP-4I users on calendar time, diabetes treatment intensity, duration of previous DPP-4I use and time-conditional high-dimensional propensity score. Cox proportional hazard models estimated the hazard ratio (HR) for VTE with SGLT2Is versus DPP-4Is.

Results

SGLT2I use was not associated with an increased risk of VTE (HR 0.65, 95% confidence interval [CI] 0.34 to 1.25). This finding was consistent among prevalent (HR 0.47, 95% CI 0.16 to 1.42) and incident (HR 0.75, 95% CI 0.33 to 1.72) new users.

Conclusions

We found that SGLT2Is were not associated with an increased risk of VTE compared to DPP-4Is. Although we observed a numerically decreased risk of VTE with SGLT2Is, estimates were accompanied by wide 95% CIs. Nonetheless, given the morbidity associated with VTE, our results provide some reassurance regarding the safety of SGLT2Is with respect to VTE.

Disponible en: https://doi.org/10.1111/bcp.15787

Examining the effectiveness and duration of adjuvanted vs. non-adjuvanted influenza vaccines in protecting older adults against symptomatic SARS-CoV-2 infection

Francesco Lapi, Alexander Domnich, Ettore Marconi, Alessandro Rossi, Ignazio Grattagliano, Claudio Cricelli

Abstract

Annual influenza vaccination is one of the main public health measures able to drastically reduce the burden of this infectious disease. Some evidence suggests 'trained immunity' triggered by influenza vaccine might reduce the risk of SARS-CoV-2 infection. Adjuvanted influenza vaccines are known to induce a broader cross-reactive immunity. No studies investigated the effect of adjuvanted vs. non-adjuvanted influenza vaccines on the risk of symptomatic SARS-CoV-2 infection. A case–control analysis nested in a cohort of subjects aged ≥65 years and immunized with adjuvanted or non-adjuvanted influenza vaccines was conducted. Although no statistically significant (OR = 0.87; P = .082) difference between the two vaccine types was observed for the 9-month follow-up period, a 17% (OR = 0.83; P = .042) reduction in the odds of COVID-19 was observed for adjuvanted vaccines with a 6-month follow-up. Further evidence is needed, but these results might have implications given the complexity of the upcoming winter seasons, in which the co-occurrence of influenza, SARS-CoV-2 and other respiratory infections (e.g., syncytial virus) might be unpredictable.

Disponible en: https://doi.org/10.1111/bcp.15940

Drug Safety

Use of Bisphosphonates and the Risk of Skin Ulcer: A National Cohort Study Using Data from the French Health Care Claims Database

Clément Jambon-Barbara, Claire Bernardeau, Julien Bezin, Matthieu Roustit, Sophie Blaise, Jean-Luc Cracowski & Charles Khouri

Abstract

Introduction

Previous pre-clinical and pharmacovigilance disproportionality analyses highlighted a safety signal of cutaneous ulcer with bisphosphonate use. Therefore, our objective is to evaluate this risk and assess whether unmeasured confounding factors could explain this association.

Methods

This study is a population-based cohort study from a representative sample (1/97th) of the French health insurance claims database: Echantillon Généraliste des Bénéficiaires (EGB) from 2006 to 2019. To limit the impact of our study design and methodological choices on any association between skin ulceration and exposure to bisphosphonates, we used several methods: a Cox proportional hazards analysis and a prior event rate ratio (PERR) analysis, using two propensity matched control groups, and either the first episode of incident ulceration or multiple event-time outcomes.

Results

There were 7402 individuals newly exposed to bisphosphonates matched to 29,605 unexposed individuals on propensity score. The primary outcome was skin ulcer occurrence assessed by at least 2 deliveries of wound dressing during the period of one month. Among 6911 individuals newly exposed to bisphosphonates and 28,072 unexposed individuals with no previous skin ulcer, the Cox regression yielded a hazard ratio (HR) of 1.40 (95% CI 1.26–1.56) for newly exposed individuals. Among 7402 exposed and 29,605 unexposed individuals, the PERR analysis found a non-significant HR of 1.03 (95% CI 0.87–1.24). Results were similar on the different sensitivity analyses.

Conclusion

No association between bisphosphonate and skin ulcers was found in the French population. The association observed in previous pharmacovigilance studies and in the Cox regression analysis is likely due to unmeasured confounding factors.

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Sharing Adverse Drug Event Reports Between Hospitals and Community Pharmacists to Inform Re-dispensing: An Analysis of Reports and Process Outcomes

Amber Cragg, Serena S. Small, Erica Lau, Adrianna Rowe, Anthony Lau, Katherine Butcher, Corinne M. Hohl

Abstract

Introduction

Adverse drug events (ADEs) are a leading cause of unplanned hospital visits. We designed ActionADE, an online ADE reporting platform, and integrated it with PharmaNet, British Columbia's (BC's) provincial medication dispensing system, to overcome identified barriers in ADE reporting and communicate ADEs to community pharmacies.

Our objectives were to characterise ADEs reported in ActionADE, explore associations between patients' age, sex and ADE characteristics, and estimate the re-dispensation rate of culprit medications in community pharmacies.

Methods

We conducted a prospective observational study of ADE reporting in four BC hospitals between April 1, 2020 and October 31, 2022. We described the characteristics of ADEs reported into ActionADE, used logistic regression modelling to examine associations between age and sex and ADE characteristics, and calculated rates of avoided culprit drug re-dispensations using community pharmacists' responses to ActionADE alerts.

