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REVISIÓN BIBLIOGRÁFICA FEBRERO Y MARZO 2023
Selección de artículos

REVISTAS GERIÁTRICAS

Age and Ageing

The 'Bermuda Triangle' of orthostatic hypotension, cognitive impairment and reduced mobility: prospective associations with falls and fractures in The Irish Longitudinal Study on Ageing

Desmond O Donnell, Roman Romero-Ortuno, Sean P Kennelly, Desmond O'Neill, Patrick O Donoghue, Amanda Lavan, Conal Cunningham, Paul McElwaine, Rose Anne Kenny, Robert Briggs

Abstract

Background

Orthostatic hypotension (OH), cognitive impairment (Cog) and mobility impairment (MI) frequently co-occur in older adults who fall. This study examines clustering of these three geriatric syndromes and ascertains their relationship with future falls/fractures in a large cohort of community-dwelling people ≥ 65 years during 8-year follow-up.

Methods

OH was defined as an orthostatic drop ≥ 20 mmHg in systolic blood pressure (from seated to standing) and/or reporting orthostatic unsteadiness. CI was defined as Mini Mental State Examination ≤ 24 and/or self-reporting memory as fair/poor. MI was defined as Timed Up and Go ≥12 s. Logistic regression models, including three-way interactions, assessed the longitudinal association with future falls (explained and unexplained) and fractures.

Results

Almost 10% (88/2,108) of participants had all three Bermuda syndromes. One-fifth of participants had an unexplained fall during follow-up, whereas 1/10 had a fracture. There was a graded relationship with incident unexplained falls and fracture as the number of Bermuda syndromes accumulated. In fully adjusted models, the cluster of OH, CI and MI was most strongly associated with unexplained falls (odds ratios (OR) 4.33 (2.59–7.24); $P < 0.001$) and incident fracture (OR 2.51 (1.26–4.98); $P = 0.045$). Other clusters significantly associated with unexplained falls included OH; CI and MI; MI and OH; CI and OH. No other clusters were associated with fracture.

Discussion

The 'Bermuda Triangle' of OH, CI and MI was independently associated with future unexplained falls and fractures amongst community-dwelling older people. This simple risk

identification scheme may represent an ideal target for multifaceted falls prevention strategies in community-dwelling older adults.

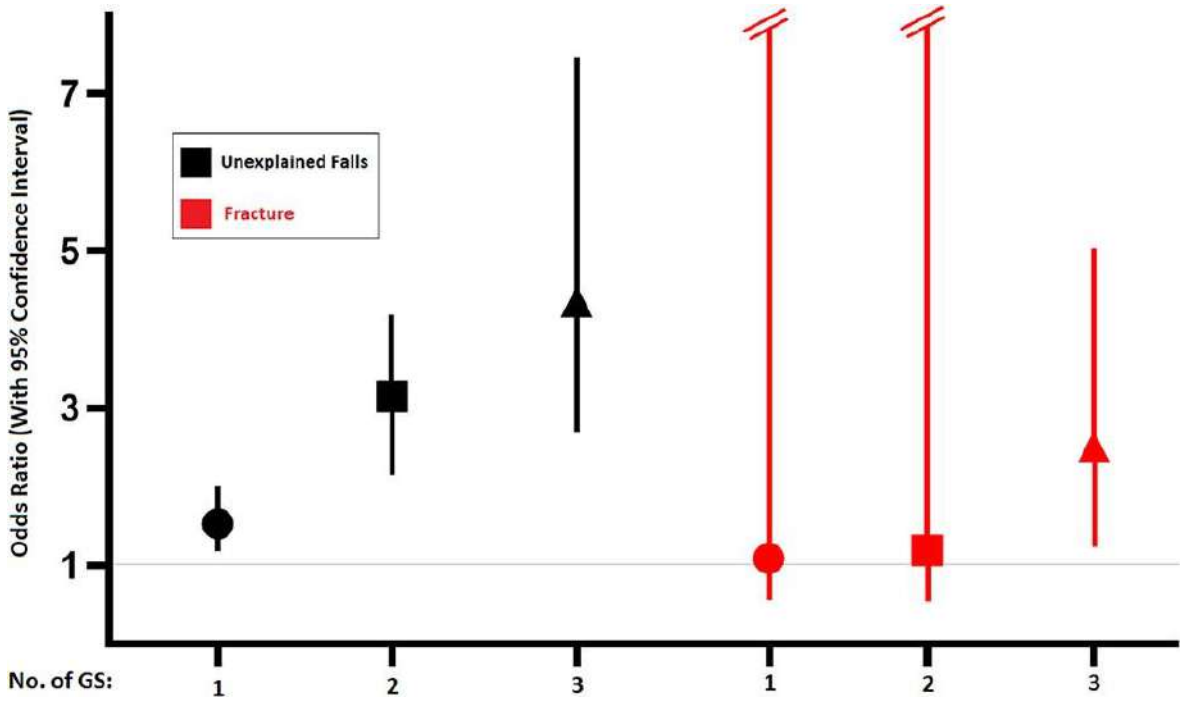

Figure 2 OR with 95% confidence intervals with unexplained falls and fracture as dependent variables by number of geriatric syndromes. Notes: the Bermuda Triangle of Falls comprises OH, cognitive impairment and MI. OH was defined as a drop of ≥20 mmHg in SBP when measured after standing from a seated position and/or reporting unsteadiness when getting up from a chair. Blood pressure was measured using an Omron digital cuff. Cognitive impairment was defined as an MMSE Score ≤ 24 and/or self-reporting memory as fair or poor. MI was defined as a Timed Up and Go Score ≥ 12 s. Unexplained Falls defined as falls not because of slips or trips, with no clear reason for the fall. Fracture defined as self-report of incident hip, wrist, vertebral or other fracture during follow-up. Abbreviation: No. of GS, number of geriatric syndromes. OR from logistic regression models with unexplained falls and fractures as dependent variables. Analysis adjusted for follow-up time, age, sex, educational attainment, alcohol excess, heart disease, polypharmacy and chronic disease burden.

