Effectiveness of pharmacist-led medication reviews in improving patient outcomes in chronic pain: A systematic review protocol

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Background

Chronic pain has become a major public health challenge in developed countries due to associated morbidity, loss of productivity and high consumption of health care resources.^{1,2} Longitudinal studies have documented a considerable increase in the prevalence of chronic pain in the past decades.^{3,4} It has been estimated that 10 million adults in the UK⁵ and 116 million in the US⁶ suffer from chronic pain.

Medications are widely employed for the treatment of chronic pain, and pharmacists, being experts in pharmacotherapy, have a role in chronic pain management by ensuring the safe and effective use of medicines. Suboptimal use of analgesics,⁷ inadequate monitoring of repeat prescriptions⁸ and self-medication with over-the-counter (OTC) analgesics in combination with prescribed analgesics, sometimes resulting in overdose or polypharmacy,⁹ have been reported in the literature and pose a threat to the successful management of chronic pain. Medication review, defined as “a structured, critical examination of a patient’s medicines with the objective of reaching an agreement with the patient about treatment, optimizing the impact of medicines, minimizing the number of medication-related problems and reducing waste,”¹⁰ has the potential to overcome all the above-mentioned obstacles in chronic pain management. Theoretically, pharmacist-led medication review may improve pain-related outcomes by optimizing the choice and dose of analgesics, improving adherence to prescribed medication, reducing adverse effects and resolving drug-related

problems (DRPs). However, limited and inconsistent clinical and research evidence is available to support these claims in the context of chronic pain.¹¹⁻¹⁴

A systematic review evaluating effectiveness of pharmacist-led educational interventions for chronic pain management reported a statistically significant reduction in pain intensity of 0.5 on a scale of 0 to 10, a reduction in adverse effects by 50% and an improvement in patient satisfaction with the treatment equivalent to 1 point on a 0 to 10 point rating scale in patients receiving interventions as compared to the control group.¹⁵ To date, no systematic review has evaluated the effectiveness of pharmacist-led medication review for chronic pain management. We intend to undertake the systematic review with the aim of evaluating the effectiveness of pharmacist-led medication review for chronic pain management in adult patients. The specific research questions are: 1) Does pharmacist-led medication review decrease pain intensity? 2) Does it reduce medication-related adverse effects? 3) Does it improve patients’ physical functioning and quality of life? 4) Are patients satisfied with the service provided by the pharmacist?

Methods

Study selection

The following databases will be searched from the date of their inception to the date of the search.

- MEDLINE (via Ovid)
- EMBASE (via Ovid)
- Cochrane Central Register of Controlled Trials

(CENTRAL)

- Cumulative Index to Nursing and Allied Health Literature (CINAHL) (via EMBSCO)
- PsycINFO
- International Pharmaceutical Abstracts (via Ovid)

Randomized controlled trials (RCTs) and non-randomized studies (quasi-experimental, controlled before-and-after studies) having at least one control group will be considered for inclusion. Nonrandomized studies are defined as “any quantitative study estimating the effectiveness of an intervention (harm or benefit) that does not use randomization to allocate units to comparison groups.”¹⁶ Nonrandomized studies will only be included in the review if fewer than 3 RCTs are eligible for inclusion.¹⁷ Waiting list controls, usual care, attention only and any other active control will be accepted as appropriate controls. Studies will be considered for inclusion if one of the arms is receiving either pharmacist-led medication review delivered independently or as part of more complex multidisciplinary interventions, provided that the pharmacist is a part of the multidisciplinary team. In addition to database searches and websites of national pharmacists’ associations (American, British and Canadian), the reference lists of the retrieved articles and reviews will be searched for eligible studies. Only studies published in English (full text or abstract) will be considered. The corresponding authors of all the included studies will be contacted to obtain additional information where necessary and to identify any other unpublished studies.