Results

In total, 3591 ADE reports were initiated by hospital clinicians, 3174 of which were included in this analysis. Serious or life-threatening ADEs resulting in permanent disability, hospitalisation, extended hospitalisation, and/or death accounted for 28.5% (906/3174; 95% CI 27.0–30.1%) of reports. Males were more likely to have non-adherence reported compared to females and experienced life threatening ADEs at a younger age than females. Of 592 patients who had ≥ 1 adverse drug reaction or allergy report (a subset of ADEs) transmitted to community pharmacies, 200 subsequently attempted to re-fill the culprit or a same class drug. Community pharmacists responded to preventative alerts by avoiding re-dispensation in 33.0% (66/200; 95% CI 26.5–39.5%).

Interpretation

ActionADE is the first interoperable system that communicates ADEs via a central medication database to community pharmacies. Every 10th ADE reported in ActionADE and shared to PharmaNet resulted in community pharmacists' avoiding one culprit or same class drug re-exposure. Further research is needed to understand ActionADE's impact on patient and health system outcomes.

Disponible en: https://doi.org/10.1007/s40264-023-01348-7

Adverse Drug Reactions to Opioids: A Study in a National Pharmacovigilance Database

Moa Gustafsson, Cristiano Matos, João Joaquim, Joep Scholl & Florence van Hunsel

Abstract

Introduction

Opioids are commonly used as analgesics; however, like any medicine, they can produce adverse drug reactions (ADRs), including nausea, constipation, dependence, and respiratory depression, that result in harmful and fatal events. Therefore, it is essential to monitor the safety of these drugs in clinical practice.

Objective

This study aimed to characterize the safety profile of opioids by conducting a descriptive study based on a spontaneous reporting system (SRS) for ADRs in The Netherlands, focusing on abuse, misuse, medication errors, and differences between sexes.

Methods

Reports submitted to the Netherlands Pharmacovigilance Centre Lareb from January 2003 to December 2021 with an opioid drug as the suspected/interacting medicine were analyzed. Reporting odds ratios (RORs) for drug-ADR combinations were calculated, analyzed, and corrected for sex and drug utilization (expenditure) for the Dutch population.

Results

A total of 8769 reports were analyzed. Tramadol was the opioid with the most reports during the period (n = 2746), while oxycodone or tramadol had the highest number of reports per year in the study period. The most reported ADRs from opioid use were nausea, followed by dizziness and vomiting, independent of sex, and all of them were more often reported in women. Vomiting associated with tramadol (ROR females/males = 2.17) was significantly higher in women. Buprenorphine was responsible for most ADRs when corrected for expenditure, with high RORs observed with application site hypersensitivity, application site reaction, and application site rash. Fentanyl gave rise to most of the reports of ADRs concerning abuse, misuse, and medication errors.

Conclusion

Patients treated with opioids experienced ADRs, primarily nausea, dizziness, and vomiting. For those groups of drugs, no significant differences were found between the sexes, except for the vomiting associated with tramadol. In general, ADRs related to opioids presented higher RORs when uncorrected and corrected for sexes and expenditure than other drugs.

There was more disproportionate reporting for ADRs concerning abuse, misuse, and medication errors for opioids than other drugs in the Dutch SRS.

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European Journal of Clinical Pharmacology

Use of overactive bladder anticholinergic medications associated with falls leading to emergency department visits: results from the ADRED study

Katja S. Just, Karen A. Schultze, Harald Dormann, Thomas Seufferlein, Ingo Gräff, Catharina Scholl, Matthias Schwab & Julia C. Stingl

Abstract

Purpose

Drug intake might be a modifiable factor for the individual fall-risk of older adults, and anticholinergic properties of drugs need to be considered. This study is aimed at analyzing the association of older adults' individual anticholinergic load with particular focus on use of overactive bladder anticholinergic medications with falls in multi-medicated patients.

Materials and Methods

Cases of the prospective, observational, multi-center study on adverse drug reactions leading to emergency departments (ADRED study) between 2015 and 2018 in Germany were analyzed comparing the exposure of overactive bladder anticholinergic medications on the chance to present with a fall with patients without exposure. Logistic regression analysis was used adjusting for pre-existing conditions, drug exposure, and the individual anticholinergic burden by drug use. To this end, a combination of seven expert-based anticholinergic rating scales was used.

Results

The anticholinergic burden was higher in patients with overactive bladder anticholinergic medications (median 2 [1; 3]) compared to not taking drugs of interest. Presenting with a fall was associated with overactive bladder anticholinergic medications (odds ratio (OR) 2.34 [95% confidence interval 1.14–4.82]). The use of fall-risk increasing drugs was likewise associated (OR 2.30 [1.32–4.00]). The anticholinergic burden itself seemed not to be associated with falls (OR 1.01 [0.90–1.12]).

Conclusions

Although falls occur multifactorial in older adults and confounding by indication cannot be ruled out, the indication for a drug treatment should be decided with caution when other, non-pharmacological treatment options have been tried.

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Pharmacotherapy

Efficacy and Safety of Factor Xa Inhibitors in Low Body Weight Patients

Yingcong Tan, Cynthia Hubbard, Holly Owens, James Pitt, Christopher Giuliano, Bradley Haan, Thomas Breeden, Dumitru Sirbu, Kelsey Pena, Trevlyn Haddox, Stephanie B. Edwin

Abstract

Objective

To provide evidence for the safety and efficacy of factor Xa inhibitors in patients with a weight ≤ 60 kg or body mass index (BMI) < 18.5 kg/m2.

Methods

A multicenter, retrospective cohort study was conducted to compare rates of bleeding and thrombosis in low body weight adult patients (weight ≤ 60 kg or BMI < 18.5 kg/m2) receiving factor Xa inhibitors (apixaban or rivaroxaban) or warfarin treatment for atrial fibrillation or venous thromboembolism. The primary outcome was time to major bleeding over the 12 months following the index admission.