Disponible en: https://doi.org/10.1093/ageing/afad005

The differential risk of severe hyponatraemia based on the use patterns of hyponatraemia-inducing medications in older adults

Kwanghee Jun, Young-Mi Ah, Jaekyu Shin, Ju-Yeun Lee

Abstract

Background

The identification and minimization of hyponatraemia-inducing medication (HIM) usage is among the effective strategies for preventing hyponatraemia. However, the differential risk of severe hyponatraemia is unknown.

Objective

To evaluate the differential risk of severe hyponatraemia associated with newly started and concurrently used HIMs in older people.

Design and setting

A case–control study using national claims databases.

Methods

We identified patients aged >65 years with severe hyponatraemia as those hospitalised with a primary diagnosis of hyponatraemia or who had received tolvaptan or 3% NaCl. A 1:20 matched control with the same visit date was constructed. Multivariable logistic regression was performed to assess the association of newly started or concurrently used HIMs comprising 11 medication/classes with severe hyponatraemia after covariate adjustment.

Results

Among 47,766,420 older patients, we identified 9,218 with severe hyponatraemia. After adjusting for covariates, all HIM classes were found to be significantly associated with severe hyponatraemia. Compared with persistently used HIMs, newly started HIMs increased the likelihood of severe hyponatraemia for eight classes of HIMs, with the highest increase being observed for desmopressin (adjusted odds ratio: 3.82, 95% confidence interval: 3.01–4.85). Concurrent use increased the risk of severe hyponatraemia compared to that with individually administered HIMs: thiazide-desmopressin (4.86, 3.90–6.07), medications causing the syndrome of inappropriate anti-diuretic hormone secretion (SIADH)-desmopressin (2.65, 2.25–3.11), medications causing SIADH-thiazides (1.87, 1.75–1.98) and combination among medications causing SIADH (1.36, 1.28–1.45).

Conclusions

In older adults, newly started and concurrently used HIMs increased the risk of severe hyponatraemia compared with persistently and singly used HIMs.

Disponible en: https://doi.org/10.1093/ageing/afad026

Archives of Gerontology and Geriatrics

Does the incidence of frailty differ between men and women over time?

Dayane Capra de Oliveira, Roberta de Oliveira Máximo a, Paula Camila Ramírez, Aline Fernanda de Souza, Mariane, Maicon Luis Bicigo Delinocente, Andrew Steptoe, Cesar de Oliveira, Tiago da Silva Alexandre

Abstract

Background

The mechanisms, risk factors and influence of sex on the incidence of frailty components are not fully understood. The aim of this study was to analyse sex differences in factors associated with the increase in the number of frailty components.

Methods

A 12-year follow-up analysis was conducted with 1,747 participants aged ≥ 60 of the ELSA Study with no frailty at baseline. Generalised linear mixed models were used to analyse the increase in the number of frailty components stratified by sex, considering socioeconomic, behavioural, clinical and biochemical characteristics as exposure variables.

Results

The increase in the number of frailty components in both sexes was associated with an advanced age (70 to 79 years and 80 years or older), low educational level, sedentary lifestyle, elevated depressive symptoms, joint disease, high C-reactive protein levels, perception of poor vision and uncontrolled diabetes ($p < 0.05$). Osteoporosis, low weight, heart disease, living with one or more people and perception of poor hearing were associated with an increase in the number of frailty components in men. High fibrinogen concentration, controlled diabetes, stroke and perception of fair vision were associated with the outcome in women ($p < 0.05$). Obese women and men and overweight women had a lower increase in the number of frailty components compared to those in the ideal weight range.

Conclusions

Socioeconomic factors, musculoskeletal disorders, heart disease and low weight seem to sustain the frailty process in men, whereas cardiovascular and neuroendocrine disorders seem to sustain the frailty process in women.

Disponible en: 10.1016/j.archger.2022.104880

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BMC Geriatrics

Risk factors for self-reported medication adherence in community-dwelling older patients with multimorbidity and polypharmacy: a multicenter cross-sectional study

Jiaming Liu, Yongpei Yu, Suying Yan, Yan Zeng, Su Su, Tiantian He, Zimin Wang, Qian Ding, Ruixue Zhang, Wenchao Li, Xin Wang, Lan Zhang & Xiaolin Yue

Abstract

Background

Medication nonadherence is a significant public health problem as it contributes to poor clinical outcomes and increased healthcare costs. Older patients with multimorbidity and polypharmacy often have low medication adherence. These patients also have a high prevalence of potentially inappropriate medication (PIM) use.

Aim

To explore risk factors related to medication nonadherence in older patients with multimorbidity and polypharmacy and examine the association between medication nonadherence and PIM use.

Method

A multicenter cross-sectional study was conducted from May to December 2019 in 16 tertiary hospitals from 12 provinces and cities in China. Data were collected from outpatients 65 years or older with multimorbidity and polypharmacy. The PIMs were evaluated using the 2019 Beers Criteria. Self-reported medication adherence was assessed using the Visual Analog Scale (VAS).

Results

A total of 773 outpatients were recruited. The prevalence of medication nonadherence was 31.8%. In the univariate analysis, nonadherence was significantly associated with sex, cognitive impairment, stroke, visiting the same physicians, self-administration of medication, the percentage of drug costs ≥ 10% of the medical expenses, and PIMs for the alimentary tract and metabolism. In the multivariate analysis, the results almost paralleled those of the univariate associations. Notably, the use of PIM was significantly associated with medication adherence.

Conclusion

Several factors that influence medication adherence were identified. Targeted interventions can be implemented to improve medication adherence, such as encouraging self-administering medications and reducing medication expenses.

Disponible en: https://doi.org/10.1186/s12877-023-03768-7

Clinical prediction rule for identifying older patients with toxigenic clostridioides difficile at the time of hospital admission

Ki-Byung Lee, Mina Lee, Jin Woong Suh, Kyung-Sook Yang, Youseung Chung, Jeong Yeon Kim, Sun Bean Kim, Jang Wook Sohn & Young Kyung Yoon

Abstract

Background

This study aimed to develop and validate a clinical prediction rule to screen older patients at risk of being toxigenic Clostridioides difficile carriers at the time of hospital admission.

