CORRESPONDENCE

Frequent Adverse Drug Reactions, and Medication Groups Under Suspicion

A Descriptive Analysis Based on Spontaneous Reports to the German Federal Institute for Drugs and Medical Devices from 1978–2016

by Diana Dubrall, Prof. Dr. rer. nat. Matthias Schmid, Dr. med. vet. Eva Alešik, Dr. med. Norbert Paeschke, Prof. Dr. med. Julia Stingl, and Prof. Dr. med. Bernhardt Sachs in issue 23/2018

Unanswered Questions

The extensive title is followed by a misleading article that omits more questions and presents facts in a biased manner, rather than clarifying them or opening up approaches to clarification.

For example, both tables separated the group of psycholeptic drugs in ways that were impossible to comprehend—in part using pharmacologically/pharmaceutically very dubious allocations: *Table 1* lists “psycholeptics (antipsychotics)” separately from “psychoanaleptics (antidepressants)”; the rate for psychoactive (not including antiepileptic) drugs is 13.9%. *Table 2* lists these medications differently again: diazepam is listed with clozapine and olanzapine, whereas risperidone is listed separately from selective serotonin reuptake inhibitors (SSRIs), and so on. In total the neuroleptics group (excluding anticonvulsive drugs) accounts for 9% and 5%. Artificially separating out the reporting rates thus results in a lack of clarity, rather than validity, in the differentiated analysis of an unquestionably complex subject.

The problem of drug interactions is not mentioned at all. The—in all experience—substantial proportion of polypharmacy and drug combinations (not least in neuroleptic/antipsychotic therapy) was neither addressed nor quantified in the methods section or the discussion.

The relevance of adverse drug reactions as listed by rates, with regard to threat to life, extent of impaired quality of life, unfitness to work, emergency hospital admission, and follow-on costs did not receive any attention whatsoever in the extensive set of figures.

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References

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In Reply:

Our objective was to analyze descriptively all spontaneous adverse drug reaction (ADR) reports received since the start of the ADR database (1978).

As we described in our article, for the classification of the drugs we followed the anatomic therapeutic chemical classification system

(ATC) code (1). The ATC code has five different hierarchical levels. The evaluations in *Table 1* applied the second ATC level and those in *Table 2*, the fourth level. Consequently, *Table 2* shows a more detailed and different classification of drug groups than *Table 1*. Regardless of these differentiated evaluations, the abstract summarizes early on: “At the least detailed level of analysis, ‘drugs for the treatment of nervous system disorders’ were the most common class of drugs under suspicion of causing the reported adverse drug reactions (23.1%).”

As described in our article, we analyzed all drugs that were reported as suspicious/interacting. Evaluations of interacting drugs in general were not the objective of our analysis and should be studied separately, owing to the complexity of the question.

We explicitly stated that about 66.9% of all spontaneous reports are classified as serious. As described, the classification (“serious adverse reaction”) is based on the legal definition (e.g., the ADR results in death, is life-threatening, requires inpatient hospitalization, results in permanent disability, and/or is a congenital anomaly) and not on clinical criteria (2). We have no data on resultant consequential costs, inability to work, etc, at our disposal and therefore we cannot analyze such data.

The ADR reports of adverse drug reactions are included in the database in a pseudonymized form and do not allow any conclusions about the relevant patient. According to the formal requirements of the German Federal Institute for Drugs and Medical Devices (BfArM), forwarding spontaneous ADR reports to BfArM does not require a written form of consent from the affected patient, even under the new General Data Protection Regulation (GDPR).

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2. Dubrall D, Schmid M, Alešik E, Paeschke N, Stingl J, Sachs B: Frequent adverse drug reactions, and medication groups under suspicion—a descriptive analysis based on spontaneous reports to the German Federal Institute for Drugs and Medical Devices from 1978–2016. *Dtsch Arztebl Int* 2018; 115: 393–400.

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Conflict of interest statement

The authors of both letters to the editor declare that no conflict of interest exists.