

REVISIÓN BIBLIOGRÁFICA JUNIO 2022: Selección de artículos

REVISTAS FARMACÉUTICAS

Drug safety

Incidence, Pathogenesis, and Management of Proton Pump Inhibitor-Induced Nephrotoxicity

[Xiao Wei, Jun Yu, Zhengkun Xu, Chun Wang, Yonggui Wu](#)

Abstract

Proton pump inhibitors are widely used in the treatment of various acid-related diseases and are among the most commonly used drugs. Studies estimate that 25–70% of proton pump inhibitors are prescribed for inappropriate treatments, doses, and indications, where the benefits of proton pump inhibitor use may be less than the risk of adverse drug reactions for many patients. Acute interstitial nephritis is an immune-mediated atypical kidney injury in the long-term use of proton pump inhibitors that causes problems for clinicians and patients. In this review, we summarize the current knowledge of proton pump inhibitors inducing acute interstitial nephritis, chronic kidney disease, and even end-stage renal disease in terms of incidence, pathogenesis, factors, clinical features, and diagnosis. We discuss how these factors change under conditions of acute interstitial nephritis, chronic kidney disease, and end-stage renal disease. The purpose of this review is to assess the current evidence to help clinicians and patients interpret the potential causal relationship between proton pump inhibitor intake and nephrotoxicity. This prompts clinicians to consider the appropriate dose and duration of proton pump inhibitor therapy to avoid inappropriate use.

European Journal of Clinical Pharmacology

Exploring heterogeneities of cardiovascular efficacy and effectiveness of SGLT2 inhibitors in patients with type 2 diabetes: an umbrella review of evidence from randomized clinical trials versus real-world observational studies

[Bojung Seo, Jialin Su, Yiqing Song](#)

Purpose

We aimed to explore possible contributors to discrepancies between randomized controlled trials (RCTs) and real-world observational studies (OS) in cardiovascular benefits of sodium-glucose cotransporter 2 (SGLT2) inhibitors in type 2 diabetes (T2D) patients.

Methods

We searched PubMed and EMBASE to identify meta-analyses of RCTs and OS on cardiovascular effects of SGLT2 inhibitors in T2D patients. Cardiovascular outcomes included major adverse cardiovascular events (MACE), myocardial infarction (MI), stroke, cardiovascular mortality (CVM), all-cause mortality (ACM), hospitalization for heart failure (HHF), and atrial fibrillation (AF). We examined the summary relative risk (RR) and 95% confidence interval (CI) for each endpoint from meta-analyses of RCTs.

Results

We identified and included 15 eligible meta-analyses, 13 for RCTs and 2 for OS, with moderately strong evidence. The results revealed a significant discrepancy between RCTs and OS for MI (RR, 95% CI 1.05, 0.82–1.38; $I = 91.5\%$ versus odds ratio (OR), 95% CI 0.77, 0.73–0.81; $I = 15.0\%$), stroke (RR, 95% CI 0.99, 0.76–1.29; $I = 93.4\%$ versus OR, 95% CI 0.75, 0.72–0.78; $I = 23.0\%$), and AF (RR, 95% CI 0.72, 0.62–0.85; $I = 0.0\%$ versus OR, 95% CI 0.92, 0.83–1.02; $I = 0.0\%$).

Conclusion

OS presented significant benefits of SGLT2 inhibitors both on primary and secondary preventions of MACE, MI, stroke, ACM, CVM, and HHF; RCTs did not. Given the spectrum of T2D patient characteristics and the strength of overall evidence, our review underscored the importance of constant integration of all available information and critical interpretation of all inconsistencies to optimize evidence-based diabetes care.

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The Annals of Pharmacotherapy

The Impact of a Diabetes Transitions of Care Clinic on Hospital Utilization and Patient Care

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Abstract

Background

There is currently limited guidance from the American Diabetes Association regarding transitions of care for patients with diabetes.

Objective

This study's aim was to determine the impact of a diabetes-specific transitions of care clinic (TOCC) on hospital utilization and patient outcomes in recently discharged patients with diabetes.

Methods

This retrospective study evaluated patients seen by TOCC as compared with similar patients discharged from the study institution the year prior. The primary outcome was a composite of the number of unique patients with readmissions/emergency department (ED) visits within 30 days of discharge. Secondary outcomes included a subcomponent analysis of readmissions/ED visits, index hospital length of stay (LOS), and to describe clinical interventions made in clinic. This study was approved by the institutional review board of the Office of Responsible Research Practice at the Ohio State University Wexner Medical Center.