Methods

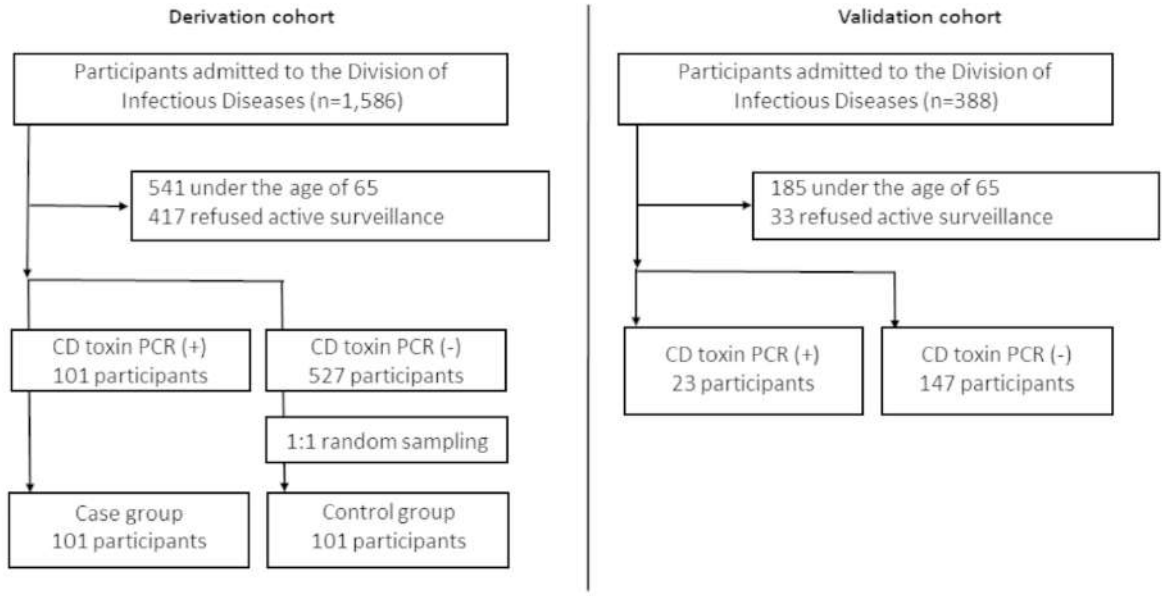
This retrospective case-control study was performed at a university-affiliated hospital. Active surveillance using a real-time polymerase chain reaction (PCR) assay for the toxin genes of C. difficile was conducted among older patients (≥ 65 years) upon admission to the Division of Infectious Diseases of our institution. This rule was drawn from a derivative cohort between October 2019 and April 2021 using a multivariable logistic regression model. Clinical predictability was evaluated in the validation cohort between May 2021 and October 2021.

Results

Of 628 PCR screenings for toxigenic C. difficile carriage, 101 (16.1%) yielded positive findings. To establish clinical prediction rules in the derivation cohort, the formula was derived using significant predictors for toxigenic C. difficile carriage at admission, such as septic shock, connective tissue diseases, anemia, recent use of antibiotics, and recent use of proton-pump inhibitors. In the validation cohort, the sensitivity, specificity, and positive and negative predictive values of the prediction rule, based on a cut-off value of ≥ 0.45, were 78.3%, 70.8%, 29.5%, and 95.4%, respectively.

Conclusion

This clinical prediction rule for identifying toxigenic C. difficile carriage at admission may facilitate the selective screening of high-risk groups. To implement it in a clinical setting, more patients from other medical institutions need to be prospectively examined.



Flow chart illustrating the inclusion of the study participants

Disponible en: https://doi.org/10.1186/s12877-023-03808-2

DRUGS AND AGING

Status Epilepticus in Older Adults: Diagnostic and Treatment Considerations

Gamaleldin M. Osman & Sara E. Hocker

Abstract

Status epilepticus (SE) is one of the leading life-threatening neurological emergencies in the elderly population, with significant morbidity and mortality. SE presents unique diagnostic and therapeutic challenges in the older population given overlap with other causes of encephalopathy, complicating diagnosis, and the common occurrence of multiple comorbid diseases complicates treatment. First-line therapy involves the use of rescue benzodiazepine in the form of intravenous lorazepam or diazepam, intramuscular or intranasal midazolam and rectal diazepam. Second-line therapies include parenteral levetiracetam, fosphenytoin, valproate and lacosamide, and underlying comorbidities guide the choice of appropriate medication, while third-line therapies may be influenced by the patient's code status as well as the cause and type of SE. The standard of care for convulsive SE is treatment with an intravenous anesthetic, including midazolam, propofol, ketamine and pentobarbital. There is currently limited evidence guiding appropriate therapy in patients failing third-line therapies. Adjunctive strategies may include immunomodulatory treatments, non-pharmacological strategies such as ketogenic diet, neuromodulation therapies and surgery in select cases. Surrogate decision makers should be updated early and often in refractory episodes of SE and informed of the high morbidity and mortality associated with the disease as well as the high probability of subsequent epilepsy among survivors.

Disponible en: https://doi.org/10.1007/s40266-022-00998-z

EUROPEAN GERIATRIC MEDICINE

Are higher antidepressant plasma concentrations associated with fall risk in older antidepressant users?

A. C. Pronk, E. P. van Poelgeest, L. J. Seppala, K. J. Ploegmakers, B. H. Stricker, K. M. A. Swart, S. C. van Dijk, S. Oliai Araghi, L. C. P. G. M. de Groot, N. M. van Schoor, R. A. A. Mathôt & N. van der Velde

Abstract

Purpose

Antidepressants are well-established fall-risk increasing drugs (FRIDs) and therefore falls should be considered an important adverse drug event (ADE) of antidepressants. However, not all antidepressant users experience fall incidents and factors associated with increased fall risk among antidepressant users are incompletely understood. Our objective was to explore whether antidepressant plasma concentrations are associated with falls in older antidepressant users.

Methods

For this study, we included antidepressant users of the multicenter B-PROOF study. Fall incidents were recorded prospectively using fall calendars. Antidepressant plasma concentrations were analyzed by Liquid chromatography-mass spectrometry (LC–MS) at baseline and at 2 years follow-up. The associations between the observed antidepressant concentration and fall risk were assessed using Cox proportional hazard and logistic regression models and adjusted for potential confounders.

