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REVISIÓN BIBLIOGRÁFICA NOVIEMBRE 2020: Selección de artículos

REVISTAS GERIÁTRICAS

Age and Ageing

In-hospital adverse drug reactions in older adults; prevalence, presentation and associated drugs—a systematic review and meta-analysis. Emma L M Jennings, Kevin D Murphy, Paul Gallagher, Denis O'Mahony

Background

the prevalence of adverse drug reactions (ADRs) in hospitalised older patients, their clinical presentations, causative drugs, severity, preventability and measurable outcomes are unclear, **ADRs being an increasing challenge to older patient safety.**

Methods

we systematically searched PubMed, Embase, EBSCO-CINAHL, the Cochrane Library, 'rey' literature and relevant systematic review bibliographies, published from database inception to March 2020. We included any study reporting occurrence of in-hospital ADRs as primary or secondary outcomes in hospitalised older adults (mean age ≥ 65 years). Two authors independently extracted relevant information and appraised studies for bias. Study characteristics, ADR clinical presentations, causative drugs, severity, preventability and clinical outcomes were analysed. Study estimates were pooled using random-effects meta-analytic models.

Results

from 2,399 abstracts, we undertook full-text screening in 286, identifying 27 studies (29 papers). Final analysis yielded a pooled ADR prevalence of 16% (95%CI 12–22%, I2 98%,τ2 0.8585), in a population of 20,153 hospitalised patients aged ≥65 years of whom 2,479 patients experienced ≥ one ADR. ADR ascertainment was highly heterogeneous. Almost 48.3% of all ADRs involved five presentations: fluid/electrolyte disturbances (17.3%), gastrointestinal motility/defaecation disorders (13.3%), renal disorders (8.2%), hypotension/blood pressure dysregulation disorders/shock (5.5%) and delirium (4.1%). Four drug classes accounted for 57.8% of causative medications i.e. diuretics (19.8%), anti-bacterials (14.8%), antithrombotic agents (12.2%) and

analgesics (10.9%). Pooled analysis of severity was not feasible. Four studies reported the majority of ADRs as preventable (55–95%).

Conclusions

on average, 16% of hospitalised older patients experience significant ADRs, varying in severity and mostly preventable, with commonly prescribed drug classes accounting for most ADRs.

Disponible en:
https://academic.oup.com/ageing/article-abstract/49/6/948/5918299?redirectedFrom=fulltext

Archives of Gerontology and Geriatrics

Self-medication in older European adults: Prevalence and predictive factors.

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Abstract

Background/objectives

Self-medication, despite some benefits, carries many risks, especially when practiced by older adults who are polymedicated. Information addressing the prevalence and associated factors of self-medication in older age in a European context is scarce and sometimes contradictory. This paper aims to estimate the prevalence of self-medication among older adults across Europe and to identify its predictive factors.

Design

Cross-sectional study.

Setting

Micro-data from the European Health Interview Survey (2006–2009) was used.

Participants

The sample comprised 31,672 community-dwelling individuals aged 65 and over living in private households in 14 European countries.

Measurements

The analyses explored the use, over the last two weeks, of any medicines, supplements, or vitamins that were not prescribed by a doctor.

Results

The mean self-medication prevalence was 26.3 %, being the highest in Poland (49.4 %) and the lowest in Spain (7.8 %). Greater odds of self-medication were found for women and for participants who were younger, divorced, or presented a higher educational degree. The presence of long-standing illness and physical pain or not using prescribed medication also significantly increased the possibility of self-medication. A wide variation in the odds of self-medication between countries was also observed (up to 8 times more for Poland, compared to Spain).

Conclusion

Self-medication is a prevalent problem among older Europeans, and even though some think it is risk-free, dangers tend to be greater with advancing age. This study will help identify the groups most likely to have this behavior so that we can focus on targeted educative and preventive initiatives.