Results

There were 165 patients in the TOCC group and 157 in the control group based on the matching criteria. There was a statistically significant decrease in the primary outcome in the TOCC group versus the control group (18% vs 36%, $P < 0.001$). In evaluation of its subcomponents, there was a statically significant decrease in patients with readmissions (11% vs 26%, $P < 0.001$) but not ED visits (10% vs 17%, $P = 0.096$). The LOS for the TOCC group was shorter at 4 days versus 5 days in the control group ($P = 0.055$).

Conclusions and Relevance

The implementation of a diabetes-specific TOCC can decrease both readmissions and ED visits and may impact hospital LOS. In addition, a TOCC can be used to identify gaps in preventive care. The results from this study may help support the creation of similar TOCC at other institutions.

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Pharmacoepidemiology and Drug Safety

Antibacterial-associated acute kidney injury among older adults: A post-marketing surveillance study using the FDA Adverse Events Reporting System

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Abstract

Purpose

Antibacterials induce a differential risk of acute kidney injury (AKI) in older adults. This study investigated the reporting risk of AKI associated with antibacterials using the individual case safety reports (ICSRs) submitted to the Food and Drug Administration Adverse Event Reporting System (FAERS) database.

Methods

A case/non-case method was used to assess AKI risk associated with antibacterials between January 1, 2000, and September 30, 2021. Cases were ICSRs for antibacterials with AKI as preferred terms included in the Medical Dictionary of Regulatory Activities (MedDRA) system organ classes 'Renal and urinary disorders' disorders. The analyses were completed on a de-duplicated dataset containing only the recent version of the ICSR. Signals were defined by a lower 95% confidence interval (CI) of reporting odds-ratio (ROR) ≥ 2 , proportional reporting ratio (PRR) ≥ 2 , information component (IC) > 0 , Empirical Bayes Geometric Mean (EBGM) > 1 , and reports ≥ 4 . Sensitivity analyses were conducted a priori to assess the robustness of signals.

Results

A total of 3,680,621 reports on ADEs were retrieved from FAERS over the study period, of which 92,194 were antibacterial reports. Gentamicin, sulfamethoxazole, trimethoprim, and vancomycin consistently gave strong signals of disproportionality on all four disproportionality measures and across the different sensitivity analyses: gentamicin (ROR = 2.95[2.51-3.46]), sulfamethoxazole (ROR = 2.97[2.68-3.29]), trimethoprim (ROR = 2.81[2.29-3.46]), and vancomycin (ROR = 3.35[3.08-3.64]).

Conclusion

Signals for gentamicin, sulfamethoxazole, trimethoprim, and vancomycin were confirmed by using antibacterials as a comparator, adjusting for drug-related competition bias and event-related competition bias.

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Initiation of antidepressant medication in people with type 2 diabetes living in the United Kingdom—A retrospective cohort study

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Abstract

Introduction

Depression is a common comorbidity in people with type 2 diabetes and it is associated with poorer outcomes. There is limited data on the treatments used for depression in this population. The aim of this study was to explore the rates of initiation of antidepressant prescriptions in people with type 2 diabetes in the UK and identify those most at risk of needing such treatment.

Research Design and Methods

This was a retrospective cohort study using data from IQVIA Medical Research Data (IMRD)-UK data. Data from general practices in IMRD-UK between January 2008 and December 2017 were used for this study.

Results

The overall rates of antidepressant prescribing were stable over the study period. The rate of initiation of antidepressant medication in people with type 2 diabetes was 22.93 per 1000 person years at risk (PYAR) with a 95%CI 22.48 to 23.39 compared to 16.89 per 1000 PYAR (95%CI 16.77 to 17.01) in an age and gender matched cohort.

The risk of being prescribed antidepressant medication with age had a U-shaped distribution with the lowest risk in the 65–69 age group. The peak age for antidepressant initiation in men and women was 40–44, with a rate in men of 32.78 per 1000 PYAR (95% CI 29.57 to 36.34) and a rate in women of 46.80 per 1000 PYAR (95% CI 41.90 to 52.26). People with type 2 diabetes with in the least deprived quintile had an initiation rate of 19.66 per 1000 PYAR (95%CI 18.67 to 20.70) compared to 27.19 per 1000 PYAR (95%CI 25.50 to 28.93) in the most deprived quintile, with a 32% increase in the risk of starting antidepressant medication (95%CI 1.22 to 1.43).