Results

In total 93 selective serotonin reuptake inhibitor (SSRI) and 41 antidepressant (TCA) users were identified. There was a significant association between baseline TCA plasma concentration and fall risk within users (HR 2.50, 95% CI 1.07–5.87, crude model). In the adjusted model, there were no significant associations between concentrations of SSRIs and fall risk.

Conclusion

There might be an association between plasma concentrations of TCAs and the risk of falling in older users. However, these results needs to be interpreted with caution considering the small sample size and accompanying limitation of confinement to crude analyses. Therefore, these novel findings need to replicated in a larger cohort, preferably including adjustment for potential confounders and more frequent measures of plasma concentrations is needed.

Disponible en: https://doi.org/10.1007/s41999-022-00742-1

Longitudinal association of lung function with frailty among older adults: The English Longitudinal Study of Ageing

Xuan Yang, Chunxiao Cheng, Wei Ma & Chongqi Jia

Abstract

Purpose

To investigate the effect of baseline lung function on the trajectory of frailty over time.

Methods

This longitudinal study included 3,658 adults aged 60 and over (average age 70.4 years old and 46.4% males) at baseline from the English Longitudinal Study of Ageing. Lung function indicators included forced vital capacity (FVC) and forced expiratory volume in the first second (FEV1), both measured at baseline examination. Frailty was defined based on Fried's frailty phenotype criteria, the measurement was repeated for four times. Linear mixed-effect regression model was applied to estimate the association of baseline lung function with the trajectory of frailty over time.

Results

Frailty score increased significantly over time ($\beta = 0.030$, $P < 0.001$). Linear mixed-effect regression model identified significant interactions between FVC ($\beta = -0.018$, $P < 0.001$) or FEV1 ($\beta = -0.022$, $P < 0.001$) and time on frailty.

Conclusion

Poor baseline lung function might accelerate the speed of frailty. Lung function might be an important predictor of the development and progression of frailty among older adults.

Disponible en: https://doi.org/10.1007/s41999-022-00732-3

Gerontology

Oral and Rectal Colonization by Antimicrobial-Resistant Gram-Negative Bacteria and Their Association with Death among Residents of Long-Term Care Facilities: A Prospective, Multicenter, Observational, Cohort Study

Kajihara T. · Yahara K. · Yoshikawa M. · Haruta A. · Kawada-Matsuo M.· Le M.N.-T. · Arai C. · Takeuchi M. · Kitamura N. · Sugawara Y. · Hisatsune J. · Kayama S. · Ohta K.· Tsuga K. · Komatsuzawa H. · Ohge H. · Sugai M.

Abstract

Introduction

The prevalence of antimicrobial-resistant bacteria (ARB) in long-term care facilities (LTCFs) remains unclear. Furthermore, the effect of ARB colonization on the clinical outcomes of LTCF residents has not been explored.

Methods

We conducted a prospective multicenter cohort study and investigated the residents (N = 178) of six Japanese LTCFs (three Welfare Facilities for the Elderly Requiring Long-term Care and three Geriatric Health Service Facilities) for oral and rectal carriage of ARB. The clinical outcomes of the residents were evaluated based on isolating bacterial strains and subjecting them to whole-genome sequencing.

Results

Of the 178 participants, 32 belonging to Geriatric Health Service Facilities with no information on their clinical outcome were excluded, and the remaining 146 were followed up for at most 21 months. Extended-spectrum β-lactamases (ESBL)-producing Enterobacterales and Pseudomonas aeruginosa were detected in 42.7% (n = 76) and 2.8% (n = 5) of the rectal swabs and 5.6% (n = 10) and 3.4% (n = 6) of the oral swabs, respectively. Detection of ARB in the oral and rectal cavities showed remarkable association with enteral nutrition. Further, P. aeruginosa was significantly associated with an increase in mortality of the residents, but there were not significant association between ESBL-producing Enterobacterales and mortality. Core-genome phylogeny of P. aeruginosa revealed a wide-spread distribution of the isolated strains across the phylogeny, which included a cluster of ST235 strains with substantially higher biofilm formation ability than the other isolated P. aeruginosa strains.

Discussion/Conclusion

This study is the first to investigate the carriage of both oral and rectal ARB, genomic relatedness and determinants of antimicrobial resistance in isolated strains, and clinical outcomes of LTCF residents. Our study provides the first direct evidence for the burden of antimicrobial resistance in LTCFs.

Oral isolates, *n* (%)			Rectal isolates, *n* (%)		
total, *n* = 41	Welfare Facility for the Elderly Requiring Long-term Care, *n* = 23	Geriatric Health Services Facility, *n* = 18	total, *n* = 127	Welfare Facility for the Elderly Requiring Long-term Care, *n* = 84	Geriatric Health Services Facility, *n* = 43
Acinetobacter spp., 15 (36.6)	*P. aeruginosa*, 7 (30.4)	*Acinetobacter* spp., 9 (50.0)	*E. coli*, 77 (60.6)	*E. coli*, 58 (69.0)	*E. coli*, 19 (44.2)
P. aeruginosa, 7 (17.1)	*Acinetobacter* spp., 6 (26.1)	Other *Pseudomonas*, 3 (16.7)	*Enterobacter* spp., 9 (7.1)	*P. mirabilis*, 6 (7.1)	Other *Pseudomonas*, 7 (16.3)
E. coli, 6 (14.6)	*E. coli*, 4 (17.4)	*E. coli*, 2 (11.1)	*Citrobacter* spp., 8 (6.3)	*Acinetobacter* spp., 5 (6.0)	*Citrobacter* spp., 6 (14.0)
Other *Pseudomonas*, 4 (9.8)	*P. mirabilis*, 2 (8.6)	*E. cloacae* complex, 1 (5.6)	*P. mirabilis*, 6 (4.7)	*P. aeruginosa*, 4 (4.8)	*Enterobacter* spp., 5 (11.6)
E. cloacae complex, 2 (4.9)	Other *Pseudomonas*, 1 (4.3)	*S. maltophilia*, 1 (5.6)	*Acinetobacter* spp., 6 (4.7)	*Enterobacter* spp., 4 (4.8)	*Acinetobacter* spp., 1 (2.3)
P. mirabilis, 2 (4.9)	*E. cloacae* complex, 1 (4.3)	*Pantoea* spp., 1 (5.6)	*P. aeruginosa*, 5 (3.9)	*Citrobacter* spp., 2 (2.4)	*P. aeruginosa*, 1 (2.3)
S. maltophilia, 1 (2.4)	*A. xylosoxidans*, 1 (4.3)	*Pigmentiphaga* spp., 1 (5.6)	*K. pneumoniae*, 3 (2.4)	*K. pneumoniae*, 2 (2.4)	*K. pneumoniae*, 1 (2.3)
Others, 4 (9.8)	*Pandoraea* spp., 1 (4.3)		Others, 13 (10.2)	Others, 3 (3.6)	Others, 3 (7.0)