Disponible en: https://www.sciencedirect.com/science/article/abs/pii/S0167494320301837

Drugs and Aging

Association between Statins Prescribed for Primary and Secondary Prevention and Major Adverse Cardiac Events among Older Adults with Frailty: A Systematic Review

Matthew Hale, Hadar Zaman, David Mehdizadeh, Oliver Todd, Harriet Callaghan, Chris P. Gale & Andrew Clegg

Background

Statins reduce the risk of major adverse cardiovascular events (MACE), however their clinical benefit for primary and secondary prevention among older adults with frailty is uncertain. This systematic review investigates whether statins prescribed for primary and secondary prevention are associated with reduced MACE among adults aged ≥ 65 years with frailty.

Methods

We conducted a systematic review of studies published between 1 January 1952 and 1 January 2019 in the MEDLINE, EMBASE, Scopus, Web of Science, Cochrane Library and International Pharmaceutical Abstracts databases. Studies that investigated the effect of statins on MACE among adults ≥ 65 years of age with a validated frailty assessment were included. Data were

extracted from the papers as per a prepublished protocol, PROSPERO: CRD42019127486. Risk of bias was assessed using the Cochrane Risk of Bias in Non-Randomised Studies of Interventions tool.

Results

Six cohort studies fulfilled the inclusion criteria; there were no randomised clinical trials. Among studies evaluating the association between statins for primary and secondary prevention and mortality, one study found statins were associated with reduced mortality (hazard ratio [HR] 0.58, 95% confidence interval [CI] 0.37–0.93), while another study found they were not (HR 0.81, 95% CI 0.61–1.08). Furthermore, one study of statins used for secondary prevention found they were associated with reduced mortality (HR 0.28, 95% CI 0.21–0.39). No studies investigated the effect of statins for primary prevention or the effect of statins on the frequency of MACE.

Conclusion

This review identified only observational evidence that among older people with frailty, statins are associated with reduced mortality when prescribed for secondary prevention, and an absence of evidence evaluating statin therapy for primary prevention. Randomised trial data are needed to better inform the use of statins among older adults living with frailty.

Disponible en: https://link.springer.com/article/10.1007/s40266-020-00798-3

Comparative Safety and Efficacy of Treatments for Overactive Bladder Among Older Adults: A Network Meta-analysis

Greta Lozano-Ortega, David R. Walker, Karissa Johnston, Alexis Mickle, Sean Harrigan, Basia Rogula, Rita M. Kristy, John C. Hairston & Carol R. Schermer

Background

Cumulative exposure to one or more anticholinergic medications (“anticholinergic burden”) is associated with an increased risk of adverse outcomes, particularly among older individuals. Mirabegron, an oral selective β3-adrenergic receptor agonist, has demonstrated efficacy in managing the symptoms of overactive bladder without contributing to anticholinergic burden. However, it is not known whether the favorable safety profile of mirabegron relative to antimuscarinics varies with increasing age among a patient population who may have a high anticholinergic burden.

Objective

The primary objective of this study was to indirectly compare the safety and efficacy profile of mirabegron relative to antimuscarinics in older adults with overactive bladder.

Methods

A systematic literature review was conducted to identify randomized controlled trials that reported safety and efficacy endpoints among patients aged ≥ 65 years. Identified randomized controlled trials were subsequently synthesized via a network meta-analysis. Preferred Reporting Items for Systematic Reviews and Meta-Analysis guidelines in designing, performing, and reporting the literature review were followed. In line with current best practices, the network meta-analysis was conducted using a Bayesian approach and according to the overall general guidance for evidence synthesis developed by the National Institute for Health and Care Excellence decision support unit. Estimates of relative safety were assessed via the odds ratio and estimates of relative efficacy were assessed via means and credible intervals.

