

REVISIÓN BIBLIOGRÁFICA **ENERO 2019**: Selección de artículos

REVISTAS GERIÁTRICAS

AGE AND AGEING

Frequency, intensity and localization of pain as risk factors for frailty in older adults

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Abstract

Background

the association between pain characteristics and frailty risk is uncertain.

Objective

to investigate the separate impact of the frequency, intensity and location of pain on frailty risk and its possible mechanisms.

Methods

prospective cohort of 1505 individuals \geq 63 years followed between 2012 and 2015 in Spain. In 2012, pain was classified into: lowest pain (Score 0), middle pain (Score 1–4) and highest pain (Score 5–6). Incident frailty was assessed in 2015 as having \geq 3 Fried criteria or a Frailty Index (FI) \geq 0.30.

Results

in multivariate analyses, the risk of frailty (measured with the Fried criteria or the FI) increased progressively with the frequency of pain, its intensity and the number of pain locations. Compared with those having the lowest pain score, the odds ratio (95% confidence interval) of Fried-based frailty was 1.24 (0.56–2.75) in the middle score and 2.39 (1.34–4.27; P-trend <0.01) in the highest score. Corresponding values for frailty as FI \geq 0.30 were 1.39 (0.80–2.42) and 2.77 (1.81–4.24; P-trend <0.01). Odds ratios did not change after adjustment for alcohol intake, Mediterranean diet adherence or sedentary time, but were reduced with adjustment for pain-associated chronic diseases (cardiovascular disease, diabetes, chronic lung disease, osteomuscular disease and depression). A higher pain score was linked to higher risk of exhaustion and low physical activity (two out of five Fried criteria) and to a worse score in all FI domains.

Conclusion

frequency, intensity and location of pain were associated with higher risk of frailty. Study associations were partly explained by pain-associated morbidity.

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ARCHIVES OF GERONTOLOGY AND GERIATRICS

Associations of potentially inappropriate medication use with four year survival of an inception cohort of nursing home residents

Kristel Paque Monique Elseviers Robert Vander Stichelea Tinne Dille Koen Pardon Luc Delien Thierry Christiaens

Abstract

Background

Survival in older adults has a high variability. The possible association of length of survival with potentially inappropriate medication (PIM) use remains unclear.

Aim

To examine the four-year survival rate, the prevalence of polypharmacy and PIM use at admission, and the association between the two, in an inception cohort of newly admitted nursing home residents

Methods

Data were used from ageing@NH, a prospective observational cohort study in nursing homes. Residents (n = 613) were followed for four years after admission or until death. PIM use was measured at admission, using STOPPFrail. The Kaplan-Meier method was used to estimate survival, using log-rank tests for subgroup analyses. Cox regression analyses was used to explore associations with PIM use and polypharmacy, corrected for covariates

Results

Mean age was 84, 65% were females. After one, two, three and four years the survival rates were respectively 79%, 60.5%, 47% and 36%. At admission, 47% had polypharmacy and 40% excessive polypharmacy, 11% did not use any PIMs, and respectively 28%, 29%, and 32% used one, two and three or more PIMs. No difference in survival was found between polypharmacy and no polypharmacy, and PIM use and no PIM use at admission. Neither polypharmacy nor PIM use at admission were associated with mortality.

Conclusion

Residents survived a relatively short time after NH admission. Polypharmacy and PIM use at admission were relatively high in this cohort, although neither was associated with mortality.

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BMC GERIATRICS

Deprescribing interventions and their impact on medication adherence in community-dwelling older adults with polypharmacy: a systematic review

Joanna Ulley, Deborah Harrop, Ali Ali, Sarah Alton and Sally Fowler Davis

Abstract

Background

Polypharmacy, and the associated adverse drug events such as non-adherence to prescriptions, is a common problem for elderly people living with multiple comorbidities. Deprescribing, i.e. the gradual withdrawal from medications with supervision by a healthcare professional, is regarded as a means of reducing adverse effects of multiple medications including non-adherence. This systematic review examines the evidence of deprescribing as an effective strategy for improving medication adherence amongst older, community dwelling adults.