Results

This study included 2538 patients between those receiving factor Xa inhibitors (n=1695) and warfarin (n=843), with a mean weight of 53.5 ± 5.5 kg and BMI of 20.7 ± 3.1 kg/m2. No significant difference in time to major bleeding was noted after controlling for potential confounders (Hazard Ratio [HR] 1.03, 95% confidence interval [CI] 0.70-1.53, p=0.87); similar results were found following propensity score matching. Thromboembolism (5.3% vs. 6.2%, p=0.38), composite major + clinically relevant non-major bleeding (9.8% vs. 11.5%, p=0.18), and all-cause mortality (10.7% vs. 12.8%, p=0.12) were similar between patients receiving factor Xa inhibitors versus warfarin.

Conclusion

No differences in safety or effectiveness were noted between factor Xa inhibitors versus warfarin. These findings provide encouraging evidence to support the use of factor Xa inhibitors in low body weight patients.

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Annals of Pharmacotherapy

The Effect of the Drug-Related Problems Prevention Bundle on Early Readmissions in Patients From the Emergency Department: A Randomized Clinical Trial

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Abstract

Background

Drug-related problems (DRPs) are prevalent and avoidable disease that patients experience due to drug use or nonuse. However, secondary prevention policies have not yet been systematized.

Objective

To assess the clinical impact of a secondary prevention bundle for DRPs in patients who visited the emergency department (ED) for medicine-related problems.

Methods

A single-center randomized clinical trial was conducted from August 28, 2019, to January 28, 2021, with 1-month follow-up. We included 769 adult patients who visited ED with a DRP associated with cardiovascular, alimentary tract, and metabolic system medications. For the intervention group, a DRP prevention bundle, consisting of a combined strategy initiated in the ED was applied. Patients in the control group received standard pharmaceutical care. Intervention was evaluated in terms of 30-day hospital readmission due to any cause.

Results

Final analysis included 769 patients, of which 68 (8.8%) were readmitted within 30 days (control group, 40 of 386 [cumulative incidence: 10.4%]; intervention group, 28 of 383 [cumulative incidence, 7.3%]). After adjustment of the model for chronic heart failure, there was a lower incidence of hospital readmission among patients in the intervention group compared with those in the control group, odds ratio: 0.59 [95% confidence interval: 0.37-0.97]; number needed to treat (NNT) = 32. No significant differences in other outcomes were observed.

Conclusion and Relevance

In this clinical trial, DRP prevention bundle in adjusted analysis decreased the rate of 30-day hospital readmission for any cause in patients who visited ED for a DRP.

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International Journal of Clinical Pharmacy

Venous thromboembolism recurrence among one-and-done direct oral anticoagulant users: a retrospective longitudinal study

Mark Alberts, Maryia Zhdanava, Dominic Pilon, Gabrielle Caron-Lapointe, Patrick Lefebvre, Brahim Bookhart & Akshay Kharat

Abstract

Background

Direct oral anticoagulants (DOACs) are the American Society of Hematology guideline-recommended treatment for venous thromboembolism (VTE) in the United States (US).

Aim

To compare risk of VTE recurrence between patients who, following the first fill, discontinued ("one-and-done") versus those who continued ("continuers") DOACs.

Method

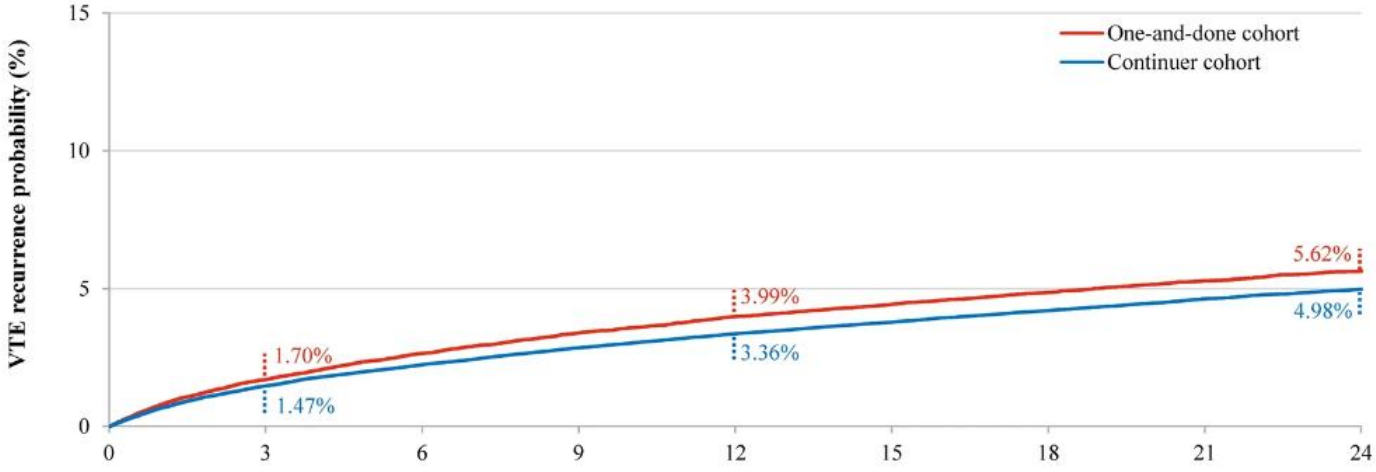
Open source US insurance claims data (04/1/2017 to 10/31/2020) were used to select adult patients with VTE initiated on DOACs (index date). Patients with only one DOAC claim during the 45-day landmark period (starting on the index date) were classified as one-and-done and the remaining as continuers. Inverse probability of treatment weighting was used to reweight baseline characteristics between cohorts. VTE recurrence based on the first post-index deep vein thrombosis or pulmonary embolism event was compared using weighted Kaplan–Meier and Cox proportional hazard models from landmark period end to clinical activity or data end.