Results

A total of 3078 abstracts, 300 of which underwent full-text screening, were identified using the search criteria. Twenty articles reporting on 21 randomized controlled trials were eligible for data extraction and synthesis. Following review, five safety and five efficacy endpoints were considered for inclusion in the network meta-analysis. Regarding findings typical of anticholinergic exposure in older adults, mirabegron was not associated with an increased odds of dry mouth (odds ratio 95% credible interval 0.76 [0.26–2.37]) or constipation (1.08 [0.39–3.02]) relative to placebo, whereas antimuscarinics were strongly associated with these events (odds ratio range 3.78–7.85 and 2.12–4.66, respectively). In this older population, mirabegron was associated with a similar odds of experiencing adverse event-related treatment discontinuations relative to placebo (0.99 [0.57–1.70]), while the odds of experiencing an adverse event-related treatment discontinuation for antimuscarinics had a range of 1.14–3.03 (in most cases, the association was mild). No increased odds of experiencing overall treatment-emergent adverse events was observed for mirabegron or antimuscarinics (odds ratio range 1.25–1.55), apart from fesoterodine (2.23 [1.37–3.37]). Finally, a similar treatment effect was observed across all efficacy endpoints between mirabegron and antimuscarinics in this older population.

Conclusions

This study indicates that the safety and efficacy profile of mirabegron remains favorable compared with antimuscarinics among older adults. This includes safety outcomes typically

associated with anticholinergic burden, which were less frequently observed in patients treated with mirabegron.

Disponible en: https://link.springer.com/article/10.1007/s40266-020-00792-9

Journal of Geriatric Oncology.

Single-arm phase II trial to evaluate efficacy and tolerance of regorafenib monotherapy in patients over 70 with previously treated metastatic colorectal adenocarcinoma FFCD 1404 – REGOLD

Thomas Aparicio,Ariane Darut-Jouve,Faiza Khemissa Akouz,Gaetan Des Guetz,Frédéric Pamoukdjian,Come Lepage, Show all authors.

Abstract

Background

Regorafenib significantly increases overall survival (OS) in patients with metastatic colorectal cancer previously treated but gives toxicities.

Objectives

to assess the efficacy and safety of regorafenib at it's approved dose in the older population.

Patients and methods

This multicenter single-arm phase II enrolled patients ≥70 years old after the failure of fluoropyrimidine-based chemotherapy, anti-VEGF, and anti-EGFR treatment. The primary endpoint was disease control rate (DCR) 2 months after initiation of regorafenib (160 mg/day, 3 weeks on/1 week off).

Results

Forty-three patients were enrolled, with a median age of 77 years. The 2 months DCR was 31.4% in the 35 evaluable patients. For the 42 patients that received at least one dose of regorafenib, median progression-free survival and OS were 2.2 and 7.5 months. The median time to autonomy degradation and quality of life degradation was 3.1 and 3.2 months, respectively. A grade 3–4 treatment-related adverse events was observed in 35/42 patients, notably: fatigue (45.2%), hand-foot skin reaction (19.0%), hypertension (21.4%), and diarrhea (7.1%). There is a trend to achieve DCR in patients ≤80 years and a trend to discontinue the study due to toxicity in patients with ECOG ≥1, over 80 years and with impaired baseline autonomy.

Conclusion

Treatment with regorafenib in pretreated patients ≥70 years is feasible and demonstrate similar efficacy that was observed in previous studies in young patients. Fatigue is the most frequent severe adverse event. However, caution should be taken for older patients with ECOG ≥1, over 80 years, and with impaired baseline autonomy.

Disponible en: https://www.geriatriconcology.net/article/S1879-4068(19)30500-4/fulltext

International Journal of Geriatric Psychiatry

Antidepressant use and orthostatic hypotension in older adults living with mild-to-moderate Alzheimer disease

Adam H Dyer Claire Murphy Robert Briggs Brian Lawlor Sean P Kennelly for the NILVAD Study Group

Objectives

Antidepressant use is often reported as a risk factor for Orthostatic Hypotension (OH), however this relationship has never been explored in those with mild/moderate Alzheimer Disease (AD), who may represent a particularly vulnerable cohort.

Methods

We performed a cross-sectional analysis of baseline data from the NILVAD study. Participants with mild-moderate AD were recruited from 23 centres in nine countries. Systolic and Diastolic Blood Pressure (SBP/DBP) was recorded in the seated position and after both 1 and 5 minutes of standing. OH was defined as a drop of ≥20 mmHg SBP/≥10 mmHg DBP. We examined the relationship between antidepressant use, orthostatic BP drop and the presence of OH, controlling for important covariates.

