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Research

Patient empowerment brochures to increase gabapentinoid deprescribing: protocol for the prospective, controlled before-and-after GABA-WHY trial

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Abstract

Background: Off-label use of gabapentinoids is common among patients admitted to hospital medical wards, who are at risk of adverse drug events. In this study, we will assess if educational brochures can increase rates of gabapentinoid deprescription among medical inpatients, compared with usual care.

Methods: We describe the protocol for a prospective before-and-after trial that will take place on 5 medical wards of 2 tertiary care hospitals in Montréal, Canada. The study intervention will include distribution of educational brochures to users of gabapentinoids during hospital admission, as well as short educational sessions for medical staff on safe gabapentinoid prescribing practices. We will include patients with a gabapentinoid prescription before admission who are aged 60 years or older. Exclusion criteria are known seizure disorder, severe cognitive impairment, expected prognosis less than 3 months and inability to read English or French. The primary outcome is the rate of gabapentinoid deprescription at 8 weeks postdischarge. We aim to recruit 160 participants, with a 1:1 distribution between intervention and control groups.

Interpretation: If successful, the use of educational brochures and staff education represents a scalable intervention to reduce gabapentinoid overuse by encouraging deprescription conversations between patients and their health care providers. Results of the study will be disseminated through publication in peer-reviewed journals and presentations at conferences. **Trial registration:** ClinicalTrials.gov, no. NCT04855578

Gabapentinoids are a class of antiepileptic drugs that includes gabapentin and pregabalin. Both drugs bind voltage-gated calcium channels in the central nervous system, inhibiting neuronal calcium influx and consequently release of neurotransmitters such as glutamate, norepinephrine and substance P.[1,2] The US Food and Drug Administration (FDA) and Health Canada have approved the use of gabapentin and pregabalin for treatment of postherpetic neuralgia, with additional indications for pregabalin, including painful diabetic neuropathy, fibromyalgia and neuropathic pain associated with spinal cord injury.[1–4]

Despite a short list of approved indications, gabapentinoid prescriptions have soared in the past decade in the United States and Canada.[5–7] In 2020, gabapentin and pregabalin were among the top 15 drugs of highest use per capita in Canada.[8] The rise in gabapentinoid prescriptions has been largely driven by its popularity for numerous off-label indications related to chronic pain, such as various types of neuropathic pain, osteoarthritis, chronic lower back pain, sciatica and cancer-related pain, despite a lack of evidence.[9] Clinical trials have shown that gabapentinoids are not beneficial for some of these indications.[10–14] In areas where there is trial evidence, the modest benefit of treatment is limited by a high risk of adverse events at studied doses, with many patients stopping the drug as a result.[14]

The prevalence of chronic gabapentinoid use is high among patients admitted to hospital, with as many as 1 in 8 patients prescribed the drug before admission.[15] Although fewer than 1 in 5 of these patients are using the drug for an indication approved by the FDA or Health Canada, the medication is rarely stopped at discharge.[15] Gabapentinoid users are also more likely to be coprescribed opioids and benzodiazepines,[15] which is concerning in light of the evidence of increased odds of opioid-related death with coprescription of pregabalin[16] or gabapentin.[17]

Competing interests: Todd Lee and Emily McDonald receive salary support from the Fonds de Recherche Québec–Santé and jointly hold the copyright for MedSafer, a deprescribing software that links to the Canadian Deprescribing Network patient empowerment brochures used in this study. Todd Lee also reports funding from the Canadian Institutes of Health Research and the Centre for Aging and Brain Health Innovation. No other competing interests were declared.

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The high prevalence of off-label use of gabapentinoids in older patients with comorbidities who are vulnerable to adverse drug events makes this class of drug an ideal target for deprescription. Multiple strategies exist to increase deprescription of potentially inappropriate medications. One promising method includes the use of direct patient education through the distribution of brochures designed by the Canadian Deprescribing Network, which have been studied for deprescribing benzodiazepines in hospital[18] and in the community.[19]

We present a protocol for evaluating the efficacy of educational brochures in increasing the deprescription of gabapentinoids among medical patients admitted to hospital.

Methods

Study design and setting

This prospective before-and-after study will take place in 5 medical units of the McGill University Health Centre, located at the Royal Victoria Hospital (Glen site) and the Montréal General Hospital, in Montréal, Canada. Both hospitals are tertiary care academic centres. The primary goal is to increase deprescription of gabapentinoids by 20%, compared with usual care, using a patient educational brochure designed in collaboration with the Canadian Deprescribing Network. Recruitment has been ongoing since May 2021.

We report this protocol in accordance with the TREND statement checklist.[20] This study is registered at ClinicalTrials.gov, no. NCT04855578.

Participants

We will evaluate any patient admitted to 1 of the 5 participating medical units who has an active prescription for gabapentin or pregabalin for the study. Patients will be identified as users of gabapentinoids from their best possible medication history, obtained by the unit's pharmacist at the time of admission. This includes reviewing the patient chart, cross-referencing community pharmacy records and conducting a detailed history with the patient. Select patient demographics, comorbidities and reason for admission will be collected from the detailed admission note available for all patients on our teaching units.