Results

27% of patients initiating DOACs were classified as one-and-done. After weighting, 117,186 and 116,587 patients were included in the one-and-done and continuer cohorts, respectively (mean age 60 years; 53% female; mean follow-up 15 months). After 12 months of follow-up, the probability of VTE recurrence was 3.99% and 3.36% in the one-and-done and continuer cohorts; the risk of recurrence was 19% higher in the one-and-done cohort (hazard ratio [95% confidence interval] = 1.19 [1.13, 1.25]).

Conclusion

Substantial proportion of patients discontinued DOAC therapy after the first fill, which was associated with significantly higher risk of VTE recurrence. Early access to DOACs should be encouraged to reduce the risk of VTE recurrence.



	3 Months	6 Months	12 Months	24 Months
Patients at risk, n (%)				
One-and-done cohort	98,525 (84.1)	85,925 (73.3)	62,456 (53.3)	24,487 (20.9)
Continuer cohort	100,307 (86.0)	88,444 (75.9)	65,290 (56.0)	26,601 (22.8)
Kaplan Meier probability of event (95% CI)				
One-and-done cohort	1.70% (1.60; 1.82)	2.65% (2.51; 2.79)	3.99% (3.81; 4.18)	5.62% (5.38; 5.87)
Continuer cohort	1.47% (1.41; 1.53)	2.24% (2.17; 2.32)	3.36% (3.27; 3.46)	4.98% (4.85; 5.12)
Log-rank test	0.0002*	<0.0001*	<0.0001*	<0.0001*

VTE recurrence (DVT or PE) probability in weighted one-and-done versus continuer cohorts.[a] *CI* Confidence interval; *DOAC* Direct oral anticoagulant; *DVT* Deep-vein thrombosis; *PE* Pulmonary embolism; *VTE* Venous thromboembolism. *Note:* (a) VTE recurrence was identified in an inpatient setting. The time to the first recurrent event was measured from day 46 post-index date (i.e., first day after the end of the landmark period); patients for whom the event was not observed during the follow-up period were censored at the end of the follow-up period

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Pharmacologic Heterogeneity and Risk of Severe Hypoglycemia with Concomitant Use of Sulfonylureas and DPP-4 Inhibitors: Population-Based Cohort Study

Jenny Dimakos, Ying Cui, Robert W. Platt, Christel Renoux, Kristian B. Filion, Antonios Douros

Abstract

Dipeptidyl peptidase-4 inhibitors (DPP-4i) interact with sulfonylureas to increase their risk of hypoglycemia. Our population-based study assessed whether intraclass pharmacologic heterogeneity among sulfonylureas (long- vs. short-acting) and DPP-4i (peptidomimetic vs. non-peptidomimetic) modifies this interaction. We conducted a cohort study using the UK's Clinical Practice Research Datalink Aurum linked to hospitalization and vital statistics data. We assembled a cohort of patients initiating sulfonylureas (2007–2020). Using a time-varying exposure definition, we assessed the risk of severe hypoglycemia (hospitalization with or death due to hypoglycemia) associated with (i) concomitant use of long-acting sulfonylureas (glimepiride and glibenclamide) with DPP-4i compared with concomitant use of short-acting sulfonylureas (gliclazide and glipizide) with DPP-4i; and (ii) concomitant use of sulfonylureas with peptidomimetic DPP-4i (saxagliptin and vildagliptin) compared with concomitant use of sulfonylureas with non-peptidomimetic DPP-4i (sitagliptin, linagliptin, and alogliptin). Time-dependent Cox models estimated confounder-adjusted hazard ratios (HRs) with 95% confidence intervals (CIs). Our cohort included 196,138 sulfonylurea initiators. During a median follow-up of 6 years, 8,576 events of severe hypoglycemia occurred. Compared with concomitant use of short-acting sulfonylureas with DPP-4i, concomitant use of long-acting sulfonylureas with DPP-4i was not associated with the risk of severe hypoglycemia (adjusted HR: 0.87, 95% CI: 0.65–1.16). Compared with concomitant use of sulfonylureas with non-peptidomimetic DPP-4i, concomitant use of sulfonylureas with peptidomimetic DPP-4i was also not associated with the risk of severe hypoglycemia (HR: 0.96, 95% CI: 0.76–1.22). Intra-class pharmacologic heterogeneity did not modify the association between concomitant use of sulfonylureas (short- vs. long-acting) and DPP-4i (peptidomimetic vs. non-peptidomimetic) and the risk of severe hypoglycemia.

Disponible en: https://doi.org/10.1002/cpt.2975

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Journal of the American Medical Directors Association

Artificial Intelligence–Based Clinical Decision Support Systems in Geriatrics: An Ethical Analysis

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Abstract

Objectives

To provide an ethical analysis of the implications of the usage of artificial intelligence–supported clinical decision support systems (AI-CDSS) in geriatrics.

Design

Ethical analysis based on the normative arguments regarding the use of AI-CDSS in geriatrics using a principle-based ethical framework.

Setting and Participants

Normative arguments identified in 29 articles on AI-CDSS in geriatrics.

Methods

Our analysis is based on a literature search that was done to determine ethical arguments that are currently discussed regarding AI-CDSS. The relevant articles were subjected to a detailed qualitative analysis regarding the ethical considerations Supplementary Datamentioned therein. We then discussed the identified arguments within the frame of the 4 principles of medical ethics according to Beauchamp and Childress and with respect to the needs of frail older adults.

