Medication Incidents in Primary Care Medicine

Protocol of a Study by the Swiss Federal Sentinel Reporting System

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Appendix 1. Results of the pilot study

Summary

From July to September 2013 in 18 Swiss family and pediatric practices, a pilot trial on medication incidents took place. 51 notifications were recorded, leading to an incident rate of 0.4 (0.4) (median, interquartile range) per family physician and week or 4 (5) per family physician and 1'000 patient contacts. Virtually no incidents were observed in pediatricians.

Aims of the pilot study

- to test the questionnaires (logistical feasibility, understandability of questions, correctness and consistency of responses)

- to limit the inclusion criteria to obtain complete information without too much redundancy with other notification systems such as the Critical Incident Reporting System (CIRS) or spontaneous reporting of ADRs (pharmacovigilance).

Study design

Prospective, explorative observational questionnaire study with a case-control design

Methods

Questionnaires and Physicians

Because questionnaires suitable for continuous reporting and adapted to our local conditions do not exist, we had to develop new ones. Therefore, based on existing literature, the study directors tested a pre-pilot version in their own praxis. The questionnaires included items on the social and clinical state of the index patients, on the kind of incident, and on possible causative factors. Before using them in a main study of the national Sentinel system, we performed a pilot study to test the questionnaires in a sample of primary care physicians or pediatricians, in each of the German, French or Italian speaking parts of Switzerland for a period of six to eight weeks. All medication-related incidents were recorded and the daily patient-to-physician contacts were counted. To identify factors correlated to specific incidents, the physicians had to collect information for each case also from a *control* patient, matched on age and sex. The initial version of the questionnaire was in German; thereafter it was translated into French. The Italian-speaking physicians could select either version. The patient information sheets were translated into Italian, too.

Inclusion criteria (Physicians)

Willingness to report 6 to 8 weeks of work from July to September 2013.

Exclusion criteria (Physicians)

Participation in the Federal Sentinel reporting system.

Inclusion criteria (Incidents)

Any unexpected event (as defined by the physician) related to the medication process which interfered with the normal course of treatment.

Exclusion criteria (Incidents)

An expected (but unavoidable) ADR, or drug-drug interaction (DDI).

Ethics

This pilot study protocol was submitted to the ethics board of the Canton Zurich, which decided that formal approval was not necessary. An informed consent form had to be signed by the patients. If patients declined participation in the study, reporting was still conducted, but without their personal data; the same applied to minor incidents when the physician was reluctant to confront the patient with information that she or he judged to be irrelevant or could cause a possible loss of confidence. Notification of incidents without informed consent is important for detection of a possible “ethical bias”.

Support

The pilot study was supported by the Bangeter-Rhyner Foundation, Basel.

Data concealing / Statistics

For the purpose of patient tracking, gender and full birth day data were indispensable. In the final dataset, the day and month from the birth information was deleted. Data are presented as median (interquartile range) or frequencies unless stated otherwise. The data sheets were sent to MG, who recorded them on an Excel spreadsheet. Descriptive statistics were performed by using SPSS. No other person had access to the raw data.

Study registration

No registration was conducted.

Results

The study took place from July to September 2013.

From the 24 physicians who were initially willing to participate our pilot trial, 6 dropped out (lack of time, did not understand the sense of the project), leading to a set of 18 to be analyzed. Their characteristics and those of their practices are summarized in Table A1. The median age of all patients was 51 (20) years for family doctors and 7 (interquartile range could not to be calculated) for pediatricians. Two of the family physicians declared that they were in care of a nursing home for the elderly, and two of the pediatricians were responsible for children's homes. Most physicians reported a rate of zero of missed notifications during the study period, but two (who admitted having missed 10% or 80% of incidents) declared not to have notified any. Four of the physicians were surprised by the frequency of the incidents, 11 were not (3 missing); 3 were surprised by the type, 11 were not (4 missing). The total time expenditure for the pilot participation was declared to be 3 (2) hours. For the planned main trial, 9 of the participants would have preferred a university institute to send in their notifications, 1 the Federal Health Agency, and the others were indifferent.