Conclusions

People with type 2 diabetes were 30% more likely to be started on antidepressant medication than people without type 2 diabetes. Women with type 2 diabetes were 35% more likely than men to be prescribed antidepressants and the risks increased with deprivation and in younger or older adults, with the lowest rates in the 65–69 year age band. The rates of antidepressant prescribing were broadly stable over the 10-year period in this study. The antidepressant medications prescribed changed slightly over time with sertraline becoming more widely used and fewer prescriptions of citalopram.

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International Journal of Clinical Pharmacy

European Society of Clinical Pharmacy definition of the term clinical pharmacy and its relationship to pharmaceutical care: a position paper

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Abstract

Many definitions of the term clinical pharmacy exist, but a number of ambiguities remain. In order to clarify the European Society of Clinical Pharmacy (ESCP) position on what defines clinical pharmacy, a consultation exercise was conducted among ESCP members with the findings used as the basis for an updated definition. The updated definition clarifies that clinical pharmacy (1) represents both a professional practice and field of research, (2) aims to optimise the utilisation of medicines in order to achieve person-centered and public health goals, (3) as a practice encompasses cognitive, managerial and interpersonal activities targeting all stages of the medicines use process, and as a field of research generates knowledge that informs clinical decision-making, health care organisation or policy, (4) as a practice is restricted to pharmacists, (5) can be practiced regardless of setting, and (6) encompasses pharmaceutical care but is not restricted to it.

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A Retrospective, Longitudinal External Study of the robustness and reproducibility of National Antibacterial Prescribing Survey Data

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Abstract

Background

Point prevalence surveys are used internationally to audit antibacterial use as well as the impact of interventions on improving prescribing and resistance rates. The annual National Antibacterial Prescribing Survey provides data on the appropriateness of antibacterial agent prescribing in Australian hospitals. Assessing the survey's robustness and result reproducibility is essential to its role in improving antibacterial prescribing practice.

Aim

To evaluate the reproducibility of internal assessments of antibacterial agent prescribing of both guideline compliance and appropriateness from a Western Australian hospital.

Method

Census data of 1051 prescriptions from 2013 to 2017 surveys were independently assessed for compliance based on Australian Therapeutic Guidelines - Antibiotics, and appropriateness, based on agent selection, therapy duration and microbiological test results. Concordance of these findings with internal hospital assessments was analysed.

Results

This external study did not reproduce internal hospital audit results for compliance with guideline parameters. Non-compliant prescribing rate was significantly ($p < 0.001$) higher externally at 50.7% (533/1051) than internal assessment at 34.9% (367/1051). External analysis also found a significantly smaller proportion of prescriptions to be appropriate (551/1051, 52.4%) compared to internal analysis (745/1051, 70.9%) $p < 0.001$. Cohen's Kappa analysis found a moderate agreement for compliance (0.49) and appropriateness (0.50) between the external and internal evaluations.

Conclusion

The lack of adequate reproducibility of compliance and appropriateness assessments may limit the generalisability of the audit's results. Validating point prevalence surveys that assess antibacterial agent prescribing can increase confidence and improve reproducibility of their findings; as they provide important data for antimicrobial stewardship programs.

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REVISTAS GERIÁTRICAS

Age and ageing

The impact of frailty on short-term mortality following primary total hip and knee arthroplasty due to osteoarthritis

[Michael J Cook, Mark Lunt, Timothy Board, Terence W O'Neill](#)

Abstract

Background

We determined the association between frailty and short-term mortality following total hip and knee arthroplasty (THA/TKA) for osteoarthritis and also the impact of THA/TKA on short-term mortality compared with a control population.

Methods

Frailty was assessed using a frailty index (categorised: fit, mild, moderate, severe frailty). The association between frailty and short-term mortality following THA/TKA was assessed using Cox regression. Mortality following THA/TKA was also compared with a control population with osteoarthritis but no previous THA/TKA, matched on year of birth, sex and quintile of index of multiple deprivation.