Results

We found a total of 5089 articles; 29 articles met the inclusion criteria and were subsequently subjected to a detailed qualitative analysis. We could not identify any systematic analysis of the ethical implications of AI-CDSS in geriatrics. The ethical considerations are very unsystematic and scattered, and the existing literature has a predominantly technical focus emphasizing the technology's utility. In an extensive ethical analysis, we systematically discuss the ethical implications of the usage of AI-CDSS in geriatrics.

Conclusions and Implications

AI-CDSS in geriatrics can be a great asset, especially when dealing with patients with cognitive disorders; however, from an ethical perspective, we see the need for further research. By using AI-CDSS, older patients' values and beliefs might be overlooked, and the quality of the doctor-patient relationship might be altered, endangering compliance to the 4 ethical principles of Beauchamp and Childress.

Disponible en: https://doi.org/10.1016/j.jamda.2023.06.008

Hospitalization and the Risk of Initiation of Antipsychotics in Persons With Parkinson's Disease

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Abstract

Objectives

The use of antipsychotics in persons with Parkinson's disease (PD) is common, although their use may aggravate the symptoms of PD. Clozapine and quetiapine are the only antipsychotics recommended in PD treatment guidelines. Information on factors associated with initiation of antipsychotics is needed. We investigated whether recent hospitalization is associated with initiation of antipsychotics in persons with PD, and whether discharge diagnoses differ between those who had antipsychotics initiated and those who did not.

Design

Nested case-control study in the nationwide register-based Finnish Study on Parkinson's disease (FINPARK).

Setting and Participants

The FINPARK study includes 22,189 persons who received an incident, clinically verified PD diagnosed during 1996–2015 and were community-dwelling at the time of diagnosis. The cases were 5088 persons who had antipsychotics initiated after PD diagnosis, identified with 1-year washout. The controls were 5088 age-, sex-, and time from PD diagnosis-matched persons who did not use antipsychotics on the matching date (antipsychotic purchase date). Recent hospitalization was defined as discharge in the 2-week period preceding the matching date.

Methods

Associations were investigated with conditional logistic regression.

Results

Quetiapine was the most commonly initiated antipsychotic (72.0% of cases), followed by risperidone (15.0%). Clozapine was initiated rarely (1.1%). Recent hospitalization associated strongly with antipsychotic initiation [61.2% of cases and 14.9% of controls, odds ratio (OR) 9.42, 95% CI 8.33-10.65], and longer hospitalizations were more common among cases. PD was the most common discharge diagnosis category (51.2% of hospitalized cases and 33.0% controls), followed by mental and behavioral disorders (9.3%) and dementia (9.0%) among cases. Antidementia and other psychotropic medication use were more common among cases.

Conclusions and Implications

These results suggest that antipsychotics were initiated because of neuropsychiatric symptoms or aggravation of those symptoms. Antipsychotics should be prescribed after careful consideration to avoid adverse effects in persons with Parkinson's disease.

Disponible en: https://doi.org/10.1016/j.jamda.2023.04.004

Impact of a Multifaceted, Pharmacist-Led Intervention on Psychotropic Medication Use for Residents of Aged Care Facilities: A Parallel Cluster Randomized Controlled Trial

Hend Almutairi, PhD Andrew Stafford, PhD Christopher Etherton-Beer, PhD Patrick Fitzgerald, PhD Leon Flicker, PhD

Abstract

Objective

To investigate the effect of a multifaceted intervention on reduction in psychotropic medication use, falls, agitation, emergency department (ED) visits, and hospitalization in residential aged care facilities (RACFs).

Design

Parallel cluster randomized controlled trial. RACFs were randomized to the multifaceted intervention, Medication Management Consultancy (MMC) (n = 5) or control (n = 6) groups. MMC, comprising online education, medication audits, and resources on psychotropic medications and nonpharmacological strategies, educates RACF staff to help reduce the use of antipsychotic medication among RACF residents through a comprehensive understanding of behavioral and psychological symptoms of dementia.

Setting and Participants

A total of 439 residents from 11 RACFs in Western Australia.

Methods

The primary outcome was change in monthly total equivalent doses (mg) of antipsychotic, antidepressant, and benzodiazepine medication use over 12 months compared with a control group. Clinical outcomes included falls, restraints, agitation, ED visits, hospitalization, and knowledge of psychotropic medications among RACF staff at pre- and postintervention were measured. The duration of the intervention was 3 to 6 months. Data were collected at T0 (baseline), T1 (6 months), and T2 (12 months).

Results

The MMC group showed a significant 44% reduction in antipsychotic use compared with the control group at T1 (incidence rate ratios [IRR], 0.56; 95% CI, 0.32–0.99; *P* = .048) and also significantly reduced the number of ED visits at T1 (IRR, 0.15; 95% CI, 0.06–0.35; *P* < .0005) and T2 (IRR, 0.04; 95% CI, 0.01–0.13; *P* < .0005). Staff knowledge about psychotropic medications improved significantly from T0 to T1 and from T0 to T2. Reduction in antidepressant use at either T1 or T2 and benzodiazepine use, compared with control, at T1 and T2 were not significantly different. Other clinical outcomes showed limited impact.

Conclusion and Implications

The MMC intervention reduced the use of antipsychotics and ED visits and improved staff knowledge in RACFs, which impacts the safety and quality of aged care in Australia.

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Long-Term Opioid Use and Dementia Risk in Patients With Chronic Pain

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Abstract

Objective

This study aimed to investigate the association between long-term opioid use and the risk of dementia in patients with chronic pain.

Design

A head-to-head propensity score–matched (PSM) comparative cohort study was conducted to examine the effect of long-term opioid use on dementia risk. A time-varying Cox regression analysis was performed to calculate adjusted hazard ratios (aHRs) with 95% CIs to identify independent predictors of dementia risk.