Disponible en: https://doi.org/10.1159/000525759

Journal of Clinical Interventions In Aging

Older Adults and Immune Thrombocytopenia: Considerations for the Clinician

Etienne Crickx, Matthieu Mahévas, Marc Michel, Bertrand Godeau

Abstract

Many epidemiological studies have shown that the incidence of immune thrombocytopenia (ITP) increases after age 60 years and peaks in patients over age 80 years. Therefore, ITP is a concern for physicians taking care of older patients, especially regarding its diagnosis and management. The diagnostic work-up should exclude other causes of thrombocytopenia and secondary ITP, including myelodysplastic syndrome and drug-induced ITP.

The treatment decision is influenced by an increased risk of bleeding, infectious diseases and thrombosis in this population and should take into account comorbidities and concomitant medications such as anticoagulant drugs.

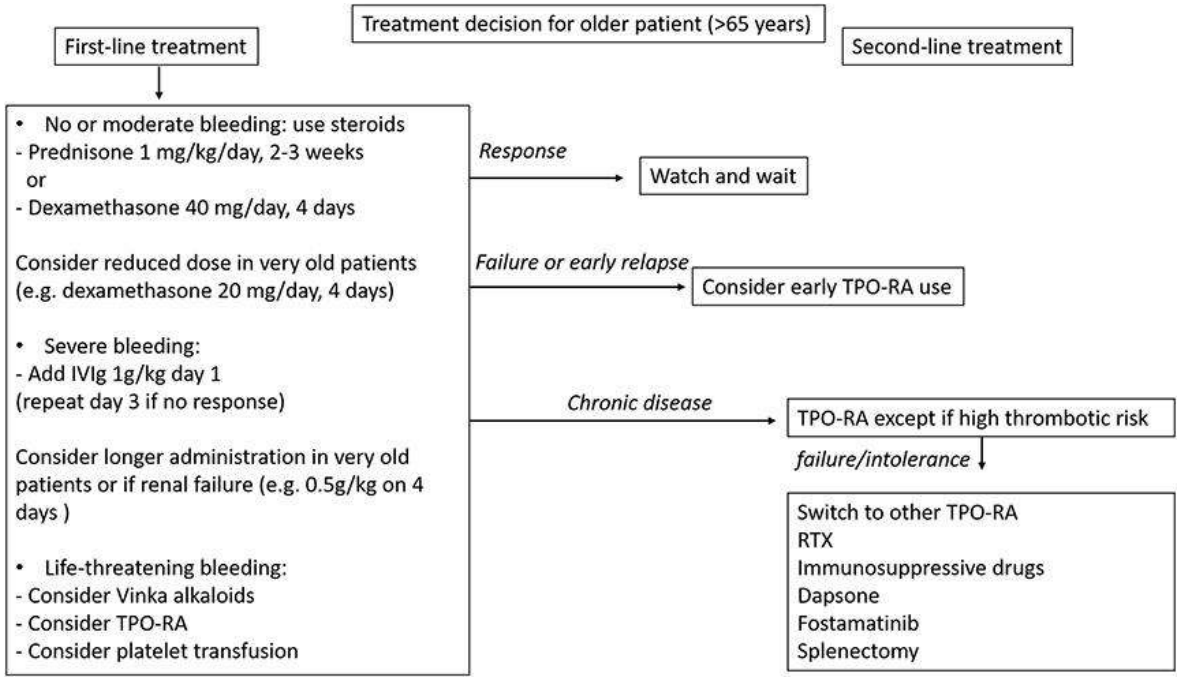
Firstline treatment is based on short corticosteroids courses and intravenous immunoglobulin, which should be reserved for patients with more severe bleeding complications, with their higher risk of toxic effects as compared with younger patients. Second-line treatment should be tailored to the patient's history, comorbidities and preferences. Preferred second-line treatments are thrombopoietin receptor agonists for most groups and guidelines given their good efficacy/tolerance ratio, but the thrombotic risk is increased in older people. Other second-line options that can be good alternatives depending on the clinical context include rituximab, dapsone, fostamatinib or immunosuppressive drugs. Splenectomy is less often performed but remains an option for fit patients with chronic refractory disease.

Emerging treatments such as Syk or Bruton tyrosine kinase inhibitors and FcRn antagonists are becoming available for ITP and may modify the treatment algorithm in the near future. The aim of this review is to describe the particularities of the diagnosis and treatment of ITP in older people, including the response and tolerance to the currently available drugs.

We also discuss some situations related to comorbidities that can frequently lead to adapt the management strategy in older patients.

Secondary ITP	Non-Immune Thrombocytopenia
Associated auto-immune disorder Evans syndrome Systemic lupus erythematosus Antiphospholipid syndrome Other auto-immune disorders **Drug-induced ITP and vaccine-induced ITP** **Infectious diseases** HIV HCV Helicobacter pylori **Lymphoproliferative disorders** Chronic lymphocytic leukemia Indolent B-cell lymphoma Angioimmunoblastic T-cell lymphoma **Primary immune deficiencies/inborn error of immunity** Common variable immune deficiency Autoimmune lymphoproliferative syndrome	**Splenic sequestration** Portal hypertension Splenomegaly Splenic infiltrative diseases **Decreased production** Inherited thrombocytopenia Primary and secondary bone-marrow failures Hematological drug toxicity, alcohol toxicity Folate and/or B12 deficiency Viral infections: HIV, HBV, HCV EBV, CMV, parvovirus B19 **Peripheral platelet consumption** Disseminated intravascular coagulation Thrombotic microangiopathy Sepsis **Alloimmune thrombocytopenia**

Abbreviations: ITP, immune thrombocytopenia; CMV, cytomegalovirus; EBV, Epstein-Barr virus; HBV, hepatitis B virus; HCV, hepatitis C virus; HIV, human immunodeficiency virus.