The process of study selection consists of the following 3 steps: 1) One author (MAH) will run the predefined specific search strategy on each of the chosen databases. All the search results will be exported to an Endnote file. 2) Two authors (MAH and DPA) will independently screen the titles and abstracts of the studies. The full text of the article will be obtained where a decision cannot be made on inclusion. 3) Finally, all potentially relevant studies meeting the predefined inclusion criteria will be included in the review. Disagreements will be resolved by a third review author (MB). We will state the number of excluded articles, giving reasons for exclusion, and present this using a PRISMA diagram.¹⁸

Types of participants

Studies involving chronic pain patients aged 18 years and older will be included irrespective of their gender or the type and etiology of chronic pain. In this systematic review, the International Association for the Study of Pain’s (IASP) defini-

FIGURE 1 Work flow of the systematic review

tion of chronic pain will be used, i.e., “pain without apparent biological value that has persisted beyond the normal tissue healing time (usually taken to be 3 months).”¹⁹ Studies involving patients with malignant or cancer pain will be excluded, as they will introduce clinical heterogeneity.

Outcome measures

Pain intensity will be the primary outcome measured using a validated scale (e.g., numerical rating scale). The secondary outcome measures include: 1) reduction in adverse effects; 2) physical functioning measured by a validated scale (e.g., Brief Pain Inventory);²⁰ 3) patient satisfaction using a validated scale; and 4) quality of life measured using a validated scale (e.g., SF-36).²¹

Assessment of risk of bias

The methodological quality of all the included studies will be assessed by 2 authors (MAH, SJC) independently. The risk of bias will be assessed using the Cochrane Collaboration’s tool for assessing risk of bias¹⁶ covering the following criteria: 1) random sequence generation; 2) allocation concealment; 3) blinding of participants and personnel; 4) blinding of outcome assessment; 5) incom-

plete outcome data; and 6) selective reporting and other bias (e.g., baseline differences between control and active arms, use of invalid questionnaires). We will assess each criterion as low risk of bias, high risk of bias or unclear risk of bias based on the recommendations of Higgins and Green.¹⁶ The quality of nonrandomized studies will be assessed using the Newcastle-Ottawa Scale (NOS).²² Disagreements will be resolved through discussion and if consensus is not reached, a third reviewer (MB) will be considered.

Data extraction

Data will be extracted by one author (MAH) and checked by another author (MB) using a standardized data collection form. The data collection form will be piloted. Disagreements will be resolved by involving a third review author (SJC).

Data synthesis

The data will be analyzed using the Cochrane Collaboration's Review Manager (RevMan 5.1). Data from the randomized and nonrandomized studies will be synthesized and presented separately. For all continuous variables (e.g., pain intensity), we will calculate mean difference (MD) when outcomes are measured using the same scale and standardized mean difference (SMD) when different scales are used, with corresponding 95% confidence

intervals. For dichotomous variables, relative risk (RR) with 95% confidence interval will be calculated. Pooling of data using meta-analysis will be performed depending on clinical homogeneity in terms of the population, intervention, outcome measures and timing of outcome measures. Only data from the randomized controlled trials meeting the inclusion criteria will be considered for meta-analysis. For nonrandomized studies, a narrative summary will be presented.

Clinical heterogeneity will be determined by discussion among the review authors and clinically heterogeneous trials will not be combined statistically. Statistical heterogeneity will be determined by using the chi-square (χ^2) and I^2 statistic. Statistical heterogeneity will determine the choice of using the random-effects model or fixed-effects model for meta-analysis. A χ^2 *p*-value of greater than 0.1 and an I^2 value of less than 50% will be used to indicate statistical homogeneity.¹⁶ The random-effects model will be used to combine clinically homogeneous but statistically heterogeneous clinical trials, whereas clinical and statistical homogeneous trials will be combined using the fixed-effects model. We will present a narrative summary if it is not possible to combine outcome data due to differences in reporting or significant heterogeneity. ■

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