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Publishing Histories of Adverse Reactions to Medicaments Anecdotally

The PHARMA guidelines for Reporting Suspected Adverse Drug Reactions

I was interested to read the recent guidelines proposed by Kelly et al. for reporting cases of adverse events (i.e. suspected adverse drug reactions), published under the aegis of the International Society of Pharmacoepidemiology (ISPE) and the International Society of Pharmacovigilance (ISoP) in *Drug Safety*[1] and simultaneously in *Pharmacoepidemiology and Drug Safety*.[2]

However, I was surprised and disappointed that the authors wrote that they had found "only one [other] set of usable guidelines," since I published a usable and readily accessible set of guidelines, called PHARMA (Publishing Histories of Adverse Reactions to Medicaments Anecdotally) in 2003. The PHARMA guidelines were published as table 3 in the appendix to the editorial that Kelly et al. cited as reference 3 in their paper.[3] The appendix to that editorial also included extensive discussion of the PHARMA guidelines.[4]

I have compared PHARMA with the ISPE/ISoP guidelines, item by item. For the most part, they are identical or only trivially different; however, there are some important omissions from the latter, which I shall now outline.

Title: Kelly et al.[1,2] mention the title of a case report, but do not discuss how it should be structured. The importance of the title should not be underestimated. In one study, 25% of all papers in a known corpus dealing with adverse drug reactions could not be retrieved from MEDLINE and EMBASE because their titles, abstracts, and indexing terms did not contain sufficient information.[5] A clear descriptive title is an important element in the retrieval of relevant publications. The title should be a non-declaratory formulation that mentions the adverse event, the drug that was suspected to have caused it, and any important susceptibility factors. The words 'associated with' should be used in preference to 'caused by' or 'due to'. Here is an example of a clear title: "Pulmonary infarction associated with crack cocaine use in a previously healthy 23-year-old woman."[6] Other examples are given in the appendix to the PHARMA guidelines.[4]

Abstract: All anecdotal case reports should include a structured abstract. Abstracts are searchable in databases such as Medline and EMBASE and can also provide helpful information for the reader who does not always have ready access to the journal. A structured abstract should include at least the first four of the following items: (i) the adverse event; (ii) the drug implicated, the dosage, and other drugs used; (iii) the duration of therapy and the time course of the event; (iv) the patient (important details, including age, sex and susceptibility factors); (v) evidence that links the drug to the event; (vi) management, if relevant; (vii) mechanism, if known or hypothesized; (viii) implications for use of the drug; and (ix) hypotheses to be tested as a result of the observation.

Information about the dosage, time course, and susceptibility factors is particularly important for adequate classification of the suspected adverse drug reaction.[7]

Introduction: Kelly et al.[1,2] do not discuss the introduction to the report, which should mention the suspected drug and the adverse event with which it was associated, any previous similar reports, and the purpose of the report.

Discussion: Kelly et al.[1,2] do not ask for some important features in the discussion, such as possible mechanisms, possible methods of monitoring and management, the implications of the report for clinical practice, and hypotheses that require further study. These should be optional features. It is particularly important to stress the need for further studies to test hypotheses and to confirm or refute the suggested association, since in most cases anecdotal reports are not subjected to formal studies of this sort, although the adverse events may nevertheless

be subsequently mentioned as adverse reactions in Summaries of Product Characteristics.[8]

Anecdotal reports form a major source of information about suspected adverse drug reactions – about 30% of the published world literature.[9] In some cases an anecdote can even provide definitive proof that a drug and an adverse event are causally associated.[10,11] It is proper that there should be agreed guidelines on how anecdotal reports should be published. The ISPE/ISoP guidelines should be revised to make good the important omissions outlined above. Journals that publish anecdotal reports of suspected drug reactions should be encouraged to ask authors to follow such guidelines, or should at least bring such guidelines to their attention.

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