

42. Consequences of Security Alerts on Spontaneous Reporting: Four Analyses from the French Pharmacovigilance Database

F. Gregoire, A. Pariente, F. Haramburu, N. Moore

Pharmacology Department, Bordeaux 2 University, Bordeaux, France

Background: The French Pharmacovigilance database includes adverse drug reactions spontaneously reported by health professionals. Security alerts might influence reporting. Increased reporting could generate spurious disproportionality signals within the database (notoriety bias).

Objective: To explore the consequences of four security alerts on reporting and security signals.

Methods: We considered alerts concerning a possible risk of valvulopathies with pergolide, tuberculosis with infliximab, strokes with atypical antipsychotics and rhabdomyolysis with statins (after cerivastatin withdrawal). We considered two equal time periods of reporting, before and after each alert. We identified all reports relevant for the alert and estimated the reporting odds ratio (ROR) before and after the alert.

Results: There was no report of valvulopathy with pergolide before the alert but 63 after, with an ROR of 9.369 (95%CI: 4.338-20.237). Five of these events actually occurred before the alert but were reported after. There were 25 reports mentioning rhabdomyolysis with statins (not including cerivastatin) before the alert (ROR = 5.8; 95%CI: 3.8-9.0), and 63 after (ROR = 9.4; 95%CI: 7.0-12.6). About 280 reports concerning cerivastatin were reported after its withdrawal. Tuberculosis with infliximab concerned 2 reports before the alert (ROR = 1529; 95%CI: 134-17458) and 7 after (ROR = 434; 95%CI: 111-1703). There was 1 report mentioning stroke with atypical antipsychotics before the alert (ROR = 0.09; 95%CI = 0.01-0.64) and 16 after (ROR = 1.13; 95%CI: 0.69-1.87). After excluding events involving antiaggregant and anticoagulant agents, these estimates were respectively 0.14 (95%CI: 0.02-1.03) before the alert and 2.02 (95%CI: 1.21-3.35) after.

Discussion: Security signals generated by disproportionality measures using spontaneous reporting databases seem to vary after a security alert. This could result from preferential reporting of highlighted events. All reports concerning pergolide and valvulopathy came after the alert. The signal varied for statins and the large reporting of events after the product withdrawal could constitute another effect of notoriety. There were not enough reports concerning infliximab to comment on the results (3 tuberculosis with other drugs after the alert vs. one before). Atypical antipsychotics were negatively associated to reports of stroke before the alert. This disproportionality could not be explained by the high weight of antiaggregant and anticoagulant agents in stroke, as it persisted after excluding reports involving those drugs.

Conclusion: Knowledge and publicisation of an alert will alter disproportionality measures in spontaneous reporting databases, which should therefore not be used to estimate known alerts. This notoriety bias could also create a "ripple" effect, altering the reporting balance of other drugs involved with the same effect.