Methods

A mixed methods review was undertaken. Eight bibliographic database and two clinical trials registers were searched between May and December 2017. Results were double screened in accordance with pre-defined inclusion/exclusion criteria related to polypharmacy, deprescribing and adherence in older, community dwelling populations. The Mixed Methods Appraisal Tool (MMAT) was used for quality appraisal and an a priori data collection instrument was used. For the quantitative studies, a narrative synthesis approach was taken. The qualitative data was analysed using framework analysis. Findings were integrated using a mixed methods technique. The review was performed in accordance with the PRISMA reporting statement.

Results

A total of 22 original studies were included, of which 12 were RCTs. Deprescribing with adherence as an outcome measure was identified in randomised controlled trials (RCTs), observational and cohort studies from 13 countries between 1996 and 2017. There were 17 pharmacy-led interventions; others were led by General Practitioners (GP) and nurses. Four studies demonstrated an overall reduction in medications of which all studies corresponded with improved adherence. A total of thirteen studies reported improved adherence of which 5 were RCTs. Adherence was reported as a secondary outcome in all but one study.

Conclusions

There is insufficient evidence to show that deprescribing improves medication adherence. Only 13 studies (of 22) reported adherence of which only 5 were randomised controlled trials. Older people are particularly susceptible to non-adherence due to multi-morbidity associated with polypharmacy. Bio-psycho-social factors including health literacy and multi-disciplinary team interventions influence adherence. The authors recommend further study into the efficacy and outcomes of medicines management interventions. A consensus on priority outcome measurements for prescribed medications is indicated.

Trial registration

PROSPERO number CRD42017075315.

Disponible en: https://bmcgeriatr.biomedcentral.com/track/pdf/10.1186/s12877-019-1031-4



Consensus and evidence-based medication review to optimize and potentially reduce psychotropic drug prescription in institutionalized dementia patients

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Abstract

Background

Dementia patients often show neuropsychiatric symptoms, known as behavioral and psychological symptoms of dementia (BPSD). These are a common motive for medical consultations, hospitalizations, and nursing home stays. Various studies have suggested that the high prevalence of psychotropic drug use to treat BPSD in institutionalized dementia patients may lead to impaired cognitive capacity, rigidity, somnolence, and other complications during the course of the illness. The aim of this study was to design a consensus-based intervention between care levels to optimize and potentially reduce prescription of psychotropic drugs in institutionalized patients with dementia and assess the changes occurring following its implementation.

Methods

Design: Prospective, quasi-experimental, pre/post intervention, multicenter study. **Scope**: 7 nursing homes associated with a single primary care team. **Inclusion Criteria**: Institutionalized patients diagnosed with dementia and under treatment with 1 or more psychotropic drugs for at least 3 months. **Sample**: 240 individuals; mean age, 87 years (SD: 6.795); 75% (180) women. **Intervention**: Creation of evidence-based therapeutic guidelines for psychotropic drug use in the treatment of BPSD by consensus between reference professionals. Joint review (primary care and geriatric care nursing home professionals) of the medication based on the guidelines and focusing on individual patient needs. **Primary variable**: Number of psychotropic drugs used per patient. **Assessment**: Preintervention, immediate postintervention, and at 1 and 6 months.

Results

Overall, the number of psychotropic drugs prescribed was reduced by 28% (from 636 before to 458 after the intervention). The mean number of psychotropic drugs prescribed per patient decreased from 2.71 at baseline to 1.95 at 1 month postintervention and 2.01 at 6 months (p < 0.001 for both time points). Antipsychotics were the drug class showing the highest reduction rate (49.66%). Reintroduction of discontinued psychotropic drugs was 2% at 1 month following the intervention and 12% at 6 months.

Conclusions

A consensus guidelines-based therapeutic intervention with a patient-centered medication review by a multidisciplinary team led to a reduction in prescription of psychotropic drugs in institutionalized dementia patients.

