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Adverse event reporting in nonpharmacologic, noninterventional pain clinical trials: ACTTION systematic review

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ABSTRACT

Assessment of treatment safety is 1 of the primary goals of clinical trials. Organizations and working groups have created reporting guidelines for adverse events (AEs). Previous research examining AE reporting for pharmacologic clinical trials of analgesics in major pain journals found many reporting inadequacies, suggesting that analgesic trials are not adhering to existing AE reporting guidelines. The present systematic review documented AE reporting in 3 main pain journals for nonpharmacologic, noninterventional (NP/NI) trials examining pain treatments. To broaden our pool of nonpharmacologic trials, we also included trials examining acupuncture, leech therapy, and noninvasive stimulation techniques (eg, transcutaneous electrical nerve stimulation). We documented AE reporting at 2 levels of specificity using coding manuals based on the Consolidated Standards of Reporting Trials (CONSORT) harms reporting standards and Analgesic, Anesthetic, and Addiction Clinical Trial Translations, Innovations, Opportunities, and Networks (ACTTION) AE reporting checklist. We identified a number of inadequacies in AE reporting across the 3 journals. For example, using the ACTTION coding manual, we found that less than one-half of the trials reported specific AE assessment methods; approximately one-third of the trials reported withdrawals due to AEs for each study arm; and about one-fourth of the trials reported all specific AEs. We also examined differences in AE reporting across several trial characteristics, finding that AE reporting was generally more detailed in trials with patients versus those using healthy volunteers undergoing experimentally evoked pain. These results suggest that investigators conducting and reporting NP/NI clinical trials are not adequately describing the assessment and occurrence of AEs.

1. Introduction

One of the primary goals of a clinical trial is to assess treatment safety, which is needed alongside efficacy information for a trial to be clinically informative [8,12,14,15,17,18,20,26,31]. A major way to assess safety is through the reporting of adverse events (AEs) and serious adverse events (SAEs)—also referred to as harms—that arise during trials. Regulatory agencies and clinicians rely on this information to understand the possible risks of a treatment decision. Incomplete AE reporting can lead to the underestimation of risk [2,3,9,11,19,20,27,28,32], potentially compromising regulatory approval and informed clinical use of treatments.

Professional groups have created standards for AE reporting, resulting in the International Conference on Harmonization (ICH) [13] and Good Clinical Practice (GCP) [10] standards. GCP requires that AEs and SAEs be recorded during a trial and reported to the trial sponsor, all investigators involved, and any appropriate regulatory authorities. These standards do not apply to AE reporting in

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