During the pilot, the median number of patient contacts per physician was 686 (320); resulting in 93 (37) per week and physician for family physicians, and 87 (45) for pediatricians. For family physicians, the median number of incidents per week was 0.4 (0.4), and per 1'000 contacts 4 (5), while for pediatricians they were virtually zero.

Fifty-one detailed notification sheets were sent to the study director. Concerning the patient data, 26 were male, 20 female, in 4 cases the gender was not reported, and in 1 case the reporting did not apply to a specific patient. The median age was 67 (23) years. Informed consent was achieved in 22 patients, while in 19 patients, the physician did not ask; in 2 cases the patient refused to participate, in 3 cases the physician could not ask the patient because of dementia, in 4 cases this information was missing, and in 1 case there was no relation to a specific patient to be asked.

In 46% of the cases, the incident was observed by the reporting physician or the staff in his practice, in 36% by the patient or his family, in 8% by the pharmacist, in 6% by the community nurse or the institution they were living in, in 2% by another physician (1 missing information). Types of incidents are listed in Table A2. In 69% of the notifications, one or more organ systems were involved; they are listed in Table A3; 31% were without any damage. The causes of the incidents as defined by the physicians are listed in Table A4; in 31% there was no distinct cause (e.g. unexpected ADR). In reaction to the incident, 24% of the physicians changed standard operating procedures (SOPs) within his practice, in 6% of the cases he made an arrangement with others, in 2% of the cases he wrote a Swissmedic ADR notification ("yellow leaflet"), in 2% a CIRS notification was made, in 32% other reactions were mentioned, and in 34% there wasn't any

reaction to the incident at all (multiple answers, 5 missing information). In 1 case the physician declared that he had a similar incident within the study period, while in the other 44 this was not the case. The notification without a specific patient concerned the interruption of cholecalciferol ampoules production by Streuli Co.

Concerning the drugs involved in the incidents, there were 9 naming of anti-hypertensives, 7 anticoagulants, 5 anti-diabetics, 5 antibiotics (2x amoxicillin, 1x amoicillin+clavulanic acid, 2x clarithromycin, 1x co-trimoxozole), 5 antidepressants, 3 neuroleptics, 3 analgesics, 2 statins, 2 vaccines, 1 antiepileptic (lamotrigin), 1 benzodiazepine, and 17 other groups.

Within the 3 cases of alleged DDI, there were 3 naming of antibiotics, 2 anti-hypertensives, 2 antidepressants, 2 non-steroidal anti-inflammatory drugs, and 7 other groups.

Within the 18 cases with an ADR, 1 Swissmedic-ADR leaflet was filled (visual hallucinations after valaciclovir). Within the 24 other cases, mostly related to an error, one CIRS notification was made (hypoglycemia in an insulin-treated diabetic after application of amoxicilline+clavulanic acid and clarithromycine).

Harm by the incident was declared to be: no harm at all 32%, mild 26%, moderate 26%, severe 16% (6 times question did not apply, and 2 missing information). Within the 25 cases with harm, the duration was: “days” 68%, “weeks” 20%, “longer” 4%, and “not yet defined” 8% (3 times missing information). Recovery was described as complete 93%, and not yet defined 8%. Treatment was none 58%, ambulatory 31%, hospital care 11%.

To discern predisposing factors to become victim of an incident, we also collected information from control patients. Table A5 compares the patient data with them.

Many physicians were not able to report the mean age of their patients, and many of them could not estimate the percentage of prescribed medications as compared to the ones directly delivered to the patients. Many respondents had difficulties understanding our concept of drug applications, meant to be the number of distinct medications times the number of their daily applications (e.g.: medication A 1 – 0 – 0, and medication B 1- 0 – 1 are *three* applications). Several physicians stated that they didn’t understand the distinction between foreseen but accepted risk vs. unexpected ADR or DDI.

Discussion

In a group of 18 family physicians or pediatricians, for 138 weeks of work and among 12’451 patient-to-physicians contacts, our pilot study resulted in 51 medication incidents.