Setting and Participants

The study included 41,636 patients after PSM, with 20,968 in the opioid use group (≥180 defined daily doses per year) and 20,968 in the non–opioid use group.

Methods

Multivariate Cox regression analysis was conducted to compare the dementia risk between the opioid use and non–opioid use groups. The incidence of dementia was calculated as the number of cases per 10,000 person-years for each group. Adjusted incidence ratios were determined to assess the dementia risk associated with opioid use.

Results

The multivariate Cox regression analysis showed that the aHR for dementia risk in the opioid use group, compared with the non–opioid use group, was 1.86 (95% CI 1.25-2.09; *P* < .001). The incidence of dementia was higher among opioid users (44.09 per 10,000 person-years) compared with nonusers (38.85 per 10,000 person-years). The adjusted incidence ratio for dementia risk in the opioid use group, compared with the nonuse group, was 1.13 (95% CI: 1.07-1.21, *P* < .001).

Conclusions and Implications

Long-term opioid use may be associated with an increased risk of dementia in patients with chronic pain. These findings highlight the need for cautious prescribing and monitoring of opioid use in this population, considering the potential long-term cognitive implications.

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Antipsychotic Drug Reduction through the Implementation of a Neurologically Oriented, Interdisciplinary Psycho-Diagnostic and Antipsychotic Stewardship Program

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Abstract

Antipsychotic utilization in skilled nursing facilities (SNFs) is a major focus of regulatory compliance and a key theme in resident care. This created opportunities for innovations in clinical care of behavioral and psychological symptoms of dementia (BPSD). In a shared initiative with one of our SNF operators, the authors implemented a joint clinician/facility program focused on rigorous clinical diagnosis and “best practices” in clinical care, specifically aimed at assessing and reducing antipsychotic use where appropriate.

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European Journal of Internal Medicine

The spectrum of hospitalization-associated harm in the elderly

Ami Schattner

Highlights

- Older patients often require hospitalization, which may not infrequently be avoidable, for example, by 'hospital-at home' which may be safer and less costly for selected patients.
- The whole wide spectrum of hospitalization-associated patient harm is rarely discussed, and may not be fully appreciated by providers.

Abstract

Acutely ill patients are not infrequently referred to the hospital and admitted, when they could be diagnosed and managed in the ambulatory setting or by hospital-level care at home. Avoidable admissions are particularly regrettable when the wide spectrum of hospitalization-associated patient harm is considered.

It includes acute discomfort to the patient due to multiple disturbing hospital stressors; an emotional trauma; the burden of multiple redundant tests begetting false-positive and incidental findings triggering further testing and cascades; highly prevalent adverse events and serious harm associated with medical care, such as nosocomial infections, delirium, falls, and adverse drug events; and a complex array of post-discharge complications including significant physical and functional decline; cognitive decline; flawed transitions of care; common post-discharge adverse events; and a substantial risk of readmission, restarting the vicious cycle and compromising patient well-being, safety, and outcomes.

Elderly patients are especially vulnerable, but in-hospital patient harm is not limited to older adults and is associated with increased length of stay, escalating costs, and mortality. The myriad types of harm that often accompany hospital admission is often not fully appreciated.

Better awareness may result in better preventive strategies, in finding alternatives to hospital admission in some cases, and may contribute towards an improved patient experience and safety when hospitalization is mandatory, and the provision of enhanced care in the vulnerable post-discharge period.

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Management of diabetic ketoacidosis

Abstract

Diabetic ketoacidosis (DKA) is an acute life-threatening emergency in patients with diabetes, it can result in serious morbidity and mortality. Management of DKA requires reversing metabolic derangements, correcting volume depletion, electrolyte imbalances and acidosis while concurrently treating the precipitating illness.

There are still controversies regarding certain aspects of DKA management. Different society guidelines have inconsistencies in their recommendations, while some aspects of treatment are not precise enough or have not been thoroughly studied. These controversies may include issues such as optimal fluid resuscitation, rate and type of Insulin therapy, potassium and bicarbonate replacement. Many institutions follow common society guidelines, however, other institutions either develop their own protocols for internal use or do not routinely use any protocols, resulting in inconsistencies in treatment and increased risk of complications and suboptimal outcomes. The objectives of this article are to review knowledge gaps and controversies in the treatment of DKA and provide our perspective on these issues.

Moreover, we believe that special patient factors and comorbidities should receive more careful attention and consideration. Factors like pregnancy, renal disease, congestive heart failure, acute coronary syndrome, older age, use of sodium-glucose cotransporter-2 (SGLT2) inhibitors and site of care all impact the treatment approach and require tailored management strategies.

However, guidelines often lack sufficient recommendations regarding specific conditions and comorbidities, we aim to address unique circumstances and provide an approach to managing complex patients with specific conditions and co-morbidities. We also sought to examine changes and trends in the treatment of DKA, illuminate on aspects of latest research with a perspective towards future developments and modifications.

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JAMA

Aspirin and Hemocompatibility Events With a Left Ventricular Assist Device in Advanced Heart FailureThe ARIES-HM3 Randomized Clinical Trial

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Abstract

Importance

Left ventricular assist devices (LVADs) enhance quality and duration of life in advanced heart failure. The burden of nonsurgical bleeding events is a leading morbidity. Aspirin as an antiplatelet agent is mandated along with vitamin K antagonists (VKAs) with continuous-flow LVADs without conclusive evidence of efficacy and safety.

Objective

To determine whether excluding aspirin as part of the antithrombotic regimen with a fully magnetically levitated LVAD is safe and decreases bleeding.

