

Upper Bound for Performance of Incident Reporting Systems Based on Experience with Phase III Adverse Event Reporting

Michael O'Connor, M.D.; Avery Tung, M.D.; Mark Nunnally, M.D.; Suanne Daves, M.D.; Richard Cook, M.D.
Anesthesia and Critical Care, University of Chicago, Chicago, Illinois

Introduction: Experts have advocated incident reporting systems as a means for improving safety in medicine. The features of an ideal incident reporting system have been discussed extensively and include detailed, immediate reporting by involved participants coupled with sound, relevant, technical analysis distributed to the appropriate group of end-users. We hypothesized that the FDA's adverse event identification system for drugs in phase III trials has many of the features of an ideal incident reporting system, and sought to characterize its performance and contrast it with the likely performance of general medical incident reporting systems.

Methods: We examined drugs approved for use in anesthesia during the past ten years, seeking to identify which agents had significant side effects identified during post-marketing surveillance. We then compared this experience with the expected performance of incident reporting systems, including the JCAHO sentinel event system.

Results: Two of the 11 new drugs had significant side effects that were not identified via the Phase III incident reporting system and only became apparent during post-marketing surveillance. Rapid increases in concentration of desflurane were identified as a cause of hypertension and tachycardia. Rapacuronium was discovered to cause significant histamine release, resulting in its withdrawal from the market.

Discussion: Surveillance for adverse events during phase III drug trials is close to the described ideal: Carefully selected patients are treated with study drug in a strict protocol alongside a control regime. Incident reports are written up by investigators familiar with the patient population, procedures, and drug under investigation, and distributed to all investigators. Despite this, new drugs frequently come to market with side effects which are not detected with this incident reporting regime. Approximately 3-4% of new drugs are ultimately withdrawn as a consequence of side effects discovered during post-marketing surveillance (1). Recognition of the limitations of Phase III trials have led to efforts to increase the sensitivity of practitioners to the possibility that incidents with 'approved' drugs may occur. Examples of such efforts include labeling new drugs with black triangles, and aggressive education campaigns (2). In spite of this, estimates of under-reporting run as high as 98% in post-marketing surveillance (3).

Compared to the Phase III incident reporting system, existing and proposed healthcare incident reporting systems are considerably removed from the ideal. The reports they gather are heterogeneous collections of events that span the breadth of medical care and encompass large variations in patient population, practice patterns, circumstances of care, resources, and outcomes. Such incident reporting systems, therefore, likely to be of less utility as tools for detecting and characterizing new forms of failure than adverse event reporting systems employed during phase III drug trials.