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A systematic review identifies shortcomings in the reporting of crossover trials in chronic painful conditions

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Abstract

Objectives: To investigate the reporting of study features of interest in abstracts and full texts of journal publications of crossover trials in chronic painful conditions.

Study Design and Setting: Systematic review based on a MEDLINE (PubMed) search (January 1990−August 2014).

Results: Ninety-eight publications on crossover studies with 3,513 study participants were eligible for inclusion. Double-blind status and randomized allocation to treatment groups are commonly reported in both abstracts and full texts (90 of 98 publications and 82 of 98 publications, respectively). Adverse events are reported in both abstract and full text in 49 of 98 publications and in the full text only in 44 of 98. A breakdown of results by treatment period is provided only in 23 of 98 publications, and if so, is reported only in the full text, never in the abstract. There is a time trend for the reporting of randomization in abstracts; it is more likely to be reported in recent studies ($P = 0.0094$). No time trends are detected in the reporting of double-blind status ($P = 0.1087$) and adverse events ($P = 0.6084$).

Conclusion: The reporting of adverse events in the abstract and the reporting of results specified by crossover period in the full texts of journal publications on crossover pain trials should be improved.

Keywords: Chronic pain; Crossover study; Reporting; Abstract; Full text; Systematic review

1. Introduction

In journal publications on clinical trials, study features are reported in abstracts and full texts, with the former being more concise due to space constraints in journals and databases. What information is reported in abstracts, however, is of importance. Readers may choose whether to read a article in full based on the abstract. Abstracts are normally accessible free of charge, and often in English, even if the full texts of publications are available by subscription only and may be in another language. Inclusion or exclusion of studies in systematic reviews is often based on information presented in abstracts. Yet the reporting quality of abstracts is often deemed suboptimal, even for recent studies [1−3].

We aim to investigate to what extent selected study features of relevance in crossover trials in chronic painful conditions are reported in abstracts and full texts of journal publications: double-blind and randomized status, adverse events, results specified by period (i.e., before or after the crossover). Double blinding, that is, blinding of the study participants and the outcome assessors, and randomization are key features that guard against biases and, where feasible, should arguably be requirements for the inclusion of treatment studies in systematic reviews, at least in the pain field [4]. Information on adverse events is needed alongside information on treatment efficacy if a benefit vs. risk assessment is to be made, and adverse event outcomes are among the suggested core outcomes for reporting in clinical trials and reviews in chronic pain [4]. Reporting results specifically by period is of relevance to trials with a crossover design. As carry-over effects or unblinding may occur in patients who experience active treatment before placebo treatment and due to concerns about treatment wash-out, it may be appropriate to use first period data only (i.e., data before the crossover). This is indeed the approach taken in some systematic reviews [5]. Knowing to what extent study features and outcomes of interest are

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What is new?

Key findings

- In the reporting of crossover trials in chronic painful conditions features such as double blind status and randomised allocation to treatment groups are commonly included in both abstracts and full texts.
- Adverse events are reported in both abstract and full text in half of the publications and in the full text only in slightly less than half of the publications.
- A breakdown of results by treatment period is provided only in one of four publications, and if so, is reported only in the full text, never in the abstract.
- Randomisation is more likely to be reported in recent studies. No time trends are detected in the reporting of double blind status and adverse events.

What this adds to what was known?

- There are some marked shortcomings in the reporting of cross-over trials in chronic painful conditions, in particular with regard to adverse events and reporting by crossover period.

What is the implication and what should change now?

- The reporting of adverse events in the abstract and the reporting of results specified by crossover period in the full texts of journal publications on crossover pain trials should be improved.

likely to be reported in abstracts and full texts of publications on clinical trials may help, for example, in conducting systematic reviews, with regard to choosing to assess either abstracts or full texts of publications for such features. Taken together the reporting in abstracts and full texts informs about reporting quality in crossover pain trials and might inform future guidance for the conduct and reporting of crossover trials.

2. Methods

MEDLINE (PubMed) was searched with this search strategy: ''((chronic AND (pain OR pain*)) OR neuropathy OR neuralgia) AND placebo AND (cross-over OR cross over OR crossover),'' with the filter ''humans.'' We searched for articles published between January 1, 1990, and August 31, 2014. For inclusion, studies need to be crossover clinical trials conducted in subjects with any chronic painful condition, be placebo controlled, and be published in English or German. Our aim was to investigate a convenience sample of fairly recent studies to examine the reporting of the study features of interest.

Data were extracted on publication details, study characteristics (conditions studied, interventions investigated, number of total study participants and women participants, duration of studies, and duration of crossover periods), as well as our study features of interest, namely, the reporting of randomization, double blinding, adverse events and results specified by crossover period, in the abstracts and full texts of the publications.

Methodological study quality (risk of bias) is assessed with the Oxford Quality Scale, a widely used instrument that assesses the domains randomization, double blinding, and withdrawals or dropouts, and scores study quality on an overall scale of zero to five points [6].

To contrast the reporting of our study features of interest in the abstract vs. the rest of a article, we use the term ''full text'' to refer to the text of a journal publication without the abstract. Summary data are presented as proportions of article abstracts or full texts reporting the features of interest.

Following ideas described by Friede et al. [7], we investigate whether interventions such as the publication of the CONSORT statement for abstracts in 2008 led to any changes in the reporting of study features by testing for a change point using the likelihood ratio test proposed by Worsley [8].

The steps for this systematic review were planned a priori, but no formal protocol was published. This research is based on anonymized published data only, and therefore, no approval by an ethics committee/institutional review board is required. Searching, data extraction, and study quality assessment were done by one of the authors (B.W.) under close supervision of the others (T.F. and S.S.). Where decisions on study inclusion or quality assessment were not straightforward, this was discussed among the authors and consensus was reached.

3. Results

3.1. Searching and study characteristics

Database searching revealed 534 hits, of which 98 publications are eligible for inclusion [9–106] (Fig. 1). The studies included in this systematic review were conducted in a range of chronic painful conditions, used a variety of treatments and included a total of 3,513 study participants. In 94 publications with 3,353 participants, the participant sex is specified; the percentage of women in these studies is between 0% and 100%, on average it is 54%.

Total study duration varies between 7 days and 36 months. Crossover period duration is between 2 days and 24 months. Studies were mostly of good methodological quality: 40 publications achieve the maximum score of five points on the Oxford Quality Scale, 29 publications score four points, 16 three points, and 13 publications score