	Avoid if Increased Thrombotic Risk	Avoid if Increased Infectious Risk	Avoid if Rapid Response Needed	Avoid if ITP is Secondary to Lymphoproliferative Disorder	Avoid if Severe Co-Morbidities	Avoid in Non-Chronic Patients
TPO-RA	x					
Rituximab		x				
Immunosuppressive drugs		x	x	x	x	
Dapsone			x			
Danazole	x		x			
Splenectomy	x	x		x	x	x
Fostamatinib				?		

Abbreviations: ITP, immune thrombocytopenia; TPO-RA, thrombopoietin receptor agonist.

Disponible en: 10.2147/CIA.S369574

REVISTAS FARMACÉUTICAS

Drug Safety

Colchicine Drug Interaction Errors and Misunderstandings: Recommendations for Improved Evidence-Based Management

Philip D. Hansten, Malinda S. Tan, John R. Horn et al

Abstract

Colchicine is useful for the prevention and treatment of gout and a variety of other disorders. It is a substrate for CYP3A4 and P-glycoprotein (P-gp), and concomitant administration with CYP3A4/P-gp inhibitors can cause life-threatening drug–drug interactions (DDIs) such as pancytopenia, multiorgan failure, and cardiac arrhythmias.

Colchicine can also cause myotoxicity, and coadministration with other myotoxic drugs may increase the risk of myopathy and rhabdomyolysis. Many sources of DDI information including journal publications, product labels, and online sources have errors or misleading statements regarding which drugs interact with colchicine, as well as suboptimal recommendations for managing the DDIs to minimize patient harm. Furthermore, assessment of the clinical importance of specific colchicine DDIs can vary dramatically from one source to another. In this paper we provide an evidence-based evaluation of which drugs can be expected to interact with colchicine, and which drugs have been stated to interact with colchicine but are unlikely to do so. Based on these evaluations we suggest management options for reducing the risk of potentially severe adverse outcomes from colchicine DDIs. The common recommendation to reduce the dose of colchicine when given with CYP3A4/P-gp inhibitors is likely to result in colchicine toxicity in some patients and therapeutic failure in others. A comprehensive evaluation of the almost 100 reported cases of colchicine DDIs is included in table form in the electronic supplementary material.

Colchicine is a valuable drug, but improvements in the information about colchicine DDIs are needed in order to minimize the risk of serious adverse outcomes.

Disponible en: https://link.springer.com/article/10.1007/s40264-022-01265-1

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European Journal of Clinical Pharmacology

Increased major bleeding incidence in atrial fibrillation patients with apixaban: a review of Japanese post-marketing surveillance studies of direct oral anticoagulants

Akinori Sairaku & Yukiko Nakano

ABSTRACT

Large-scaled post-marketing surveillance studies (PMSSs) of 4 direct oral anticoagulants (DOACs) for stroke prevention in non-valvular atrial fibrillation (AF) were conducted since 2011 in Japan, and the results of the last one have recently been published. Each reported a more than acceptable ischemic stroke prevention. The major bleeding rates were also acceptably low and comparable to each other in the PMSSs of dabigatran (J-dabigatran), rivaroxaban (XAPASS), and edoxaban (ETNA-AF-Japan). However, the incidence in PMSS of apixaban (STANDARD) was more than double the others. This finding appeared to contradict the globally accepted theory that apixaban is less likely than other DOACs to cause bleeding events. Possible responsible mechanisms included (1) the age and kidney function, (2) concomitant antiplatelet therapy, (3) drug actions, (4) follow-up duration, and (5) dose reduction criteria. Similarities in the clinical background shared by the 4 different PMSSs' participants and knowledge from previous studies did not support a dominant contribution of any of those former 4 factors to the increased major bleeding incidence in STANDARD. A possibility of the 5th factor was then examined. An estimated calculation we created showed that apixaban's dose reduction criteria was strict enough to considerably reduce the opportunity for participants to take its reduced rather than standard dose. We then successfully simulated how the "strict" dose reduction criteria would have increased the bleeding event rates under DOAC therapy. The discussion in this review may therefore raise a question about the validity of the current dose reduction criteria of apixaban for Japanese AF patients.

Disponible en: https://link.springer.com/article/10.1007/s00228-023-03471-x

Evaluation and subgroup analysis of the efficacy and safety of intensive rosuvastatin therapy combined with dual antiplatelet therapy in patients with acute ischemic stroke

Ting Deng, Tong Zhang, Haitao Lu, Jingmian Chen, Xiaomeng Liu, Wei He & Xiao-hua Yao

Objectives

We investigated the efficacy of intensive rosuvastatin therapy plus 7-day dual antiplatelet therapy (DAPT) in reducing stroke recurrence for patients with acute ischemic stroke (AIS) and compared subgroups of patients.

Methods

We enrolled patients with AIS whose time of onset to medication was ≤ 72 h, and the baseline scores of NIHSS (bNIHSS) were 0–10. The patients received intensive rosuvastatin therapy plus 7-day DAPT with aspirin and clopidogrel (study group) or rosuvastatin plus single antiplatelet therapy (SAPT, control group). The primary outcomes were recurrence of ischemic stroke, bleeding, statin-induced liver injury, and statin-associated myopathy (SAM) within 90 days. We also performed a subgroup analysis to assess the heterogeneity of the two therapy regimens in reducing recurrent stroke.

Results

Recurrent stroke occurred in 10 patients in the study group and 42 patients in the control group (hazard ratio [HR], 0.373, 95% confidence interval [CI], 0.178–0.780; P = 0.009). Bleeding events occurred in 9 patients in the study group and 14 patients in the control group (HR, 1.019; 95%CI, 0.441–2.353; P = 0.966). Statin-induced liver injury and SAM were not recorded. Intensive rosuvastatin plus 7-day DAPT was generally effective in reducing the risk of recurrent stroke, except in the subgroup with bNIHSS ≤ 2. The therapy was particularly efficient in the elderly, male, high-bNIHSS, and hypertension, diabetes, and hyperlipidemia subgroups, with P < 0.02.