Disponible en: https://bmcgeriatr.biomedcentral.com/track/pdf/10.1186/s12877-018-1015-9



DRUGS AND AGING

Relation Between Delirium and Anticholinergic Drug Burden in a Cohort of Hospitalized Older Patients: An Observational Study

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Abstract

Background

Delirium is a neuropsychiatric syndrome which occurs on average in one out of five hospitalized older patients. It is associated with a number of negative outcomes, including worsening of cognitive and functional status, increasing the burden on patients and caregivers, and elevated mortality. Medications with anticholinergic effect have been associated with the clinical severity of delirium symptoms in older medical inpatients, but this association is still debated.

Objective

The aim was to assess the association between delirium and anticholinergic load according to the hypothesis that the cumulative anticholinergic burden increases the risk of delirium.

Methods

This retrospective, cross-sectional study was conducted in a sample of older patients admitted to the Acute Geriatric Unit (AGU) of the San Gerardo Hospital in Monza (Italy) between June 2014 and January 2015. Delirium was diagnosed on admission using the 4 'A's Test (4AT), a validated screening tool for delirium diagnosis, which has shown good sensitivity and specificity to detect this condition in elderly patients admitted to an AGU. Each patient's anticholinergic burden was measured with the Anticholinergic Cognitive Burden (ACB) scale, a ranking of anticholinergic medications to predict the risk of adverse effects on the central nervous system in older patients. **Results**

Of the 477 eligible for the analysis, 151 (31.7%) had delirium. According to the ACB scale, 377 patients (79.0%) received at least one anticholinergic drug. Apart from quetiapine, which has a strong anticholinergic effect, the most commonly prescribed anticholinergic medications had potential anticholinergic effects but unknown clinically relevant cognitive effects according to the ACB scale (score 1). Patients with delirium had a higher anticholinergic burden than those without delirium, with a dose–effect relationship between total ACB score and delirium, which was significant at univariate analysis. A plateau risk was found in patients who scored 0–2, but patients who scored 3 or more had about three or six times the risk of delirium than those not taking anticholinergic drugs. The dose–response relationship was maintained in the multivariate model adjusted for age and sex [odds ratio (OR) 5.88, 95% confidence interval (CI) 2.10–16.60, p = 0.00007], while there was only a non-significant trend in the models adjusted also for dementia and Mini Nutritional Assessment (OR 2.73, 95% CI 0.85–8.77, p = 0.12).

Conclusions

Anticholinergic drugs may influence the development of delirium due to the cumulative effect of multiple medications with modest antimuscarinic activity. However, this effect was no longer evident in multivariable logistic regression analysis, after adjustment for dementia and malnutrition. Larger, multicenter studies are required to clarify the complex relationship between drugs, anticholinergic burden and delirium in various categories of hospitalized older patients, including those with dementia and malnutrition.

Disponible en: https://link.springer.com/article/10.1007/s40266-018-0612-9



JOURNAL OF THE AMERICAN GERIATRICS SOCIETY

Tools for Deprescribing in Frail Older Persons and Those with Limited Life Expectancy: A Systematic

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Abstract

Objectives

To summarize available tools that can assist clinicians in identifying and reducing or stopping (deprescribing) potentially inappropriate medications and that specifically consider frailty or limited life expectancy.

Design

Systematic review and narrative synthesis.

Setting

We searched medline (via ovid sp), embase (via ovid sp), and cinahl from inception to december 2017, along with grey literature. We included articles that described a tool to guide deprescribing of medications.

Participants

Frail older persons and older persons with limited life expectancy.

Measurements

Narrative description of tools.

Results

We identified 15 tools and organized them into three main categories: tools (n = 2) that described a model or framework for approaching deprescribing, tools (n = 9) that outlined a deprescribing approach for the entire medication list, and tools (n = 4) that provided medication-specific advice. The complexity of the tools ranged from simple lists to detailed, step-wise protocols. The development methodology varied widely, and the methods used to synthesize the tools were generally not well described. Most tools were based on expert opinion. Only four of the 15 tools have been tested in clinical practice (in very low-quality studies).

