

REVISIÓN BIBLIOGRÁFICA OCTUBRE 2020: Selección de artículos

REVISTAS GERIÁTRICAS

BMC Geriatrics

Health-related quality of life in hospitalized older patients with versus without prolonged use of opioid analgesics, benzodiazepines, and z-hypnotics: a cross-sectional study

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Background

Central nervous system depressant medications (CNSDs) such as opioid analgesics and sedative-hypnotics are commonly prescribed to older patients for the treatment of chronic pain, anxiety and insomnia. Yet, while many studies reported potential harms, it remains unknown whether persistent use of these medications is beneficial for older patients' self-reported health-related quality of life (HRQoL). The present study clarified this knowledge gap through comparing HRQoL of hospitalized older patients with versus without using CNSD drugs for ≥ 4 weeks. Moreover, we explored the relationship between such use and HRQoL, adjusting for the effects of polypharmacy, comorbidity burden and other clinically relevant covariates.

Methods

The study was cross-sectional and included 246 older patients recruited consecutively from somatic departments of a large regional university hospital in Norway. We defined prolonged CNSD use as using opioids, benzodiazepines and/or z-hypnotics for ≥ 4 weeks. Patients' self-reported HRQoL were measured with scales of the EuroQol EQ-5D-3L instrument. Data analyses were mainly descriptive statistics and regression models.

Results

Patients with prolonged use of CNSDs reported lower scores on both EQ-5D index and EQ VAS compared with those without such use ($p < 0.001$). They had higher odds of having more problems performing usual activities (OR = 3.37, 95% CI: 1.40 to 8.13), pain/discomfort (OR = 2.06, 95% CI: 1.05 to 4.04), and anxiety/depression (OR = 3.77, 95% CI: 1.82 to 7.82).

In multivariable regression models, there was no significant association between prolonged CNSD use and HRQoL when including pain as a predictor variable. In models not including pain, CNSD use was strongly associated with HRQoL (adjusted for sociodemographic background, polypharmacy, comorbidity, anxiety and depressive symptoms, regression coefficient – 0.19 (95% CI, – 0.31 to – 0.06).

Conclusions

Older patients with prolonged CNSD use reported poorer HRQoL. They also had more pain and higher depression scores. Prolonged use of CNSDs was not independently associated with higher HRQoL.

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The associations of the number of medications and the use of anticholinergics with recovery from tubal feeding: a longitudinal hospital-based study

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Background

Several medications, such as anticholinergics, are considered to affect the swallowing function adversely; however, whether or not anticholinergics or polypharmacy should be avoided to prevent eating dysfunction in elderly populations remains unclear. We therefore examined whether or not the number of medications or the use of anticholinergics was associated with recovery from tubal feeding in elderly inpatients.

Methods

We conducted a retrospective 1-year observation study in 95 Japanese hospitalized patients (83.3 ± 9.7 years old) receiving nutrition through a feeding tube. The anticholinergic cognitive burden scale (ACBs) was used as an index for quantifying the anticholinergic action.

Results

Thirty-six (37.9%) subjects recovered from tubal to oral feeding during the observation period. The logistic regression models showed that an increased number of prescribed medications and an increase in ACBs decreased the incidence of recovery from tubal feeding (odds ratio [95% confidence interval]: 0.66 [0.50–0.87], $P = 0.003$ and 0.52 [0.29–0.92], $P = 0.024$, respectively). Furthermore, the cumulative incidence of recovery from tubal feeding was significantly lower in the subjects who were given an additional ≥ 3 medications during the observation period than in those who were not (hazard ratio [95% confidence interval]: 0.08 [0.01–0.59], $P = 0.014$).

Conclusions

The findings of this study suggest that an increased exposure to medications, especially anticholinergics, may be an important factor interfering with recovery from tubal feeding in hospitalized elderly patients.

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Drugs and Aging

Anticholinergic Burden and Fractures: A Systematic Review with Methodological Appraisal

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Introduction

Medications with anticholinergic activity (MACs) are used to treat diseases common in older adults. Evidence on the association between anticholinergic burden (AB) and increased risk of fractures and osteoporosis or reduced bone mineral density (BMD) is inconsistent. Our aim was to conduct a systematic review of observational studies on AB with fractures and osteoporosis or reduced BMD and provide methodological appraisal of included studies.