Results

A total of 103,563 cases who had a THA, 125,367 who had a TKA and matched controls contributed. Among those who had surgery, mortality increased with increasing frailty; adjusted hazard ratio (HR) (95% CI) at 30 days in severely frail versus fit: following THA, 2.85 (1.84, 4.39) and following TKA, 2.14 (1.29, 3.53). The predicted probability of 30-day mortality following THA/TKA varied by age, sex and frailty: following THA, from 0.05% among fit women aged 60–64 years to 6.55% among men with severe frailty aged ≥ 90 years. All-cause 30-day mortality was increased in fit cases following THA and TKA, respectively, versus fit controls (adjusted HR (95% CI), 1.60 (1.15, 2.21) and 2.98 (1.81, 4.89)), though not among cases with mild, moderate or severe frailty versus controls in the same frailty category.

Conclusion

Short-term mortality increased with increasing frailty following THA/TKA. Comparison of mortality among cases and controls may be affected by a 'healthy surgery' selection effect.

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[Apo protein E* \$\epsilon\$ 2 carriers exhibit high aspirin-treated platelet reactivity and low cardiovascular risk during long-term aspirin treatment](#)

[Xiao-Li Li, Qiang Wang, Guo-Dong Jia, Hui-Jun Yin, Yao-Hui Wang, Chao Hu, Xiao-Qing Wang, Yang Yang](#)

Objective

Apolipoprotein E (APOE) loci, including rs429358 (ϵ 4) and rs7412 (ϵ 2), are involved in cardiovascular (CV) health. However, their effect on the CV-protective effect of aspirin remains unknown.

Methods

A total of 515 aspirin-treated individuals with existing CV diseases were recruited, and their APOE genotypes, platelet functions and other routine laboratory parameters were assessed when they enrolled. The first major CV events (myocardial infarction, stroke, revascularisation and CV death) and all CV events (major CV events plus unstable angina and transient ischaemic attack) during a mean 5.2-year follow-up period were recorded.

Results

After adjusting for age, gender, BMI, lifestyle, lipid profiles and other CV drugs and comorbidities, $\epsilon 2$ carriers were found to exhibit ~80% lower risk of major CV and 60% lower risk of all CV (HR = 0.186, CI: 0.048–0.715, $P = 0.014$; HR = 0.435, CI: 0.234–0.812, $P = 0.009$, respectively) than $\epsilon 2$ noncarriers. Furthermore, high incidence of high platelet reactivity assessed by arachidonic acid-induced light transmission aggregometry (23.4 vs. 13.7%, $P = 0.038$), triglyceride and haemoglobin and low low-density lipoprotein were observed. $\epsilon 4$ carriers had slightly increased cholesterol and hypercholesterolemia incidence relative to $\epsilon 4$ noncarriers.

Conclusions

Our results demonstrated that APOE* $\epsilon 2$ carriers can derive additional CV benefit from long-term aspirin treatment. Moreover, it was observed that APOE2 interacts with cyclooxygenase-1 (COX-1) and upregulates its activity. The CV-protective effect of aspirin in $\epsilon 2$ carriers is likely attributed to APOE2 upregulating vascular COX-1-mediated CV protective pathway, together with aspirin partially inhibiting platelet COX-1-mediated platelet aggregation.

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Journal of the American Geriatrics Society

Prevalence of sarcopenia and mortality rate in older adults with hip fracture

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Abstract

Background

Several international study groups adopted appendicular skeletal muscle mass (ASM) index adjusted by (1) height squared, (2) weight, and (3) body mass index (BMI) in the diagnosis of sarcopenia. However, different prevalence rates of sarcopenia by each index and clinical implications were not well known. The purpose of this study was to compare the differences in (1) the percentage of sarcopenia in hip fracture patients and (2) the relative mortality rate according to the sarcopenia criteria of three ASM indices.

Methods

Between January 2009 and December 2020, 1003 older adult hip fracture patients at a tertiary institution were eligible and retrospectively reviewed for this study. Based on the ASM measured on dual-energy X-ray absorptiometry, three indices were calculated, and sarcopenia was diagnosed. The proportion of sarcopenia was evaluated according to each index. One, two, and five-year mortality rates were compared between each sarcopenia group and a normal musculature group, based on ASM criteria.