Results

Of 509 participants (72.9 ± 8.3 years, 61.9% female), two-fifths (39.1%; 199/509) were prescribed a regular antidepressant. Antidepressant use was associated with a significantly greater SBP and DBP drop at 5 minutes (β: 1.83, 0.16-3.50, P = .03 for SBP; β: 1.13, 0.02-2.25, P < .05 for DBP). Selective Serotonin Reuptake Inhibitor (SSRI) use was associated with a significantly greater likelihood of OH (OR 2.0, 1.1-3.6, P = .02). Both findings persisted following robust covariate adjustment.

Conclusions

In older adults with AD, antidepressants were associated with a significantly greater SBP/DBP drop at 5 minutes. SSRI use in particular may be a risk factor for OH. This emphasises the need to screen older antidepressant users, and particularly those with AD, for ongoing orthostatic symptoms in order to reduce the risk of falls in this vulnerable cohort.

Disponible en: https://onlinelibrary.wiley.com/doi/10.1002/gps.5377

REVISTAS FARMACÉUTICAS

Drug Safety

Potential Safety Issues with Use of Sodium-Glucose Cotransporter 2 Inhibitors, Particularly in People with Type 2 Diabetes and Chronic Kidney Disease

Tamara Y. Milder, Sophie L. Stocker, Richard O. Day & Jerry R. Greenfield

Abstract

Sodium-glucose cotransporter 2 (SGLT2) inhibitors are a major advance in the fields of diabetology, nephrology, and cardiology. The cardiovascular and renal benefits of SGLT2 inhibitors are likely largely independent of their glycaemic effects, and this understanding is central to the use of these agents in the high-risk population of people with type 2 diabetes and chronic kidney disease. There are a number of potential safety issues associated with the use of SGLT2 inhibitors. These include the rare but serious risks of diabetic ketoacidosis and necrotising fasciitis of the perineum. The data regarding a possibly increased risk of lower limb amputation and fracture with SGLT2 inhibitor therapy are conflicting. This article aims to explore the potential safety issues associated with the use of SGLT2 inhibitors, with a particular focus on the safety of these drugs in people with type 2 diabetes and chronic kidney disease. We discuss strategies that clinicians can implement to minimise the risk of adverse effects including diabetic ketoacidosis and volume depletion. Risk mitigation strategies with respect to SGLT2 inhibitor-associated diabetic ketoacidosis are of particular importance during the current coronavirus disease 2019 (COVID-19) pandemic.

Disponible en: https://doi.org/10.1007/s40264-020-01010-6
Comentarios: Probablemente se cuelen en las GPC de IC, asi que veo bien inclurilo.

European Journal of Clinical Pharmacology

Appropriate use of essential medicines in the elderly: a comparison of the WHO essential medicines list and PIM criteria

Xin Ma, Xuxu Yin, Meng Li, Yanwen Wang, Hongxia Xin & Wei Liu.

Abstract

Purpose

The elderly are not only threatened by bad medicines (overtreatment) but also by undertreatment with "good" medicines. Symmetry is required in any patient-centred approach to properly treat older people. The purpose of this study was to perfect the development of an EML and criteria according to the advantages of each and promote the appropriate use of essential medicines in the elderly.

Method

We compared the EML with four PIM criteria and calculated the proportion of essential medicines included in the criteria. We also summarized the rationale for including medicines in each criterion and analysed higher risk drugs and drug risks.

Results

Of essential medicines, 26% are included in at least one criterion as PIM. In 11 drug categories of the EML, more than 50% of drugs of each category are included in at least one criterion, and in four categories, all drugs are included. The potentially inappropriate essential medicines (PIEMs) for the elderly focus on cardiovascular drugs and central nervous system drugs. Fifty-nine drugs have been explicitly identified as increasing the risk of falls, increasing mortality and/or having inappropriate long-term use, and the main risk of PIEMs is falls (30.3% of PIEMs). Additionally, 17.9% of essential medicines are labelled as positive drugs in START and/or FORTA (A/B).

Conclusion

Improving medication information for the elderly in the EML and establishing an essential medicines list for the elderly will promote appropriate drug use in older people worldwide.