Methods

We searched MEDLINE, EMBASE, Science Citation Index and CENTRAL as well as grey literature from database inception up to August 2020. Eligibility criteria were: observational design, AB-exposure measured through a scale, fracture of any type or osteoporosis or reduced BMD as outcome, and reported measure of association between exposure and outcome. No restrictions related to time, language or type of data were applied. Eligibility and risk of bias assessment as well as data extraction were performed independently by two reviewers. Risk of bias of the included studies was assessed using the Newcastle–Ottawa Scale and the RTI Item Bank.

Results

The majority of the nine included studies had low risk of bias but heterogeneous methodology. No study used a new user design. Seven studies reported an increased risk of fractures associated with AB. In four studies using the Anticholinergic Risk Scale (ARS), adjusted risk of fractures was increased by 2–61% for ARS = 1, by 0–97% for ARS = 2, by 19–84% for ARS = 3, and by 56–96% for ARS \geq 4; in three studies the ARS was aggregated, risk increased by 39% for ARS = 1–2 and 17% for ARS = 2–3. Two studies reported increased risk of fractures of 14 and 52% in the highest AB-category and one study reported that change in ARS of \geq 3 during hospitalization was associated with a 321% increased risk in fractures. Two studies did not find an association between AB and fractures. The association between AB and osteoporosis or reduced BMD could only be

assessed in two studies, one reporting increased risk of lower BMD at Ward's triangle, the other reporting no association between AB and BMD T-score change at the femoral neck.

Discussion

Our study suggests an association between AB and increased risk of fractures with possible dose-exposure gradient in studies using the ARS. The low number of studies and heterogeneity of methods calls for the conduct of more studies.

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European Geriatric Medicine

Unreported urinary incontinence: population-based prevalence and factors associated with non-reporting of symptoms in community-dwelling people ≥ 50 years

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Purpose

Concerns exist around under-detection and under-treatment of urinary incontinence (UI) in specific patient groups, particularly older people. The aim of this study is to ascertain the prevalence of unreported UI in a large sample of older adults, to profile factors associated with under-reporting of UI and the association of unreported UI with quality of life (QOL).

Methods

This study was embedded within the Irish Longitudinal Study on Ageing, involving a population-representative sample of almost 7,000 older adults (55% female, mean age 65 years). UI was defined as involuntary loss of urine from the bladder occurring on average at least twice per month. Unreported UI had not yet been reported to a healthcare professional. QOL was measured using the Control, Autonomy, Self-realisation and Pleasure-19 Scale (CASP-19).

Results

Almost 40% (285/750) of participants with UI had not reported symptoms to a healthcare professional despite visiting their general practitioner (GP) on average over 4 times in the last year. Logistic regression modelling demonstrated that under-reporting of UI was associated with female sex, taking < 5 medications, less severe symptoms and lower number of GP visits. Linear regression models show that unreported UI was associated with significantly lower CASP-19 ($\beta = -1.20$ (95% CI: -2.19 to -0.20)).

Conclusion

Only 40% of older people with UI report symptoms to a healthcare professional despite frequent symptoms, and a significant association with poorer QOL. This highlights the need to educate older people around seeking help for UI, as well as opportunistically addressing UI as part of comprehensive age-attuned care.

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Journal of gerontology A biol sci med sci

Long-term Effects of Calcium β -Hydroxy- β -Methylbutyrate and Vitamin D3 Supplementation on Muscular Function in Older Adults With and Without Resistance Training: A Randomized, Double-blind, Controlled Study

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Abstract

The primary aim of this study was to determine whether supplementation with calcium β -hydroxy- β -methylbutyrate (HMB) and vitamin D3 (D) would enhance muscle function and strength in older adults. Older adults over 60 years of age with insufficient circulating 25-hydroxy-vitamin D (25OH-D) levels were enrolled in a double-blinded controlled 12-month study. Study participants were randomly assigned to treatments consisting of: (a) Control + no exercise, (b) HMB+D + no exercise, (c) Control + exercise, and (d) HMB+D + exercise. The study evaluated 117 participants via multiple measurements over the 12 months that included body composition, strength, functionality, and questionnaires. HMB+D had a significant benefit on lean body mass within the nonexercise group at 6 months (0.44 ± 0.27 kg, HMB+D vs -0.33 ± 0.28 kg, control, $p < .05$). In nonexercisers, improvement in knee extension peak torque ($60^\circ/s$) was significantly greater in HMB+D-supplemented participants than in the nonsupplemented group ($p = .04$) at 3 months, 10.9 ± 5.7 Nm and -5.2 ± 5.9 Nm, respectively. A composite functional index, integrating changes in handgrip, Get Up, and Get Up and Go measurements, was developed. HMB+D + no exercise resulted in significant increases in the functional index compared with those observed in the control + no exercise group at 3 ($p = .03$), 6 ($p = .04$), and 12 months ($p = .04$). Supplementation with HMB+D did not further improve the functional index within the exercising group. This study demonstrated the potential of HMB and vitamin D3 supplementation to enhance muscle strength and physical functionality in older adults, even in individuals not engaged in an exercise training program.