Conclusion

Tools exist to help clinicians deprescribe in frail older persons and those with limited life expectancy. These tools may assist clinicians at various stages in the deprescribing process. However, it remains to be investigated whether use of such tools in practice is likely to improve clinical outcomes or reduce inappropriate medication use

Disponible en: https://onlinelibrary.wiley.com/doi/epdf/10.1111/jgs.15616



<u>REVISTA ESPAÑOLA DE GERIATRÍA Y</u> <u>GERONTOLOGÍA</u>

¿Cuál es el papel de la valoración geriátrica integral en Oncogeriatría?

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RESUMEN

El aumento creciente de la población mundial y el envejecimiento generalizado se han acompañado de un incremento en la prevalencia de cáncer en el anciano. El envejecimiento se asocia a determinados cambios fisiológicos, algunos de los cuales se potencian por la propia neoplasia. Junto a esto, el anciano oncológico suele tener más problemas que el resto de los individuos de edad avanzada, y es habitual que presente multitud de déficits. Estas características hacen necesario un manejo especial del mismo, utilizando, para ello, la principal herramienta empleada en Geriatría, la valoración geriátrica integral. Con este manuscrito se pretende analizar cuál es la trascendencia de la valoración geriátrica integral en dicho grupo poblacional, prestando especial atención a su capacidad para predecir la toxicidad a la quimioterapia y la supervivencia del anciano oncológico, y su capacidad para clasificar a estos pacientes en grupos que faciliten la toma de decisiones posterior.

Disponible en: http://www.elsevier.es/es-revista-revista-espanola-geriatria-gerontologia-124-articulo-cual-es-el-papel-valoracion-S0211139X1830619X

GERIATRICS AND GERONTOLOGY INTERNATIONAL

Change in number of potentially inappropriate medications impacts on the nutritional status in a convalescent rehabilitation setting

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Abstract

Aim

The association between potentially inappropriate medications (PIM) use and nutritional status is unclear in Japan. The aim of the present study was to establish whether PIM use during hospitalization affects the nutritional status among geriatric patients in the convalescing stage.

Methods

This retrospective longitudinal cohort study included consecutive geriatric patients admitted and discharged from convalescent rehabilitation wards between 2010 and 2016. Participants were divided based on the presence or absence of increased PIM from admission to discharge. Demographic data, laboratory data and the Functional Independence Measure were analyzed between groups. We used the 2015 American Geriatrics Society Beers Criteria to screen for PIM, and the primary outcome was the Geriatric Nutritional Risk Index at discharge. A multiple linear regression analysis was used to examine whether Geriatric Nutritional Risk Index at discharge was independently associated with increased PIM.



Results

In total, 643 participants (220 men, 423 women; interquartile range 73–85 years) were included in the present study. Multiple linear regression analysis for increased PIM, adjusting for confounding factors, showed that PIM use was independently and negatively correlated with Geriatric Nutritional Risk Index at discharge. In particular, first-generation antihistamine, antipsychotic, benzodiazepine, proton pump inhibitor and non-steroidal anti- inflammatory drug use increased significantly from admission to discharge.

Conclusions

Increased PIM might be a predictor of nutritional status in geriatric patients.

Disponible en: https://onlinelibrary.wiley.com/doi/epdf/10.1111/ggi.13561

JOURNAL OF GERIATRIC ONCOLOGY

Clinical pharmacology of oncology agents in older adults: A comprehensive review of how chronologic and functional age can influence treatment-related effects

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Abstract

Unique challenges exist when managing older adults with cancer. Associations between cancer and age-related physiologic changes have a direct impact on pharmacokinetics and pharmacodynamics of cancer therapies and can affect drug dosing, dose intensity, efficacy, safety and quality of life. The breadth and depth of these issues, however, have not been fully evaluated because the majority of clinical trials have focused on a younger and healthier population. As a consequence, little information is available to support clinicians in making evidence-based decisions regarding treatment with cancer therapies in older adults, especially those over age 75. Prior clinical pharmacology reviews summarized the literature on how age-related physiologic changes can influence and affect conventional and targeted anti-cancer treatments. Our article provides an updated review with expanded information that includes small molecule kinase inhibitors, monoclonal antibodies, immunotherapies, hormonal, conventional, and miscellaneous agents. Additionally, our article integrates how functional age, determined by the geriatric assessment (GA), can also influence treatment-related effects and health outcomes. Broadening cancer therapy trials to capture not only chronologic age but also functional age would allow clinicians to better identify subsets of older adults who benefit from treatment versus those most vulnerable to morbidity and/or mortality.