Disponible en: https://doi.org/10.1007/s00228-020-03038-0

Potentially inappropriate medication in older psychiatric patients

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Abstract

Purpose

Many psychotropic drugs are listed as potentially inappropriate medication (PIM) in the older population. Potentially inappropriate means that prescription of those drugs in older adults may cause significant harm. The objective of this study was to analyze the prevalence and sort of PIM prescribing in a naturalistic, real-world psychiatric setting.

Methods

The retrospective analysis gathered data from a large pharmacovigilance study, conducted at 10 psychiatric hospitals. Data from inpatients aged ≥ 65 years were included for the analysis. The

number and sort of PIM, as defined by the German PRISCUS list, were controlled by analyzing the patients' medication profile.

Results

In total, 4760 patient cases (59.2% female) with a mean (mean ± standard deviation (SD)) age of 77.33 ± 7.77 years were included into the study. Altogether, 1615 cases (33.9%) received at least 1 PRISCUS-PIM per day (regular and as-needed medication included). The most frequently prescribed PRISCUS-PIM (n = 2144) were zopiclone > 3.75 mg/day (n = 310), lorazepam > 2 mg/day (n = 269), haloperidol > 2 mg/day (n = 252), and diazepam (n = 182). Cases with PRISCUS-PIM were younger (75.7 vs. 78.2 years, $p < 0.001$) and had a longer (26 vs. 22 days, $p < 0.001$) hospital length of stay. Replacing benzodiazepines and z-substances, haloperidol > 2 mg, tricyclic antidepressants, first generation antihistaminergic drugs, and clonidine by non-PIM could reduce 69.9% of PRISCUS-PIM-prescribing.

Conclusions

The prevalence of PRISCUS-PIM is high in the hospitalized psychiatric setting. Rational deprescribing of inappropriate anticholinergics, benzodiazepines, and antipsychotics in the older population is a key component to reduce the risk of adverse drug reactions. More tolerable medications should be prescribed.

Disponible en: https://doi.org/10.1007/s00228-020-03012-w

Potentially inappropriate medication in acute hospitalized elderly patients with polypharmacy: an observational study comparing PRISCUS, STOPP, and Beers criteria

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Abstract

Purpose

To compare the prevalence of potentially inappropriate medication (PIM) in the elderly according to the PRISCUS list, STOPP criteria, and Beers criteria. Secondary, to describe the differences using the three criteria focused on the inappropriate prescription of psychotropic drugs in the elderly.

Methods

A retrospective study was performed at Severo Ochoa University Hospital. The study included 365 patients, aged 80 years and older, living in Madrid, Spain.

Results

93.42% of patients received at least one PIM during hospitalization. Using the PRISCUS list, this changed from 32.6 to 2.7% at discharge. Applying STOPP criteria lowered the percentage from 65.20 to 10.95%, and with Beers criteria from 80.27 to 10.13. Lower Barthel index at admission was associated with an increased relative risk for receiving at least one PIM (OR 1.79, 95% CI 1.15–2.80, p = 0.024) using PRISCUS list as a tool in conjunction with STOPP criteria (OR 1.44, 95% CI 0.89–2.33, p = 0.037). Polypharmacy at admission predicted the presence of PIMs with STOPP criteria (OR 1.74, 95% CI 1.07–2.84, p = 0.001). Regarding psychotropic medicines, 208 patients

(56.98%) received at least one psychotropic medicine during hospitalization. A total of 26.30% of patients were treated with psychotropic medicines, detected by the PRISCUS list, and 53.97% and 29.85% with STOPP and Beers, respectively.

Conclusions

Explicit criteria are a useful tool for identifying during hospitalization of the elderly patients. As indicated by the results, new research is needed to carry out an adaptation in our country that includes an evaluation of the strengths of the three tools to decrease PIMs and improve prescription in the elderly.

Disponible en: https://doi.org/10.1007/s00228-020-03022-8

Pharmacotherapy

Prescription Medication Use in Older Adults Without Major Cardiovascular Disease Enrolled in the Aspirin in Reducing Events in the Elderly (ASPREE) Clinical Trial

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Abstract

Background

Efforts to minimize medication risks among older adults include avoidance of potentially inappropriate medications. Contemporary analysis of medication use in community-dwelling older people compared with the general population is lacking.