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Journal of the American Geriatrics Society

Low Vitamin D Levels and Risk of Incident Delirium in 351,000 Older UK Biobank Participants

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Abstract

BACKGROUND/OBJECTIVES

Delirium is common in older adults, especially following hospitalization. Because low vitamin D levels may be associated with increased delirium risk, we aimed to determine the prognostic value of blood vitamin D levels, extending our previous genetic analyses of this relationship.

DESIGN

Prospective cohort analysis.

SETTING

Community-based cohort study of adults from 22 cities across the United Kingdom (the UK Biobank).

PARTICIPANTS

Adults aged 60 and older by the end of follow-up in the linked hospital inpatient admissions data, up to 14 years after baseline (n = 351,320).

MEASUREMENTS

At baseline, serum vitamin D (25-OH-D) levels were measured. We used time-to-event models to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) for the association between vitamin D deficiency and incident hospital-diagnosed delirium, adjusted for age, sex, assessment month, assessment center, and ethnicity. We performed Mendelian randomization genetic analysis in European participants to further investigate vitamin D and delirium risk.

RESULTS

A total of 3,634 (1.03%) participants had at least one incident hospital-diagnosed delirium episode. Vitamin D deficiency (<25 nmol/L) predicted a large incidence in delirium (HR = 2.49; 95% CI = 2.24–2.76; P = 3*10⁻⁶⁸, compared with >50 nmol/L). Increased risk was not limited to the deficient group: insufficient levels (25–50 nmol/L) were also at increased risk (HR = 1.38; 95% CI = 1.28–1.49; P = 4*10⁻¹⁸). The association was

independent of calcium levels, hospital-diagnosed fractures, dementia, and other relevant cofactors. In genetic analysis, participants carrying more vitamin D-increasing variants had a reduced likelihood of incident delirium diagnosis (HR = .80 per standard deviation increase in genetically instrumented vitamin D: .73–.87; $P = 2 \times 10^{-7}$).

CONCLUSION

Progressively lower vitamin D levels predicted increased risks of incident hospital-diagnosed delirium, and genetic evidence supports a shared causal pathway. Because low vitamin D levels are simple to detect and inexpensive and safe to correct, an intervention trial to confirm these results is urgently needed.

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REVISTAS FARMACÉUTICAS

British Journal of Clinical Pharmacology

Exposure–response relationships of dapagliflozin on cardiorenal risk markers and adverse events: A pooled analysis of 13 phase II/III trials

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Abstract

Aims

Dapagliflozin is a sodium–glucose co-transporter 2 inhibitor that has been developed as oral glucose lowering drug. The original dose-finding studies focused on optimal glycaemic effects. However, dapagliflozin also affects various cardiorenal risk markers and provides cardiorenal protection. To evaluate whether the currently registered doses of 5 and 10 mg are optimal for cardiorenal efficacy and safety, we characterized the relationship between dapagliflozin exposure and nonglycaemic cardiorenal risk markers as well as adverse events.

Methods

Data were obtained from a pooled database of 13 24-week randomized controlled clinical trials of the clinical development programme of dapagliflozin. The exposure–response relationship was quantified using population pharmacodynamic and repeated time-to-event models.

Results

A dose of 10 mg dapagliflozin resulted in an average individual exposure of 638 ng h/mL (95% prediction interval [PI]: 354–1061 ng h/mL), which translated to 71.2% (95% PI: 57.9–80.5%),

61.1% (95% PI: 58.0–64.8%), 91.3% (95% PI: 85.4–94.6%) and 25.7% (95% PI: 23.5–28.3%) of its estimated maximum effect for fasting plasma glucose, haematocrit, serum creatinine and urinary albumin–creatinine ratio, respectively.

Conclusion

We demonstrate that doses higher than 10 mg could provide additional beneficial effects in haematocrit, systolic blood pressure, urinary albumin–creatinine ratio and uric acid, without obvious increases in the rate of adverse events. These results raise the question whether future outcome studies assessing the benefits of higher than currently registered dapagliflozin doses are merited.

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European Journal of Hospital Pharmacy

Deprescribing practices for anticonvulsants after benign seizures secondary to high-dose tranexamic acid in a single, large UK cardiothoracic centre.