Conclusions

Without increasing bleeding and statin-associated adverse events, intensive rosuvastatin therapy plus 7-day DAPT significantly reduced the risk of recurrent stroke, especially for subgroups with high-risk factors. Clinical trial registration. China Clinical Trial Registration Center (ChiCTR1800017809).

Disponible en: https://link.springer.com/article/10.1007/s00228-022-03442-8

British Journal of Clinical Pharmacy

Anticholinergic burden in middle and older age is associated with lower cognitive function, but not with brain atrophy

Jure Mur, Riccardo E. Marioni, Tom C. Russ, Graciela Muniz-Terrera, Simon R. Cox

Abstract

Aims

The aim of this study is to estimate the association between anticholinergic burden, general cognitive ability and various measures of brain structural MRI in relatively healthy middle-aged and older individuals.

Methods

In the UK Biobank participants with linked health-care records (n = 163,043, aged 40–71 at baseline), of whom about 17 000 had MRI data available, we calculated the total anticholinergic drug burden according to 15 different anticholinergic scales and due to different classes of drugs. We then used linear regression to explore the associations between anticholinergic burden and various measures of cognition and structural MRI, including general cognitive ability, 9 separate cognitive domains, brain atrophy, volumes of 68 cortical and 14 subcortical areas and fractional anisotropy and median diffusivity of 25 white-matter tracts.

Results

Anticholinergic burden was modestly associated with poorer cognition across most anticholinergic scales and cognitive tests (7/9 FDR-adjusted significant associations, standardised betas (β) range: −0.039, −0.003). When using the anticholinergic scale exhibiting the strongest association with cognitive functions, anticholinergic burden due to only some classes of drugs exhibited negative associations with cognitive function, with β-lactam antibiotics (β = −0.035, PFDR < 0.001) and opioids (β = −0.026, PFDR < 0.001) exhibiting the strongest effects. Anticholinergic burden was not associated with any measure of brain macrostructure or microstructure (PFDR > 0.08).

Conclusions

Anticholinergic burden is weakly associated with poorer cognition, but there is little evidence for associations with brain structure. Future studies might focus more broadly on polypharmacy or more narrowly on distinct drug classes, instead of using purported anticholinergic action to study the effects of drugs on cognitive ability.

Disponible en: https://doi.org/10.1111/bcp.15698

Derivation and validation of a risk prediction score for nonsteroidal anti-inflammatory drug-related serious gastrointestinal complications in the elderly

Suhyun Lee, Kyu-Nam Heo, Mee Yeon Lee, Young-Mi Ah, Jaekyu Shin, Ju-Yeun Lee

Abstract

Aims

Few studies have quantified the impact of risk factors on GI complications in elderly nonsteroidal anti-inflammatory drug (NSAID) users. This study aimed to develop and validate a risk prediction score for severe GI complications to identify high-risk elderly patients using NSAID.

Methods

We used the following two Korean claims datasets: customized data with an enrolment period 2016–2017 for model development, and the sample data in 2019 for external validation. We conducted a nested case–control study for model development and validation. NSAID users were identified as the elderly (≥65 years) who received NSAIDs for more than 30 days. Serious GI complications were defined as hospitalizations or emergency department visits, with a main diagnosis of GI bleeding or perforation. We applied the logistic least absolute shrinkage and selection operator (LASSO) regression model for variable selection and model fitting.

Results

We identified 8176 cases and 81 760 controls with a 1:10 matched follow-up period in the derivation cohort. In the external validation cohort, we identified 372 cases from 254 551 patients. The risk predictors were high-dose NSAIDs, nonselective NSAID, complicated GI ulcer history, male sex, concomitant gastroprotective agents, relevant co-medications, severe renal disease and cirrhosis. Area under the receiver operating characteristic curve was 0.79 (95% confidence interval, 0.77–0.81) in the external validation dataset.

Conclusions

The prediction model may be a useful tool for reducing the risk of serious GI complications by identifying high-risk elderly patients.

Disponible en: https://doi.org/10.1111/bcp.15696

Differences in the location of bleeding with direct oral anticoagulants vs. vitamin K antagonists: A study in the World Health Organization's pharmacovigilance database

Jean-Louis Montastruc, Samuel Tessier, Alessandra Bura-Riviere

Abstract

Aims

Clinical trials have found differences in bleeding locations between direct oral anticoagulants (DOAC) and vitamin K antagonists (VKA). The present study was performed to investigate these differences in real life using reports of adverse drug reactions registered in the World Health Organization's pharmacovigilance database, VigiBase®.

Methods

All bleeding registered between 1 January 2008 and 31 December 2021 in adults were included. The main objective was to compare bleeding locations reported with DOAC with those with VKA. As a secondary objective, we performed the same comparison with Xa vs. thrombin inhibitors. Results were presented as reporting odds ratios (RORs) adjusted on age, gender, origin of reports and co-medications with their 95% confidence interval.

Results

During this 14-year period, 142 228 instances of bleeding were registered with oral anticoagulants, including 39 570 with VKA and 102 658 with DOAC. Mean time to event was lower with DOAC (7.6 months) than with VKA (29.9 months) ($P < .001$). Significant differences in bleeding locations were found in the reports with less cerebral, urologic and nasal bleeding, more gynaecologic bleeding with DOAC than with VKA, without any significant differences in digestive and cutaneous locations. A higher risk of bleeding reports was found with Xa inhibitors vs. dabigatran whatever the locations (except digestive bleeding).

Conclusion

This real-life study shows that the differences in bleeding locations between DOAC and VKA are not limited to the brain or gastrointestinal tracts. Significant differences were also found between Xa and thrombin inhibitors.

Disponible en: https://doi.org/10.1111/bcp.15693

Annals of Pharmacotherapy

Proton Pump Inhibitors and Rhabdomyolysis: Analysis of Two Different Cross-Sectional Databases

Satoru Mitsuboshi, PhD https://orcid.org/0000-0002-6244-1253, Hirofumi Hamano, PhD, et al

Abstract

Background:

It is unclear whether use of a proton pump inhibitors (PPIs) increases the risk of rhabdomyolysis.