Participants must be 60 years or older to enter the study. We selected the 60-year cut-off as we thought that this group would benefit the most from a deprescribing intervention, given the higher prevalence of polypharmacy and risk for potential adverse drug events.[21] Exclusion criteria include having a known seizure disorder, not being enrolled in the provincial public health insurance plan, estimated life expectancy less than 3 months, inability to consent, major neurocognitive disorder and inability to read in English or French. For patients admitted more than once during the study period, the first admission will be considered the index admission and data from further admissions will not be included in the study. A research assistant will determine study eligibility according to these criteria, and any ambiguity regarding a participant's eligibility will be further reviewed by one of the study's investigators.

Trial interventions

All sites will begin in the control period of the trial, during which participants will receive usual medical care. Participants will be informed that the goal of the trial is to evaluate their usual home pain medication and any trends in deprescribing at hospital discharge. They will be unaware that gabapentinoids are specifically studied, to reduce the risk of selection bias and contamination of the control group. Health care providers on the unit will be informed of the presence of an ongoing clinical trial, without further details on its nature or objectives.

At the 12-month mark of the study, all 5 units will simultaneously transition to the intervention period. This will reduce the risk of bias introduced by any temporal trends in level of trainees or seasonal variations in medical staff workload that could affect deprescription practices. If the target number of control participants is reached before the 12-month mark, recruitment will be suspended until then.

As medical staff and trainees rotate frequently between sites and units, and as this is an educational intervention, randomization at the level of the individual participant or at the level of the unit is not feasible (including stepped-wedge design). Learned behaviour and access to the brochures would invariably lead to contamination of the control group and thus we selected a before-and-after study method to minimize this source of bias in our data.

The intervention will consist of 2 components. First, participants will receive during their hospitalization an educational brochure designed by the Canadian Deprescribing Network on gabapentinoids, available in either English or French (https://www.deprescribingnetwork.ca/patient-handouts).[22] The brochures are 10-page, letter-size documents, written in a sixth-grade level vocabulary. They contain self-assessment tests on risks of medications, provide information on evidence of efficacy and common adverse effects, propose therapeutic alternatives and suggest tapering regimens in the form of illustrated calendars. The brochure clearly states that readers should contact a health care provider before stopping or tapering their medication. This could either be the treating staff or residents during their admission, or their family physician after discharge. During the intervention period, the research assistant will give brochures to the participants at the end of the initial visit, after completion of the consent form. The participants will only be informed that the brochure is for one of their pain medications and will be encouraged to read it during their hospital stay.

The second component of the intervention is a short, 5- to 10-minute educational session about evidence for and against gabapentinoid use, the design and purpose of the study, and a brief overview of the brochures. One of the study investigators will deliver these mandatory sessions to physicians (staff, residents and medical students) at every study site at the beginning of each monthly rotation period. The goal of these educational sessions is to promote informed decision-making by clinicians when deprescribing gabapentinoids, which is fundamental to our proposed deprescription strategy.

Data collection

All participants will provide written informed consent. Trained research assistants will collect demographics, comorbidities and reason for admission from the participants and their medical records. During the index admission, the first questionnaire will be administered in person and will collect information about participant demographics, including age, sex and residence style (independent, assisted living, etc.). We will also obtain a medication history (for study drugs) and assess global functioning, pain control and cognition with adapted forms of validated Patient-Reported Outcomes Measurement Information System (PROMIS) questionnaires.[23–25]

A telephone follow-up questionnaire administered 8 weeks after hospital discharge will collect any changes in comorbidities or living situation, and will ask participants about planned or ongoing deprescribing of their gabapentinoid (decreasing dose, ongoing taper or stopping), as well as about starting or changing dosage of other pain medications, such as opioids and nonsteroidal anti-inflammatory drugs. We will also repeat the global functioning, pain control and cognition questionnaires. All study data will be securely stored using REDCap software.

Outcomes

The primary outcome will be deprescription of gabapentinoids at 8 weeks after hospital discharge, defined as complete cessation or taper with intention to stop.

Secondary outcomes assessed at 8 weeks postdischarge will include dose reduction without intention to stop, participant-reported outcomes (changes in global functioning scores, pain control and cognitive function), and initiation of new pain medications or increases in doses of preadmission nongabapentinoid pain medications.

Sample size

The estimated sample size is 160 participants, with a 1:1 distribution between the intervention and control groups. The control period event rate (gabapentinoid deprescription at 8 weeks postdischarge) is expected to be 13%.[15] We calculated the sample size to detect an absolute increase of 20% in deprescription rates (number needed to treat of 5), allowing for a 2-sided type 1 error of 5% and a type 2 error of 20% (132 subjects), and accounting for 15% loss to follow-up, including death in hospital and after discharge (156 subjects, rounded to 160). Given previous trial results showing that educational brochures for benzodiazepines can lead to an absolute increase of 43% in deprescription rates among medical inpatients (number needed to treat of 3),[18] an absolute increase in deprescription rates of 20% was thought to be a reasonable target in this trial.