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Abstract

Objective High-dose tranexamic acid (TXA) can cause seizures in patients who have undergone pulmonary endarterectomy (PTE). Seizures secondary to TXA will resolve once the drug is excreted from the body, and the patients do not have to be on long-term anticonvulsants. The aim of the study is to find out if medication review in the hospital has led to deprescribing of anticonvulsants for TXA-associated seizures on discharge from the critical care unit (CCU) and hospital.

Methods This is a single-centre retrospective study conducted at a tertiary cardiothoracic hospital between 2012 and 2017. The inclusion criteria consisted of all adult patients who have undergone PTE surgery. Patients who were started on anticonvulsants preoperatively or postoperatively for seizures secondary to organic causes were excluded.

Results A total of 933 patients underwent PTE from January 2012 to August 2017. 25 patients had TXA-related seizures postoperatively and were started on anticonvulsant therapy, giving an incidence of 2.7%. 15 patients were discharged from the CCU without anticonvulsants. A further three patients had their anticonvulsants deprescribed in the ward before being discharged from the hospital.

Conclusion Deprescribing of anticonvulsants after benign seizures secondary to high-dose TXA is facilitated by verbal and written handover, which can be improved in our hospital. A detailed handover summary, as well as a discharge letter with clearly defined instructions for drug review, is needed to make deprescribing a more robust process.

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The Annals of Pharmacotherapy

Direct Oral Anticoagulants in Select Patients With Hypercoagulable Disorders

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Abstract

Objective: To summarize the literature assessing the safety and efficacy of direct oral anticoagulants (DOACs) for the acute treatment and secondary prevention of venous thromboembolism (VTE) in select patients with hypercoagulable disorders.

Data Sources: An electronic PubMed literature search was conducted from January 2010 to July 2020 using the following keywords: DOAC, rivaroxaban, apixaban, dabigatran, edoxaban, thrombophilia, cancer, antiphospholipid syndrome, protein C deficiency, protein S deficiency, antithrombin deficiency, factor V Leiden, prothrombin G20210A gene mutation, congenital thrombophilia, hypercoagulable, hereditary thrombophilia, acquired thrombophilia.

Study Selection and Data Extraction: Articles were included if they reported clinical outcomes associated with cancer-associated VTE, antiphospholipid syndrome (APS), and other hereditary thrombophilias.

Data Synthesis: The safety and efficacy of using a DOAC is highly dependent on the type of hypercoagulable disease state. Current trials support the use of edoxaban, rivaroxaban, and apixaban for the treatment of cancer-associated thrombosis (CAT), with apixaban being preferred because of lower bleeding rates compared with standard of care. The use of DOACs, especially rivaroxaban, have been associated with worse outcomes in patients with APS, whereas data on DOAC use in hereditary thrombophilia remains scarce and limited to low-risk patients.

Relevance to Patient Care and Clinical Practice: This review evaluates the literature assessing the safety and efficacy of DOACs in patients with various hypercoagulable disorders.

Conclusions: The current body of evidence supports the use of select DOACs for the treatment of CAT. In contrast, DOAC use in patients with APS and hereditary thrombophilia should be avoided at this time

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Direct Oral Anticoagulant Use in Chronic Kidney Disease and Dialysis Patients With Venous Thromboembolism: A Systematic Review of Thrombosis and Bleeding Outcomes

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Melissa Lefebvre, BSc, MSBio, Claudia Summa-Sorgini, BSc Phm, Marisa Battistella, BSc, BScPhm, Pharm D 

Abstract

Objective:

To evaluate how treatment with DOACs for VTE affects thrombosis and bleeding outcomes compared to warfarin in CKD and dialysis patients.

Data Sources:

A literature search was conducted for studies evaluating VTE and bleeding outcomes with DOAC use in CKD and dialysis patients. Searches conducted through EMBASE, MEDLINE/PubMed, Scopus, and Cochrane Central Register of Controlled Trials, from inception to September 22, 2020.

Study Selection and Data Extraction:

Randomized controlled trials, cohort studies, and case series with ≥ 10 patients included.

Data Synthesis:

From 7286 studies, nine studies met inclusion criteria. There was no significant difference between DOACs (dabigatran, rivaroxaban, apixaban) and warfarin for reducing recurrent VTE and bleeding events in moderate CKD patients. The risk of overall major bleeding increased when the degree of kidney impairment increased. There was no significant difference between apixaban and warfarin for VTE outcomes in dialysis patients.