Disponible en: https://www.geriatriconcology.net/article/S1879-4068(18)30161-9/pdf



Patient- and tumor-related predictors of chemotherapy intolerance in older patients with cancer: A systematic review

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Abstract

Objective

The aim of this systematic review was to investigate patient-related factors (e.g. depressive symptoms, cognition, mobility, activities of daily living (ADL)) as well as tumor-related factors (e.g. tumor type, chemotherapy regimen) influencing chemotherapy intolerance in cancer patients aged 65 years or older.

Methods

We included observational studies that reported data on possible predictors of chemotherapy intolerance in older patients with cancer. We studied chemotherapy intolerance using the following outcomes: chemotherapy toxicity grade 3 to 5, unplanned hospitalization, chemotherapy discontinuation, chemotherapy dose reduction, functional decline, and chemotherapy mortality. We searched PubMed, Embase, and PsycInfo for articles between January 1995 and July 2016. The quality of the included studies was assessed using the Quality in Prognosis Studies (QUIPS) tool.

Results

The search yielded 1774 articles, and 30 articles from 27 studies were included. The patientrelated factors associated with chemotherapy intolerance, in terms of the size of the association and the consistency of the results, were more than one fall in the last six months, mobility problems, poor performance status and the presence of severe comorbid conditions. The tumorrelated factors that were associated with chemotherapy intolerance in older patients with cancer were certain regimens of chemotherapy and polychemotherapy, as compared to monochemotherapy. The number of studies on unplanned hospitalization and functional decline was small.

Conclusion

The included studies were heterogeneous with respect to endpoints and included parameters. Nevertheless, the size of the association and the consistency of results suggest that all these factors are relevant for everyday oncological practice.

Disponible en: https://www.geriatriconcology.net/article/S1879-4068(18)30138-3/pdf



INTERNATIONAL JOURNAL OF GERIATRIC PSYCHIATRY

Prescription opioid and benzodiazepine misuse is associated with suicidal ideation in older adults

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Abstract

Objectives

Suicide in older adults is a major public health issue. Past research across the US adult population has linked prescription medication misuse with suicidal ideation. No work has evaluated associations between prescription opioid or benzodiazepine misuse and suicidal ideation in older adults, and this work aimed to address that gap.

Methods/design

Data were from adults 50 years and older participating in the 2015 to 2016 National Survey on Drug Use and Health (n = 17 608). Design-based logistic regression evaluated links between any past-year prescription opioid or benzodiazepine use without misuse or prescription misuse and past-year suicidal ideation, after controlling for sociodemographic, physical health, mental health, and substance use correlates associated with suicidal ideation.

Results

After controlling for all correlates, past-year use without misuse of prescription opioids or benzodiazepines was not associated with past-year suicidal ideation in older adults. In contrast, past-year opioid misuse (AOR = 1.84, 95% CI = 1.07-3.19) and benzodiazepine misuse (AOR = 2.00, 95% CI = 1.01-3.94) were significantly associated with past-year suicidal ideation, even after controlling for all covariates. While 2.2% of US older adults not engaged in either opioid or benzodiazepine misuse reported past-year suicidal ideation, 25.4% of those who misused both medication classes endorsed such suicidality (AOR = 4.73, 95% CI = 2.07-10.79).

Conclusions

Both past-year prescription opioid and benzodiazepine misuse are associated with past-year suicidal ideation in US older adults. Clinicians encountering older adult patients at-risk for or engaged in prescription medication misuse also should screen for suicidality.