Concerning problems to get informed consent, many physicians stated that it was oftentimes only later that an incident was detected, so it was perceived that the time and energy needed to contact the patient was a waste of time. To inform him or her about a minor incident which was readily corrected by the physician and without consequences, could in the worst case disturb the relationship to and confidence in their doctor. After discussing this issue with the responsible persons of the Federal Health Agency (Brigitte Meier, Martin Götz) it was clear that some form of general consent to collect anonymized data would be sufficient for most epidemiological research, especially for the main study of our project as planned by 2015, so that we would not have to get individual consent from the patients. This is important for our project because it would require some kind of confession to declare an error to the patient, prompting the physician into non-reporting and thus leading to massive bias of up to 50% of the incidents.

Ethical concerns beside, it seems difficult enough to get unbiased information about errors. In our study, out of 18 ADR, only one led to drug authority (Swissmedic) notification! Out of 26 other medication incidents or errors, only one was subject to notification to the CIRS system. Our pilot study clearly documents a substantial rate of underreporting to these systems. Hence we presume that the population of our study physicians was exceptionally motivated about the topic, so that the average physician doing there every day’s work would perform worse leading to an even larger proportion of non-reporting.

As declared by comments of two of the pediatricians in the study, they seldom use drug treatments (out of specialized centers) and if so, only for a short duration; this may explain the low number of incidents reported in our study.

In our pilot, the two major single reasons for error were lack of alertness (of doctor and practice staff) and lack of cooperation from patients and their relatives. The former may be dealt with by clear SOPs – adapting them was the most often cited consequence of an incident – and the latter may be helped by improving communication skills. One single case stated that the patient was misled by the package leaflet of his medication. It was the case of zaleplon, a somniferous out of trade. Although rare, such cases should be reason enough to contact the manufacturer.

Most cases were without or with only minor harm, although 18 times a moderate to severe damage was reported. All were resolved without permanent consequences to patients. There were cases of theoretical incompatibility mostly with DDI, detected by electronic control systems. No harm by DDI however was recorded in our data.

A main aim of our pilot was to test the comprehension of questionnaires. Several physicians had problems with reporting the number of daily drug applications; this may be overcome by giving them detailed examples. Some participants could not indicate the mean age of their patients; in the Sentinel system, the problem of knowing the age of their patients is solved by 2x2 weeks of detailed consultation analysis, so in this respect, the difficulties of answering this item will not be of importance for the main study.

We included many items on patient risk factors in our questionnaire to discern factors that presumably predispose having an incident. To evaluate their importance, we collected information from *control cases* of the same age and sex. Although most physicians had no difficulties to define a control patient, this issue is troublesome and time consuming. If predisposing factors should be analyzed, the information from control cases is indispensable. For our main study, we decided to collect denominator information from the detailed analysis of patient-to-physician contacts and to skip the case-control method.

As for the inclusion criteria: the participant physicians judged it to be cumbersome to discern whether the risk of an ADR or DDI was to be (theoretically) foreseen but accepted vs. unexpected. For the main trial opened inclusion criteria to any ADR or DDI irrespectively from being presumed or not, provided that an error element has been involved in its evolution.

Conclusions

The prospective and systematic reporting by the physicians of the Swiss National Sentinel Reporting System by 2015 seems to be a feasible way to collect information on medication-related incidents in primary care.

Table A1. Physicians participating in the pilot study among language regions.

Linguistic region	German (9) spoken	French (6) or Italian (3) spoken
Gender		
- male	7	7
- female	2	2
Specialty		
- general internal	6	8
- pediatrician	3	1
Age	53 (21)	49 (19)
Number of physicians in practice	3x1, 3x2, 2x4, 1xM	2x1, 4x2, 1x3, 1x4, 1x7
- of them reporting to the pilot	7X1, 2x2	7x1, 2x2
Medical graduation year	1987 (23)	1986 (19)
Working hours per week,	50 (15)	50 (17)
of them in practice, %	90 (20)	80 (20)
Medication delivery by pharmacist as compared to direct delivery, %	0, 8, 70, 80, 90, 96, 3xM	30, 4x100, 4xM
Localization of practice,		
- urban	5	2
- small town	1	5
- rural	3	2
Electronic interaction control system, %	33	33
Practice certification, %	22	22
Staff meetings,		
- at least monthly, %	56	33
- less frequent, %	44	56
- none, %	0	11
Quality circle participation,		
- at least monthly, %	78	67
- less frequent, %	11	33
- none, %	11	0
Weeks of reporting to the study	7 (1)	8 (1)