Statistical analysis

We will provide a descriptive summary of the population enrolled in this study, including participant age, sex, comorbidities, reason for admission, type of gabapentinoid prescribed (pregabalin v. gabapentin), other coprescriptions, length of hospital stay and residence type.

We will use an "intention to treat" principle. We will analyze participant data according to their participation during the intervention or control period. For the primary outcome, we will perform a sensitivity analysis for patients who died or were lost to follow-up using the most recent available data on their gabapentinoid use (inpatient pharmacy records, discharge prescriptions or the provincial electronic medical record). We will assess binary outcomes using binomial regression comparing the intervention to no intervention and adjusting for age and sex. We will assess continuous outcomes (T scores) using linear regression comparing the intervention to no intervention, adjusting for baseline values, age and sex.

We will perform several preplanned subgroup analyses for the primary outcome, including an analysis of participants aged 80 or older; analyses based on reason for admission, discharge destination (community v. long-term care facility) and comorbidities; and an analysis looking at the effect of each study unit. Subgroup analyses will be treated as hypothesis generating and presented graphically with 95% confidence intervals.

Ethics approval

Ethics approval has been granted by the McGill University Health Centre Research Ethics Board.

Interpretation

The objective of this study is to evaluate the efficacy of educational brochures for increasing the deprescription of gabapentinoids among medical patients admitted to hospital. Increasing deprescription rates for potentially inappropriate medications is challenging, especially given the numerous demands on physicians' and pharmacists' time in the inpatient setting. Interventions must be simple and safe, and have strong evidence of efficacy, if they are to be adopted into the workflow of busy health care teams. Evidence-based solutions are needed to address the issue of polypharmacy.

Educational brochures, although by no means a complete solution, represent a promising starting point. They have many of the characteristics of an ideal intervention, including being low-tech, inexpensive, safe, easy to administer and aimed at bringing patients into the decision. As previous trials have shown, they have been highly effective in increasing deprescription of benzodiazepines and sedative hypnotics.[18,19] We seek to provide evidence that the gabapentinoid brochure can show similar efficacy to brochures for deprescription of benzodiazepines and sedative hypnotic drugs when targeted to patients admitted to hospital.

Results of this study will be disseminated through publication in peer-reviewed journals, as well as presentations in national conferences, such as the annual meetings for the Canadian Society of Internal Medicine and Choosing Wisely Canada. The results from the trial will also provide benchmark data for inappropriate use of gabapentinoids that can be compared across hospitals in Quebec and Canada.

Limitations

We recognize that it will not be possible to use a blinded design with participants or physicians in this study. However, this is typical in pragmatic study designs and we do not expect that this will substantially affect our results. We have selected objective outcomes whenever possible, including validated standardized questionnaires, that do not involve individual assessor judgment. In addition, during the control period of this study, all participants will be informed that the study will be evaluating medications and deprescription trends but will not be made aware that gabapentinoids will be studied specifically. We believe this will help to reduce selection bias. Accordingly, medical staff will not be aware of the specifics of the study during the control period.

Given the simultaneous crossover of all sites into the intervention period, our study may be unable to account for year-to-year temporal trends in deprescription of gabapentinoids, which could be influenced by factors such as training level of residents or time constraints from seasonal variations of workload intensity on the clinical teaching unit. However, previous retrospective data have not shown any temporal trends for gabapentinoid deprescribing on our medical wards.[15] To mitigate the risk of bias introduced by temporal trends, the sites will transition to the intervention period 12 months after the beginning of the control period.

Although we think this intervention is of low risk to participants, we are cognizant of several ethical concerns. With regard to privacy concerns, some patients may only agree to participate in the study if they are exempt from follow-up phone calls. This wish will be respected and such patients will only be enrolled if they consent to our use of the provincial electronic medical record (*Dossier Santé Québec*) to evaluate the primary outcome, and will be excluded from some of the secondary analyses.

Special consideration will also be given to patients who are cognitively impaired or otherwise unable to provide consent. Although this subpopulation of patients may still greatly benefit from deprescription of potentially inappropriate medications, the educational brochures used in this study rely on instigating motivation and providing self-capacity. Therefore, only individuals who are cognitively intact or have a minor neurocognitive disorder[26] will be considered for this trial. Although distribution of the educational brochures to the patient's proxy could be considered, this strategy is less feasible in the context of the COVID-19 pandemic, as family and caregivers often have limited access to the bedside, hindering contact with medical staff, which is crucial for initiation of the deprescription process.

Conclusion

In this study, we will assess if educational brochures can increase rates of gabapentinoids deprescription among medical inpatients. Brochures could represent a scalable intervention for combatting gabapentinoid overuse, and encourage conversations that lead to deprescribing an array of potentially inappropriate medications.

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