Disponible en: https://onlinelibrary.wiley.com/doi/epdf/10.1002/gps.4999



REVISTAS FARMACÉUTICAS

AMERICAN JOURNAL OF HEALTH SYSTEM PHARMACIST

Comparison of clinical pharmacy specialists and usual care in outpatient management of hyperglycemia in Veterans Affairs medical centers

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Abstract

Purpose

The results of a study to assess the effectiveness and safety of hyperglycemia management provided by clinical pharmacy specialists (CPSs) versus usual care in outpatients with diabetes from 53 Veterans Affairs (VA) medical centers are reported.

Methods

An historical cohort study of outpatients with baseline glycosylated hemoglobin (HbA1c) values of >9% who were referred to a CPS for management of hyperglycemia and primary care patients who were not referred to a CPS was conducted. The primary outcomes were change in HbA1c over time and time to reach an HbA1c value of <8%. Secondary outcomes included the number of visits to achieve an HbA1c value of <8%, proportion of patients with an HbA1c value of <6% who were receiving secretagogues, and proportion of patients with serious hypoglycemia.

Results

After propensity score matching by baseline characteristics, there were 12,327 patients in each group. The mean \pm S.D. number of visits to reach an HbA1c value of <8% was 2.46 \pm 1.58 in the pharmacist-managed group and 1.82 \pm 1.27 with usual care (p < 0.001). The proportion of patients with an HbA1c value of <6% who were receiving secretagogues was 39.9% with pharmacist-managed care and 38.6% with usual care (p = 0.73). Serious hypoglycemia was noted in 4.3% of pharmacist-managed patients and 3.1% of usual care patients (p < 0.001).

Conclusion

Data from 53 VA medical centers revealed that CPSs managed the care of ambulatory care patients with hyperglycemia as well as primary care providers.

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EUROPEAN JOURNAL OF CLINICAL PHARMACOLOGY

Non-steroidal anti-inflammatory drugs and risk of Parkinson's disease in the elderly population: a meta-analysis

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Abstract

Purpose

Several studies have explored the impact of non-steroidal anti-inflammatory drugs (NSAIDs) and the risk of Parkinson disease (PD). However, the extent to which NSAIDs may increase or decrease the risk of PD remains unresolved. We, therefore, performed a meta-analysis of relevant studies to quantify the magnitude of the association between NSAID use and PD risk in the elderly population.

Methods

The electronic databases such as PubMed, EMBASE, Scopus, Google Scholar, and Web of Science were used to search the relevant articles published between January 1990 and December 2017. Large ($n \ge 1000$) observational design studies with a follow-up at least 1 year were considered. Two authors independently extracted information from the included studies. Random effect model was used to calculate risk ratios (RRs) with 95% confidence interval (CI)

Results

A total of 17 studies with 2,498,258 participants and nearly 14,713 PD patients were included in the final analysis. The overall pooled RR of PD was 0.95 (95%CI 0.860–1.048) with significant heterogeneity (I2 = 63.093, Q = 43.352, p < 0.0001). In the subgroup analysis, the overall pooled RR of PD was 0.90 (95%CI 0.738–1.109), 0.96 (95%CI 0.882–1.055), and 0.99 (95%CI 0.841–0.982) from the studies of North America, Europe, and Asia. Additionally, long-term use, study design, individual NSAID use, and risk of PD were also evaluated.

Conclusion

Despite the neuroprotective potential of NSAIDs demonstrated in some experimental studies, our findings suggest that there is no association between NSAIDs and the risk of Parkinson disease at the population level. Until further evidence is established, clinicians need to be vigilant ensuring that the use of NSAIDs remains restricted to their approved anti-inflammatory and analgesic effect.

Disponible en: https://link.springer.com/article/10.1007/s00228-018-2561-y



EUROPEAN JOURNAL OF HOSPITAL PHARMACY

Selection of interventions aimed at improving medication adherence in patients with multimorbidity

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Abstract

Objectives

To select interventions aimed at improving medication adherence in patients with multimorbidity by means of a standardised methodology.