Patient-to-physician contacts per week	97 (56)	92 (29)
Number of incidents reported	3 (4)	2 (5)

Values denote median (interquartile range), M=missing value.

Table A2. Types of incident (n=51), multiple entries.

	Namings	Percent
Dose too high	10	19.6%
Dose too low	4	7.8%
Application too long	2	3.9%
Wrong route of application	1	2.0%
Wrong medication	5	9.8%
Necessary medication not applied	6	11.8%
Unexpected drug-drug interaction	4	7.8%
Unexpected adverse drug reaction	21	41.2%
Administration of expired or defective medication	1	2.0%
Medication not reimbursed by insurer	1	2.0%
Other type of incident	10	19.6%
Total	**65**	**127.5%**

Table A3. Organ system involved (n=35), multiple entries.

	Namings	Percent
Cardiovascular	6	17.1%
Central nervous system	13	37.1%
Gastro-intestinal /	5	14.3%
liver	0	0.0%
Kidney	1	2.4%
Skin	7	20.0%
Other	13	37.1%
Total	**45**	**128.6%**

Table A4. Causes of the incident (n=35), multiple entries.

	Namings	Percent
Failure of communication		
within practice	2	5.7%
with hospital	3	8.6%
with institution	2	5.7%
with community nurse	1	2.9%
with pharmacist	5	14.3%
with others	2	5.7%
Generic substitution	2	5.7%
Multiple prescriptions	2	5.7%
Lack of alertness within practice	11	31.4%
Lack of documentation	6	17.1%
Insufficient patient instruction	4	11.4%
Lack of cooperation of the patient or of his relatives	7	20.0%
Misleading package leaflet	1	2.9%
Misleading information from the Internet	1	2.9%
Administrative problems	1	2.9%
Distributor-related problems	2	5.7%
Insufficient maintenance	1	2.9%
Other types	6	17.1%
Total	**59**	**168.6%**

Table A5. Frequencies of circumstances presumed to influence the propensity to incidents*.

Item	N	Cases %	Controls %
Relationship with patient	31		
- "own" patient		94	78
- replacement of family physician		6	19
- institution's doctor		0	3
Dwelling	26		
- with family or partner		73	61
- alone		19	27
- in an institution		8	12
Social problems	28		
- none		68	68
- mild		14	14
- moderate to severe		18	18
Psychiatric illness or dementia	28		
- none		93	85
- mild		0	11
- moderate to severe		7	4
Treatment with psychotropic drugs (multiple entries)	27		
- *none*		59	78
- *antidepressants*		36	18
- *neuroleptics*		4	0
- *benzodiazepines*		7	11
- *opiates*		7	4
Linguistic problems	28		
- none		89	86
- mild		11	14
Addictions	27		

- none - alcohol - drugs		92 4 4	74 22 4
Smoking - no - yes	25	 76 24	 76 24
Vision problems or hearing loss (uncorrected or uncorrectable) - none - vision impaired - hearing loss - both	28	 89 4 7 0	 78 11 7 4
Mobility impairment - none - mild - moderate to severe	28	 89 7 4	 82 11 7
Who prepares the medication - him-/herself - relatives - community nurse - institution - other (or does not apply)	25	 76 8 4 8 4	 64 20 4 12 0
Number of daily medications (median, interquartile range) - number of distinct compounds - number of active substances - number of applications	 26 26 20	 4 (5) 5 (5) 6 (10)	 4 (5) 4 (5) 6 (5)

* No significant differences by testing with McNemar’s chi square test.