Objective:

To clarify whether use of PPIs increases the risk of rhabdomyolysis.

Methods:

This cross-sectional study analyzed data entered into the Medical Data Vision (MDV) database in Japan and into the U.S. Food and Drug Administration Adverse Event Reporting System (FAERS). The MDV data were analyzed to evaluate the association between use of PPIs and rhabdomyolysis. Then, the FAERS data were analyzed to evaluate whether the risk of rhabdomyolysis was increased further when a statin or fibrate was used concomitantly with a PPI. In both analyses, histamine-2 receptor antagonist was set as a comparator because it is used to treat gastric disease. In the MDV analysis, Fisher's exact test and multiple logistic regression analysis were performed. In the FAERS analysis, a disproportionality analysis using Fisher's exact test and multiple logistic regression analysis were performed.

Results:

Multiple logistic regression analysis of both databases showed a significant association between use of PPIs and an increased risk of rhabdomyolysis (odds ratio [OR] = 1.74-1.95, $P \leq 0.01$). However, use of a histamine-2 receptor antagonist was not significantly associated with increased risk of rhabdomyolysis. In the sub-analysis of the FAERS data, use of a PPI did not increase the risk of rhabdomyolysis in patients receiving a statin.

Conclusion and Relevance:

The data in 2 separate databases consistently suggest that PPIs may increase the risk of rhabdomyolysis. The evidence for this association should be assessed in further drug safety studies.

Disponible en: https://doi.org/10.1177/10600280231156270

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Pharmacoepidemiology & Drug Safety

High-throughput Screening for Prescribing Cascades among Real World Statin Initiators

Scott M. Vouri, Earl J. Morris, Marta Walsh, Jessica Agalliu, Alyssa Dempsey, Leonie Hochleitner, Matthew R. Muschett, Stephan Schmidt, Carl J. Pepine, Steven M. Smith

Purpose

Statins are among the most prevalent medications prescribed and associated with adverse events that may prompt additional treatment (i.e., a prescribing cascade). No comprehensive assessment of statin-related prescribing cascades has been performed to our knowledge.

Methods

We utilized sequence symmetry analysis to iteratively screen prescribing sequences of all therapeutic classes ("marker" classes) based on Level 4 Anatomical Therapeutic Chemical codes among adult statin initiators, using IBM Marketscan commercial and Medicare supplemental claims databases (2005–2019). Order of initiation and secular trend-adjusted sequence ratios were calculated for each statin-marker class dyad, among marker class initiators ±90 days of statin initiation. Among signals classified as prescribing cascades, we calculated naturalistic number needed to harm (NNTH) within one year as the inverse of the excess risk among exposed.

Results

We identified 2,265,519 statin initiators (mean±SD age, 56.4±12.0 years; 48.7% women; 7.5% with cardiovascular disease). Simvastatin (34.4% of statin initiators) and atorvastatin (33.9%) were the most commonly initiated statins. We identified 160 significant statin-marker class dyad signals, of which 35.6% (n=57) were classified as potential prescribing cascades. Of the top 25 strongest signals (lowest NNTH), 12 were classified as potential prescribing cascades, including osmotically acting laxatives (NNTH, 44, 95% CI 43-46), opioids + non-opioid combination analgesics (81, 95% CI 74-91), and first-generation cephalosporins (204, 95% CI 175-246).

Conclusions

Using high-throughput sequence symmetry analysis screening, we identified previously known prescribing cascades as well as potentially new prescribing cascades based on known and unknown statin-related adverse events.

Disponible en: https://doi.org/10.1002/pds.5607

Revista Española

Terapia farmacológica en la prevención secundaria del ictus isquémico en los muy ancianos: ¿ha mejorado en las últimas décadas?

L. Castilla-Guerraa,b, M.C. Fernández-Morenob,c, M.L. González-Iglesiasa, J. Boceta-Osunab,d, B. Gutiérrez-Gutiérrezb,d, M.D. Jiménez-Hernándezb,e

Introducción

El envejecimiento poblacional ha provocado un aumento de los ictus en los pacientes muy ancianos (PMA). Valoramos cómo ha cambiado la prevención secundaria del ictus isquémico en PMA en las últimas décadas.

Método

Estudio retrospectivo de las altas por ictus isquémico en los hospitales Virgen Macarena, Virgen del Rocío y Virgen de Valme de Sevilla (España), durante los períodos 1999-2001, 2014-2016 y 2019-2020. Se consideró PMA ≥ 80 años.

Resultado

Estudiamos a 1.806 pacientes, de los cuales 349 (19,3%) eran PMA. Con los años se han duplicado los PMA (13,5% vs. 25,9% y 28%; p=0,0001) y aumentado la edad (83,3±3 vs. 84,1±3 vs. 85,2±4; p=0,001). Comparando los períodos, los PMA tienen más hipertensión (69,9 vs. 84,8% vs. 84,6%; p=0,0001) y dislipidemia (12 vs. 41,7% vs. 52,3%; p=0,0001) y tienen prescritos más antihipertensivos (69,1% vs. 86,7% vs. 92,3%; p=0,0001), estatinas (5,3% vs. 78% vs. 81,5%; p=0,0001) y anticoagulantes (16,5% vs. 19,4% vs. 53,1%; p=0,001); también ha aumentado el número de antihipertensivos (1±0,9 vs. 1,6±0,9 vs. 1,9±0,8 fármacos; p=0,0001) y de estatinas de alta intensidad (2,3% vs. 42,7% vs. 69,2%; p=0,0001). Comparando los PMA con pacientes más jóvenes, no hubo diferencias en el tratamiento antihipertensivo en ningún período, aunque sí hubo diferencias en el tratamiento antitrombótico en el primer período y con las estatinas las diferencias se mantuvieron hasta el final.

Conclusiones

En los últimos 20 años el número de PMA se ha duplicado y supera la cuarta parte de las altas. Aunque existe mejoría en la prevención secundaria del ictus en los PMA, existe margen de mejora.

Disponible en: 10.1016/j.rce.2023.01.003