Methods

A modified Delphi methodology was used to reach consensus. Interventions that had demonstrated their efficacy in improving medication adherence in patients with multimorbidity or in similar populations were identified from a literature search of several databases (PubMed, EMBASE, the Cochrane Library, Center for Reviews and Dissemination, and Web of Science). 11 experts in medication adherence and/or chronic disease scored the selected interventions for appropriateness according to three criteria: strength of the evidence that supported each intervention, usefulness in patients with multimorbidity, and feasibility of implementation in clinical practice. The final set of interventions was selected according to appropriateness and agreement based on the Delphi methodology.

Results

566 articles were retrieved in the literature search. Nine systematic reviews were included. 33 interventions were initially selected for evaluation by the panellists. Consensus after two Delphi rounds was reached on 16 interventions. Five interventions were categorized as educational, six as behavioural and five were related to other aspects of interest.

Conclusions

The interventions selected following a comprehensive and standardized methodology, could be used to improve medication adherence in patients with multimorbidity.

Disponible en: https://ejhp.bmj.com/content/26/1/39



PHARMACOEPIDEMIOLOGY AND DRUG SAFETY

Opioid tolerance and clinically recognized opioid poisoning among patients prescribed extended-release long-acting opioids

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Abstract

Background

In recognition of potential for increased overdose risk, drug labels for extended-release and longacting (ER/LA) opioids emphasize the need for established opioid tolerance prior to initiating high dosages.

Objectives

Describe the proportion of patients with opioid tolerance prior to initiation of 90 morphine milligram equivalents (MME) ER/LA opioids and examine subsequent risk of opioid poisoning.

Methods

We used Truven Health Analytics' MarketScan Databases (2006-2015) to identify patients initiating ER/LA opioids \geq 90 MME. We examined prescription histories and describe the proportion of initiators with opioid tolerance (defined as \geq 7 days of 60 MME in the prior 14 days). We adjusted for age, sex, year of initiation, and baseline comorbidities using inverse probability of treatment weighted Cox proportional hazards models. We estimated adjusted hazard ratios and 95% confidence intervals for the effect of opioid tolerance on the risk of clinically recognized opioid poisoning (based on diagnosis codes) in specific periods (0-7, 8-30, 31-90, and 91-365 days) following initiation.

Results

Among 372 038 initiators, 38% did not meet opioid tolerance criteria. The proportion of nontolerant initiators was highest among those initiating methadone (44%) and fentanyl (42%). Nontolerant patients were 37% more likely to be diagnosed with opioid poisoning (adjusted hazard ratios = 1.37 [1.07, 1.76]) in the week following ER/LA initiation.

Conclusions

Over one-third of patients initiating \geq 90 MME ER/LA opioids did not have evidence of opioid tolerance. The 7 days following high dose ER/LA initiation may represent a high-risk period for clinically diagnosed opioid poisoning in patients who do not have prior opioid tolerance.

Disponible en: https://onlinelibrary.wiley.com/doi/epdf/10.1002/pds.4572



Monotherapy Is Good Enough for Patients with Mild-to-Moderate Alzheimer's Disease: A Network Meta-analysis of 76 Randomized Controlled Trials

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Abstract

Memantine and the Acetylcholinesterase inhibitors (AChEls) are two classes of drugs that are used to treat patients with Alzheimer's disease. We conducted a network meta-analysis of randomized controlled trials to compare the treatment effectiveness of monotherapy or combination therapy A total of 23,707 AD patients in 76 randomized trials were identified. In patients with mild-tomoderate AD, monotherapy with donepezil, galantamine or rivastigmine were superior to placebo in enhancing cognitive functions and activities of daily living (ADL), whereas monotherapy with donepezil or memantine were superior to placebo in improving behavioral symptoms. However, combination therapy with AChEls and memantine did not show additional benefit than monotherapy. In patients with moderate-to-severe AD, neither monotherapy nor combination therapy were superior to placebo in any domain measurement. Combination therapy with memantine and AChEls is confirmed to have no additional benefits over monotherapy.

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