Relevance to Patient Care and Clinical Practice:

There continues to be a controversial debate whether it may be more beneficial to use DOACs versus warfarin in CKD/dialysis patients with venous thromboembolism (VTE). The risk vs benefit of using DOACs in the CKD/ESKD population should continue to be evaluated for each individual patient.

Conclusion:

Apixaban may be used cautiously as an alternative in acute VTE treatment in severe CKD patients. Insufficient evidence is available to suggest the use of dabigatran and rivaroxaban in this patient population. The benefit of using DOACs in this population for VTE treatment should be weighed against the potential bleeding risk in patients with CKD.

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The Senior Care Pharmacist (American Society of Consultant Pharmacists)

High-Risk Medication Use in Older Residents of Long-Term Care Facilities: Prevalence, Harms, and Strategies to Mitigate Risks and Enhance Use

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Abstract

Older residents of long-term care facilities (LTCFs), also known as nursing homes, care homes, or residential aged care facilities, often have multiple health conditions and are exposed to polypharmacy. Use of high-risk medications such as opioids, glucose-lowering medications, antithrombotics, and antipsychotics is prevalent among residents of LTCFs. Ensuring appropriate use of high-risk medications is important to minimize the risk of medication-related harm in this vulnerable population. This paper provides an overview of the prevalence and factors associated with high-risk medication use among residents of LTCFs. Evidencebased strategies to optimize the use of high-risk medications and enhance resident outcomes are also discussed.

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International Journal of Clinical Pharmacy

Dipeptidyl peptidase-4 inhibitors and risk of venous thromboembolism: data mining of FDA adverse event reporting system

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Abstract

Background

A recent study is raising concerns that dipeptidyl peptidase 4 inhibitors are associated with increased risk of venous thromboembolism.

Objective

We aimed to assess the association between dipeptidyl peptidase-4 inhibitors and venous thromboembolism using the US Food and Drug Administration Adverse Event Reporting System database.

Methods

We searched the venous thromboembolism cases related to dipeptidyl peptidase-4 inhibitors from 2004 first quarter to 2018 first quarter. We compared dipeptidyl peptidase-4 inhibitors versus three groups: (1) all other glucose-lowering drugs excluding insulins; (2) sulfonylureas and sodium-glucose-cotransporter-2 inhibitors; (3) sodium-glucose-cotransporter-2 inhibitors. In each comparison, we calculated proportional rate ratios and 95% confidence ratios by SAS 9.4.

Results

We obtained 873 dipeptidyl peptidase-4 inhibitors-associated venous thromboembolism events. Compared to all other glucose lowering-drugs excluding insulins, the proportional reporting ratio for overall venous thromboembolism, deep vein thrombosis, pulmonary embolism were 0.92 (0.86, 0.99), 0.91 (0.82,1.01), and 0.82 (0.74,0.90), respectively; the proportional reporting ratio for portal vein thrombosis, splenic vein thrombosis, mesenteric vein thrombosis were 3.94 (2.96, 5.25), 10.80 (6.14, 18.99), and 4.98 (2.76,8.96), respectively.

Conclusion

Our analysis found no association between dipeptidyl peptidase-4 inhibitors and venous thromboembolism risk, while moderate to strong signals of portal vein thrombosis, splenic vein thrombosis, mesenteric vein thrombosis risks were observed.

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Deprescribing in geriatric inpatients is associated with a lower readmission risk: a case control study

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Abstract

Background Polypharmacy is prevalent in older adults and has been associated with iatrogenic harm. Deprescribing has been promoted to reduce polypharmacy. It remains however unclear whether deprescribing during hospital stay can reduce the readmission risk. **Objective** We sought to determine whether deprescribing in geriatric inpatients was associated with a lower readmission risk at three months post-discharge. **Method** A case control study was performed, using data from a prospective, controlled study in geriatric inpatients. Deprescribing was defined as the percentage of discontinued preadmission medications and was assessed upon discharge. A logistic regression analysis was used to determine the odds ratio for deprescribing and the outcome of readmissions. An adjusted odds ratio was then estimated, taking into account age, sex, mortality, the number of preadmission medications and the Charlson Comorbidity Index. **Results** Data of 166 patients were analysed, of whom 61 had experienced at least one readmission. Adjusting for age, number of preadmission medications and mortality resulted in the most informative regression model, based on the lowest Akaike information criterion (adjusted odds ratio 0.981, 95% confidence interval 0.964 to 0.998). **Conclusion** Deprescribing in geriatric inpatients was associated with a reduced readmission risk at three months post-discharge.

Disponible en: <https://link.springer.com/article/10.1007/s11096-020-01091-4>