Results

The proportion of sarcopenia patients differed according to three ASM indices. The proportion of sarcopenic patients by ASM/height² index was higher than those of the other two indices in both male and female hip fracture patients. In male patients, 61% were sarcopenic by ASM/height² index, 37% by ASM/weight index, and 44% by ASM/BMI index. In female patients, 26%, 11%, and 14% were sarcopenic, respectively. Among the three indices, only ASM/height² had significant correlations with all 1-, 2-, and 5-year mortality rates.

Conclusions and Implications

The prevalence of sarcopenia in hip fracture patients differed substantially according to ASM indices. Sarcopenic hip fracture patients had a higher mortality rate than those with normal musculature. The 1-year, 2-year, and 5-year mortality rates were discriminated by ASM/height² criteria in both men and women. Future prospective studies in a larger cohort are warranted.

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International Journal of Geriatric Psychiatry

Biweekly fluctuations of neuropsychiatric symptoms according to the Neuropsychiatric Inventory: Erratic symptoms or scores?

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Objectives

This study investigates the stability of neuropsychiatric symptoms (NPS) assessed biweekly using the Neuropsychiatric Inventory (NPI) in a memory clinic population during a six week period.

Methods

Twenty-three spousal caregivers (mean [SD] age=69.7[8.8], 82.6% women) of 23 patients (43.5% had dementia) completed all assessments. The NPI was assessed four times during six weeks. We examined whether NPI domains were present during all four assessments, studied within-person variation for each NPI domain, and calculated Spearman's correlations between subsequent time-points. Furthermore, we associated repeated NPI assessments with repeated measures of caregiver burden to examine the clinical impact of changes in NPI scores over time.

Results

The course of NPS was highly irregular according to the NPI, with only 35.8% of the NPI domains that were present at baseline persisted during all six weeks. We observed large within-person variation in the presence of individual NPI domains (61.3%, range 37.5-83.9%) and inconsistent correlations between NPI assessments (e.g. range $r_s=0.20-0.57$ for agitation, range $r_s=0.29-0.59$ for anxiety). Higher NPI total scores were related to higher caregiver burden ($r_s=0.60$, $p<0.001$), but changes in NPI total scores were unrelated to changes in caregiver burden ($r_s=0.16$, $p=0.20$).

Conclusions

We observed strong fluctuations in NPI scores within very short time windows raising the question whether this represents erratic symptoms and/or scores. Further studies are needed to investigate the origins of these fluctuations.

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Reduced Kidney Function is Associated with Poorer Domain-Specific Cognitive Performance in Community-Dwelling Older Adults

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Objectives

Whilst chronic kidney disease (CKD) has been associated with cognitive impairment, the association between reduced estimated Glomerular Filtration Rate (eGFR) and domain-specific cognitive performance is less clear and may represent an important target for the promotion of optimal brain health in older adults.

Methods

Participants aged >60 years from the Trinity-Ulster-Department of Agriculture (TUDA) study underwent detailed cognitive assessment using the Mini-Mental State Examination (MMSE), Frontal Assessment Battery (FAB) and Repeatable Battery for Assessment of Neuropsychological Status (RBANS). Poisson and linear regression models assessed the relationship between eGFR strata and cognitive performance.

Results

In 4,887 older adults (73.9 ± 8.3 years; 67.7% female), declining eGFR strata was associated with greater likelihood of error on the MMSE/FAB and poorer overall performance on the RBANS. Following robust covariate adjustment, findings were greatest for GFR <45ml/mL/1.73m² (Incidence Rate Ratio [IRR]: 1.17; 95% CI 1.08,1.27 ; p<0.001 for MMSE; IRR: 1.13; 95% CI 1.04, 1.13; p<0.001 for FAB; β: -3.66; 95% CI -5.64, -1.86; p<0.001 for RBANS). Additionally, eGFR <45ml/mL/1.73m² was associated with poorer performance on all five RBANS domains, with greatest effect sizes for immediate memory, delayed memory and attention. Associations were strongest in those aged 60-70, with no associations observed in those >80 years.

Conclusions

Reduced kidney function was associated with poorer global and domain-specific neuropsychological performance. Associations were strongest with eGFR <45 ml/min/1.73m² and in those aged 60-70 years, suggesting that this population may potentially benefit from potential multi-domain interventions aimed at promoting optimal brain health in older adults.

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