Participants

A total of 19,114 community-dwelling adults in Australia and the United States aged 70 years or older (65 years or older for U.S. minorities) without histories of major cardiovascular disease, cognitive impairment, or disability participated in a randomized, placebo-controlled trial of aspirin: ASPirin in Reducing Events in the Elderly study.

2.1 Measurements

Prescribed baseline medications obtained by self-report and medical record review were grouped by World Health Organization Anatomic and Therapeutic Chemical category. Potentially inappropriate medications were defined using a modified American Geriatrics Society Beers Criteria. Polypharmacy was defined as 5 or more medications, and hyperpolypharmacy defined as 10 or more medications. Cross-sectional descriptive statistics and adjusted odds ratios were computed.

Results

The median number of prescription medications per participant was three, regardless of age. Women had a higher medication prevalence. Cardiovascular drugs (primarily antihypertensives) were the most commonly reported (64%). Overall, 39% of the cohort reported taking at least one potentially inappropriate medication, with proton-pump inhibitors being the most commonly reported (21.2% of cohort). Of the cohort, 27% had polypharmacy, and 2% hyperpolypharmacy.

Age 75 years or older, less than 12 years of education, hypertension, diabetes mellitus, chronic kidney disease, frailty, gastrointestinal complaint, and depressive symptoms were associated with an increased likelihood of potentially inappropriate medications and polypharmacy. For almost all medication classes, prevalence was equivalent or lower than the general older population.

Conclusion

Overall medication burden and polypharmacy are low in older adults free of major cardiovascular disease, disability, and cognitive impairment. The prevalence of potentially inappropriate medications is higher than previously reported and similar to more vulnerable populations as a result of the introduction of proton-pump inhibitors to the American Geriatrics Society Beers Criteria. Longitudinal follow-up is required to further understand the balance of benefits and risks for potentially inappropriate medications and polypharmacy in community-dwelling older people.

Disponible en: https://doi.org/10.1002/phar.2461

Pharmacoepidemiology and Drug Safety

Influence of statin-potency on the risk of kidney disease – a nationwide cohort study using laboratory data

Anna Citarella PhD, Marie Linder PhD, Simona Cammarota PhD, Anders Sundström PhD, Helle Kieler MD, PhD

Abstract

Purpose

To estimate the risk of kidney disease in high-potency statin users compared to those treated with low-potency statins without history of kidney disease at statin initiation, linking the Swedish national healthcare registers and laboratory data.

Methods

Incident users of statins, ≥40 years of age, with estimated Glomerular Filtration Rate (eGFR) >60 mL/min/1.73m2 and no diagnosis of kidney disease at treatment initiation were identified between 2006 and 2007 and then followed for 2-years. The outcome was the incidence of kidney disease identified by the presence of the diagnostic code in the healthcare registers or eGFR<60 mL/min/1.73m2. We estimated hazard ratios (HRs) and 95% confidence intervals (CIs) with adjusted and propensity score (PS)-matched Cox proportional hazards models.

Results

A total of 27 385 patients were identified, 25.2% of which treated with a high-potency statin. During the follow-up, 68 (0.25%) patients were identified with a diagnosis of kidney disease from the registers. The number increased to 2498 (9.1%) when the criteria of eGFR<60 mL/min/1.73m2 was added. The adjusted HR of kidney disease in high-potency statin users was 1.14 (95%CI 1.03–1.25) compared to low-potency users; the result was unchanged after the PS approach.

Conclusions

Adding information from laboratory data to those from the national health registers, a slightly increased risk for kidney disease was found in high-potency statin users without pre-existing kidney disease at treatment initiation compared to those treated with low-potency statins.