DESIGN, SETTING, and PARTICIPANTS

This international, randomized, double-blind, placebo-controlled study of aspirin (100 mg/d) vs placebo with VKA therapy in patients with advanced heart failure with an LVAD was conducted across 51 centers with expertise in treating patients with advanced heart failure across 9 countries. The randomized population included 628 patients with advanced heart failure implanted with a fully magnetically levitated LVAD (314 in the placebo group and 314 in the aspirin group), of whom 296 patients in the placebo group and 293 in the aspirin group were in the primary analysis population, which informed the primary end point analysis. The study enrolled patients from July 2020 to September 2022; median follow-up was 14 months.

Main outcomes and measures

The composite primary end point, assessed for noninferiority (−10% margin) of placebo, was survival free of a major nonsurgical (>14 days after implant) hemocompatibility-related adverse events (including stroke, pump thrombosis, major bleeding, or arterial peripheral thromboembolism) at 12 months. The principal secondary end point was nonsurgical bleeding events.

Results

Of the 589 analyzed patients, 77% were men; one-third were Black and 61% were White. More patients were alive and free of hemocompatibility events at 12 months in the placebo group (68%) vs those taking aspirin (74%). Noninferiority of placebo was demonstrated (absolute between-group difference, 6.0% improvement in event-free survival with placebo [lower 1-sided 97.5% CI, −1.6%]; P < .001). Aspirin avoidance was associated with reduced nonsurgical bleeding events (relative risk, 0.66 [95% confidence limit, 0.51-0.85]; P = .002) with no increase in stroke or other thromboembolic events, a finding consistent among diverse subgroups of patient characteristics.

Conclusions and relevance

In patients with advanced heart failure treated with a fully magnetically levitated LVAD, avoidance of aspirin as part of an antithrombotic regimen, which includes VKA, is not inferior to a regimen containing aspirin, does not increase thromboembolism risk, and is associated with a reduction in bleeding events.

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JAMA Internal Medicine

Are New Alzheimer Drugs Better Than Older Drugs?

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Abstract

In July 2023, the US Food and Drug Administration (FDA) provided full approval for an amyloid-β–directed antibody, lecanemab (Leqembi), for treating Alzheimer disease. The prescribing information states that treatment, which is administered as an intravenous infusion, should be initiated in patients with mild cognitive impairment or the mild dementia stage of the disease, which is the population in which the treatment was studied in clinical trials. Lecanemab is the second monoclonal antibody targeting β-amyloid protein to be approved; the first was aducanumab (Aduhelm) in 2021. The FDA approved lecanemab via its accelerated approval program in January 2023 based solely on the decline in β-amyloid as estimated on positron emission tomography scans in the brains of patients taking the drug compared with placebo. The agency granted full approval of lecanemab based on clinical efficacy data from a clinical trial with 1795 participants.1 Advocacy groups were pressuring the US Centers for Medicare & Medicaid Services to pay for the drug.

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Overnight Stay in the Emergency Department and Mortality in Older Patients

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Abstract

Importance

Patients in the emergency department (ED) who are waiting for hospital admission on a wheeled cot may be subject to harm. However, mortality and morbidity among older patients who spend the night in the ED while waiting for a bed in a medical ward are unknown.

Objective

To assess whether older adults who spend a night in the ED waiting for admission to a hospital ward are at increased risk of in-hospital mortality.

Design, Settings, and Participants

This was a prospective cohort study of older patients (≥75 years) who visited the ED and were admitted to the hospital on December 12 to 14, 2022, at 97 EDs across France. Two groups were defined and compared: those who stayed in the ED from midnight until 8:00 am (ED group) and those who were admitted to a ward before midnight (ward group).

Main Outcomes and Measures

The primary end point was in-hospital mortality, truncated at 30 days. Secondary outcomes included in-hospital adverse events (ie, falls, infection, bleeding, myocardial infarction, stroke, thrombosis, bedsores, and dysnatremia) and hospital length of stay. A generalized linear-regression mixed model was used to compare end points between groups.

Results

The total sample comprised 1598 patients (median [IQR] age, 86 [80-90] years; 880 [55%] female and 718 [45%] male), with 707 (44%) in the ED group and 891 (56%) in the ward group. Patients who spent the night in the ED had a higher in-hospital mortality rate of 15.7% vs 11.1% (adjusted risk ratio [aRR], 1.39; 95% CI, 1.07-1.81). They also had a higher risk of adverse events compared with the ward group (aRR, 1.24; 95% CI, 1.04-1.49) and increased median length of stay (9 vs 8 days; rate ratio, 1.20; 95% CI, 1.11-1.31). In a prespecified subgroup analysis of patients who required assistance with the activities of daily living, spending the night in the ED was associated with a higher in-hospital mortality rate (aRR, 1.81; 95% CI, 1.25-2.61).

Conclusions and Relevance

The findings of this prospective cohort study indicate that for older patients, waiting overnight in the ED for admission to a ward was associated with increased in-hospital mortality and morbidity, particularly in patients with limited autonomy. Older adults should be prioritized for admission to a ward.

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The New England Journal of Medicine

Ferric Carboxymaltose in Heart Failure with Iron Deficiency

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Abstract

Background

Ferric carboxymaltose therapy reduces symptoms and improves quality of life in patients who have heart failure with a reduced ejection fraction and iron deficiency. Additional evidence about the effects of ferric carboxymaltose on clinical events is needed.

Methods

In this double-blind, randomized trial, we assigned ambulatory patients with heart failure, a left ventricular ejection fraction of 40% or less, and iron deficiency, in a 1:1 ratio, to receive intravenous ferric carboxymaltose or placebo, in addition to standard therapy for heart failure. Ferric carboxymaltose or placebo was given every 6 months as needed on the basis of iron indexes and hemoglobin levels. The primary outcome was a hierarchical composite of death within 12 months after randomization, hospitalizations for heart failure within 12 months after randomization, or change from baseline to 6 months in the 6-minute walk distance. The significance level was set at 0.01.

