Development and validation of an algorithm to appraise the quality of spontaneous reports of adverse drug reaction: the QADRA project

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Background: A prompt identification of potential risk signals is an essential feature of a spontaneous reporting system of adverse drug reactions (ADRs), to minimize harmful effects among drug users and allow timely regulatory interventions. The quality of an ADR report is usually based on its seriousness (WHO, 2000). In addition, other parameters, such as notoriety and plausibility of ADRs, may account for the quality of ADR reports (Kelly et al., 2007).
Aim: The present study was performed with the aim of designing and validating an algorithm for the multidimensional evaluation of the quality of ADR case reports (QADRA).
Methods: The quality criteria considered for development of the present algorithm were: causality (level of plausibility of imputation of the causative role played by the suspected drug in the adverse event); notoriety (ability of the case report to add knowledge to the known safety profile of the suspected drug); clinical relevance (level of commitment required for the case management by health care providers); completeness (degree of information completeness required for case evaluation). A sample of 153 patients was randomly and retrospectively selected from 15,906 records included in the Italian database of spontaneous ADR reports throughout 2009. This sample size was estimated to allow a 0.05 type I error with a power of 80%, given an alternative proportion (p) of 0.2. This estimate was based on the assumption that the p of 'good quality' reports in the source population was 30%. Each report was evaluated by two panels of experts blinded to one another, as well as by the algorithm developed in the present study. Each case was classified taking three parameters into consideration: plausibility, notoriety and clinical relevance. Cases were classified as "good quality" or "poor quality" on the basis of clinical introspection. The final assessment constituted the "gold standard" to validate the algorithm. Afterwards, to inspect the predictive ability of our score, receiver operator characteristic (ROC) curves were constructed, and areas under the curve (AUC) were calculated along with sensitivity and specificity values. The most discriminative cut-offs were therefore identified to categorize the score into "high", "intermediate" and "low" quality.
Results: The two panels assessed that 21.6% of reports were of 'high' quality. When applying the QADRA algorithm (score range 0-15), its median value was 6 (4-7, 25 and 75 centile, respectively). The area under the ROC curve, which assesses the ability of the risk score to predict the report quality, was 0.93 (95% CI: 0.88 - 0.97). Herein, the cut-off points ≤5, 6 or 7 and ≥8 indicated the best balance between sensitivity and specificity, and they could be used to categorize the reports as being of 'high', 'intermediate' and 'low' quality (AUC=0.87; 95% CI: 0.80-0.92), respectively.
Conclusion: Based on present findings, the QADRA algorithm is highly predictive of the quality of ADR reports. It performs as a reliable and complete tool, since it overcomes some limitations of available algorithms and definitions. This algorithm is intended to be used mainly for regulatory and pharmacoepidemiological purposes. However, several potential applications should be investigated in the future, both for scientific purposes and healthcare system management.

References

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