Disponible en: https://doi.org/10.1002/pds.5173

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Clinical Pharmacology & Therapeutics

Clinical characteristics and outcome of drug-induced liver injury in the older patients: from the young-old to the oldest-old

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Abstract

Old patients with hepatotoxicity have been scarcely studied in idiosyncratic drug-induced liver injury (DILI) cohorts. We sought for the distinctive characteristics of DILI in older patients across age groups. A total of 882 DILI patients included in the Spanish DILI Registry (33% ≥65 years) were categorized according to age: "young" (<65y); "young-old" (65-74y); "middle-old" (75-84y); and "oldest-old" (≥85y). All elderly groups had increasingly higher comorbidity burden (p<0.001) and polypharmacy (p<0.001). There was a relationship between jaundice and hospitalization (p<0.001), and both were more prevalent in the elderly age groups, especially in the oldest-old (88% and 69%, respectively) and the DILI episode was more severe (p=0.029). The proportion of females decreased across age groups from the young to the middle-old, yet in the oldest-old there was a distinct female predominance. Pattern of liver injury shifted towards cholestatic with increasing age among top culprit drugs amoxicillin-clavulanate, atorvastatin, levofloxacin, ibuprofen, and ticlopidine. The best cut-off point for increased odds of cholestatic DILI was 65y. Older patients had increased non-liver related mortality (p=0.030) as shown by the predictive capacity of MELD (OR=1.116; p<0.001), and comorbidity burden (OR=4.188; p=0.001) in the 6-month mortality. Older patients with DILI exhibited an increasingly predominant cholestatic phenotype across a range of culprit drugs other that amoxicillin-clavulanate, with increased non-liver related mortality and require a different approach to predict outcome. The oldest DILI patients exhibited a particular phenotype with more severe DILI episodes and need to be considered when stratifying older DILI populations.

Disponible en: https://doi.org/10.1002/cpt.2108

Clinical Therapeutics

Effects of Ivabradine on Cardiac Remodeling in Patients With Stable Symptomatic Heart Failure: A Systematic Review and Meta-analysis

Hongbing Wan, MD 1, Tieqiu Huang, MD 1Hongzhou Zhang, MD
Qinghua Wu, MD

Abstract

Purpose

Ivabradine reduces heart rate (HR) in patients with heart failure (HF). However, its effect on cardiac remodeling is not obvious. The goal of this study was to explore the extra effect of ivabradine on cardiac remodeling in patients with HF.

Methods

We searched PubMed from database inception to January 31, 2020, Cochrane and Embase from database inception to February 2, 2020, and Web of Science and ClinicalTrials.gov from database inception to February 3, 2020, for randomized controlled trials on ivabradine treatments in patients with stable symptomatic HF, left ventricular ejection fraction (LVEF) < 45%, and resting HR ≥ 60 beats/min in sinus rhythm. We pooled the mean differences (MDs) or standardized mean differences and their 95% CIs. An inverse variance was used to combine data. Fixed- or random-effects models were used to outline the outcomes based on heterogeneity levels. We assessed the heterogeneity among studies according to the *I* 2 statistic. A sensitivity analysis for select results was performed to assess the robustness of the outcomes.

Findings

Of 2277 trials, 9 trials fulfilled the inclusion criteria. A total of 1523 patients were enrolled in 9 studies. There were 796 participants in the ivabradine group and 727 participants in the control group. The duration of follow-up ranged from 6 weeks to 19.6 months. The mean (SD) age of the participants was 59.7 (11.2) years, and 1187 participants (77.9%) were men. Therapy with ivabradine was related to reversing cardiac remodeling with a significant increase in LVEF (MD = 3.04%; 95% CI, 2.07%–4.00%; $p < 0.001$), decrease in the left ventricular end-systolic volume index (LVESVI) (MD = −7.30 mL/m 2; 95% CI, −12.94 to −1.66 mL/m 2; $p = 0.01$), and reduction in the left ventricular end-diastolic volume index (LVEDVI) (MD = −7.27 mL/m 2; 95% CI, −14.04 to −0.50 mL/m 2; $p = 0.04$). In the subgroup of enrolled patients with a resting HR of ≥70 beats/min, greater progress in LVEF was detected in the ivabradine group (MD = 3.60%; 95% CI, 2.40%–4.81%; $p < 0.001$), and a higher improvement in LVESVI was identified in the ivabradine group (MD = −11.06 mL/m 2; 95% CI, −21.15 to −0.98 mL/m 2; $p = 0.03$).