Results

We enrolled 3065 patients, of whom 1532 were randomly assigned to the ferric carboxymaltose group and 1533 to the placebo group. Death by month 12 occurred in 131 patients (8.6%) in the ferric carboxymaltose group and 158 (10.3%) in the placebo group; a total of 297 and 332 hospitalizations for heart failure, respectively, occurred by month 12; and the mean (±SD) change from baseline to 6 months in the 6-minute walk distance was 8±60 and 4±59 m, respectively (Wilcoxon–Mann–Whitney P=0.02; unmatched win ratio, 1.10; 99% confidence interval, 0.99 to 1.23). Repeated dosing of ferric carboxymaltose appeared to be safe with an acceptable adverse-event profile in the majority of patients. The number of patients with serious adverse events occurring during the treatment period was similar in the two groups (413 patients [27.0%] in the ferric carboxymaltose group and 401 [26.2%] in the placebo group).

Conclusions

Among ambulatory patients who had heart failure with a reduced ejection fraction and iron deficiency, there was no apparent difference between ferric carboxymaltose and placebo with respect to the hierarchical composite of death, hospitalizations for heart failure, or 6-minute walk distance.

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Trial of Solanezumab in Preclinical Alzheimer's Disease

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Abstract

Background

Trials of monoclonal antibodies that target various forms of amyloid at different stages of Alzheimer's disease have had mixed results.

Methods

We tested solanezumab, which targets monomeric amyloid, in a phase 3 trial involving persons with preclinical Alzheimer's disease. Persons 65 to 85 years of age with a global Clinical Dementia Rating score of 0 (range, 0 to 3, with 0 indicating no cognitive impairment and 3 severe dementia), a score on the Mini–Mental State Examination of 25 or more (range, 0 to 30, with lower scores indicating poorer cognition), and elevated brain amyloid levels on 18F-florbetapir positron-emission tomography (PET) were enrolled. Participants were randomly assigned in a 1:1 ratio to receive solanezumab at a dose of up to 1600 mg intravenously every 4 weeks or placebo. The primary end point was the change in the Preclinical Alzheimer Cognitive Composite (PACC) score (calculated as the sum of four z scores, with higher scores indicating better cognitive performance) over a period of 240 weeks.

Results

A total of 1169 persons underwent randomization: 578 were assigned to the solanezumab group and 591 to the placebo group. The mean age of the participants was 72 years, approximately 60% were women, and 75% had a family history of dementia. At 240 weeks, the mean change in PACC score was −1.43 in the solanezumab group and −1.13 in the placebo group (difference, −0.30; 95% confidence interval, −0.82 to 0.22; P=0.26). Amyloid levels on brain PET increased by a mean of 11.6 centiloids in the solanezumab group and 19.3 centiloids in the placebo group. Amyloid-related imaging abnormalities (ARIA) with edema occurred in less than 1% of the participants in each group. ARIA with microhemorrhage or hemosiderosis occurred in 29.2% of the participants in the solanezumab group and 32.8% of those in the placebo group.

Conclusions

Solanezumab, which targets monomeric amyloid in persons with elevated brain amyloid levels, did not slow cognitive decline as compared with placebo over a period of 240 weeks in persons with preclinical Alzheimer's disease.

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Boletín Terapéutico Andaluz

Tratamiento farmacológico de la enfermedad de Parkinson

Mª Carmen Fernández Moreno.

Interesante revisión en castellano sobre la fisiopatología, diagnóstico y tratamiento de la enfermedad de Parkinson. Algunos puntos clave:

- La enfermedad de Parkinson (EP) es un proceso neurodegenerativo crónico, progresivo y multisistémico, provocado por la pérdida o degeneración de neuronas dopaminérgicas.
- El principal factor de riesgo es la edad, pero también pueden influir factores genéticos y ambientales.
- Se caracteriza principalmente por los síntomas motores (bradicinesia, temblor en reposo, rigidez e inestabilidad postural) y por otros síntomas no motores que afectan las funciones sensoriales, emocionales, cognitivas, y autonómicas. Evoluciona con diferentes estadios y su presentación clínica varía entre los individuos.
- El diagnóstico se basa en criterios clínicos y el proceso incluye: establecer la existencia de parkinsonismo, hacer diagnóstico diferencial, determinar EP establecida o probable y exploración periódica. No hay pruebas diagnósticas complementarias (marcadores bioquímicos, test genéticos o pruebas de imagen) de utilidad para orientar o confirmar el diagnóstico clínico.
- El tratamiento de la EP es sintomático y no existen terapias curativas, modificadoras de la enfermedad o neuroprotectoras. Debe abordarse de forma multidisciplinar, individualizada y consensuada con el paciente; incluyendo terapia farmacológica, medidas complementarias y en su caso, tratamientos invasivos.
- El tratamiento antiparkinsoniano debe iniciarse cuando los síntomas interfieren en la vida del paciente y establecerse individualizadamente. La terapia dopaminérgica (levodopa, agonistas dopaminérgicos, IMAO-B, inhibidores de la COMT) es la base del tratamiento de los síntomas motores, y también se utilizan otros fármacos (anticolinérgicos, amantadina), generalmente como complemento a los anteriores.
- Al avanzar la EP en pacientes tratados con terapia dopaminérgica (sobre todo levodopa), suelen desarrollarse complicaciones motoras que empeoran con la progresión de la enfermedad y requieren ajustes y cambios del tratamiento; y en algunos casos, terapias de segunda línea.

Disponible en: https://cadime.es/images/documentos_archivos_web/BTA/2023/CA-DIME_BTA_38_01.pdf