Implications

In patients with stable symptomatic HF, LVEF <45%, and resting HR ≥ 60 beats/min in sinus rhythm, ivabradine use was associated with reversing cardiac remodeling with a significant increase in LVEF, a decrease in LVESVI, and a reduction in LVEDVI.

Disponible en: https://doi.org/10.1016/j.clinthera.2020.10.005

REVISTAS DE MEDICINA GENERAL

JAMDA: Journal of the American Medical Directors Association

A New Care Model Reduces Polypharmacy and Potentially Inappropriate Medications in Long-Term Care

Carolina Tisnado Garland, Line Guénette, PhD, Edeltraut Kröger, PhD, Pierre-Hugues Carmichael, MSc, Rachel Rouleau, MSc, Caroline Sirois, PhD

Abstract

Objectives

Assess the impact of a new pharmaceutical care model on (1) polypharmacy and (2) potentially inappropriate medication (PIM) use in long-term care facilities (LTCFs).

Design

Pragmatic quasi-experimental study with a control group. This multifaceted model enables pharmacists and nurses to increase their professional autonomy by enforcing laws designed to expand their scope of practice. It also involves a strategic reorganization of care, interdisciplinary training, and systematic medication reviews.
Setting and Participants

Two LTCFs exposed to the model (409 residents) were compared to 2 control LTCFs (282 residents) in Quebec, Canada. All individuals were aged 65 years or older and residing in included LTCFs.
Measures
Polypharmacy (≥10 medications) and PIM (2015 Beers criteria) were analyzed throughout 12 months between March 2017 and June 2018. Groups were compared before and after implementation using repeated measures mixed Poisson or logistic regression models, adjusting for potential confounding variables.
Results

Over 12 months, for regular medications, polypharmacy decreased from 42% to 20% (exposed group) and from 50% to 41% (control group) [difference in differences (DID): 13%, $P < .001$]. Mean number of PIMs also decreased from 0.79 to 0.56 (exposed group) and from 1.08 to 0.90 (control group) (DID: 0.05, $P = .002$).
Conclusions and Implications
Compared with usual care, this multifaceted model reduced the probability of receiving ≥10 medications and the mean number of PIMs. Greater professional autonomy, reorganization of care, training, and medication review can optimize pharmaceutical care. As the role of pharmacists is expanding in many countries, this model shows what could be achieved with increased professional autonomy of pharmacists and nurses in LTCFs.
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In heart failure, adding empagliflozin to medical therapy reduced a composite of CV death or HF hospitalization

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Abstract
Question

In patients with chronic heart failure (HF) and reduced ejection fraction (rEF), what is the effect of adding empagliflozin to recommended therapy on cardiovascular (CV) outcomes?

Design

Randomized placebo-controlled trial (EMPEROR-Reduced [Empagliflozin Outcome Trial in Patients with Chronic Heart Failure and a Reduced Ejection Fraction]).

Blinding

Treatment allocation concealed; blinded (patients, clinicians, clinical events committee).*

Setting

520 centers in 20 countries.

Patients

3730 adults ≥18 years of age (mean age, 67 y; 76% men; 73% left ventricular ejection fraction [LVEF] ≤30%; 50% diabetes) who had chronic HF (NYHA functional class II, III, or IV) with LVEF ≤40% and were receiving recommended medical therapies (diuretics, renin–angiotensin system and neprilysin inhibitors, β-blockers, mineralocorticoid receptor antagonists, and cardiac devices as indicated). Key exclusions: major CV event in the previous 90 days, estimated glomerular filtration rate (eGFR) <20 mL/min/1.73 m2, and type 1 diabetes.

Interventions

Empagliflozin, 10 mg/d (n = 1863), or placebo (n = 1867), added to recommended medical therapy.

In HFrEF, adding empagliflozin to medical therapy reduced a composite of CV death or HF hospitalization compared with placebo, regardless of diabetes status.

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