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Effects of e-mails containing ADR information and a current case report on ADR reporting rate and quality of reports

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Abstract

Background Spontaneous reporting of adverse drug reactions (ADRs) is one approach to increasing our knowledge on the risks of drugs in clinical practice. Under-reporting is a shortcoming of this system.

Objectives To evaluate if repeated e-mails with attachments on ADR information can affect (1) the reporting of ADRs and (2) the quality of the ADR reports.

Methods All 117 heads of primary health care units in the region of Västra Götaland in Sweden were randomly allocated (1:1) to an intervention group or a control group. The intervention consisted of e-mails with attachments sent out to each of the 117 heads in January, May and September 2007. These e-mails included (1) the heading “Every ADR report is important”, (2) a current case report of an ADR and (3) instructions on how to report. The number of reports from each primary health care unit run by the same head was registered, as was the quality of the report. The quality was defined as high if the ADR was (1) serious, (2) unexpected or (3) related to the use of new drugs and not labeled as common in the summary of product characteristics. All other reports were regarded as low-quality reports.

Results The total number of reports increased from 89 in 2006 to 111 in 2007 ($P=0.037$). No difference in the

number of reports between intervention ($n=56$) and control ($n=55$) units could be detected. The proportion of high-quality reports before and after the intervention was 36 and 48%, respectively (intervention, $P=0.11$) and 40 and 36%, respectively (control, $P=0.55$).

Conclusions No apparent effect of repeated ADR e-mails on the reporting of ADRs could be detected, although an increase in the reporting rate in general was noted.

Keywords Adverse drug reaction · Quality of reports · Reporting rate

Introduction

Adverse drug reactions (ADRs) are a major health care problem and a common cause for hospital care [1–3]. Consequently, an analysis of risks and benefits is essential before initializing drug treatment in patients. Such an analysis, however, implies access to adequate knowledge on these parameters. After a drug is registered, a large number of patients with characteristics often widely differing from those in the preregistration studies are exposed to the drug, such as elderly patients, nonadherent patients and patients with concomitant diseases treated with other drugs (polypharmacy). The drug safety information is limited for these patient groups, and post-marketing surveillance is therefore an important tool for increasing our knowledge of risk and benefits of drugs.

Spontaneous reporting of ADRs is one approach by which the knowledge of the risks of a drug in clinical practice can be increased. It is an important method for detecting signals, which is one aim of pharmacovigilance. In Sweden, authorized prescribing health care providers (physicians, dentists) and nurses are obliged to report (1)

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serious ADRs, (2) ADRs not mentioned in the summary of product characteristics (SPC), (3) ADRs related to the use of new drugs (≤ 2 years on the market) except those labeled as common in the SPC and (4) ADRs whose incidence seems to increase [4], the latter obviously being difficult for any individual to identify. All ADR reports are reviewed by trained nurses (MLJ, GB) and clinical pharmacologists (SMW) at regional pharmacovigilance centers, after which they are entered in the SWedish Drug Information System (SWEDIS). The ADR reports are assessed in terms of causality and seriousness according to World Health Organization (WHO) criteria.

A serious drawback of the spontaneous reporting system is that only a small proportion of all ADRs are reported [5, 6]. Low reporting rates may be due to the lack of time and/or lack of knowledge on how to report them [7] as well as attitudes, such as the belief that (1) ADRs are well documented by the time a drug is marketed, (2) one should only report an ADR if there is no doubt that it is related to the utilized drug or (3) the single case any individual doctor may see could not contribute to medical knowledge [8, 9].

Methods that are known to increase ADR reporting include (1) education [10, 11], (2) access to report forms in combination with verbal reminders [12] and (3) distribution of a drug-safety bulletin [13] and detailed drug-specific feedback to the reporting doctor [14]. Some of these methods are time-consuming and therefore costly. Moreover, for all the methods mentioned, the effects may diminish over time. Consequently, there is an urgent need for an easily managed, but continuously up-dated method (=on-going) aimed at improving ADR reporting without too much effort or cost.

In the region of Västra Götaland in Sweden, there are 123 primary health care units directed by 117 heads. News concerning drugs is distributed via attachments in e-mails to the heads of the primary health care units, who are instructed to forward the message to their employees. The “e-mail attachment” system has been used since 2005, and approximately 25 e-mails are distributed each year. This system has been shown to influence sales of prescribed drugs, indicating that the e-mails are read by primary care doctors and considered to these individuals to be trustworthy [15].

The aim of the study reported here was to evaluate whether repeated e-mails with attachments containing ADR information can affect (1) the reporting of ADRs and (2) the quality of the ADR reports.

Methods

The 117 heads of primary health care units in the region of Västra Götaland were randomly allocated in a 1:1 fashion

to an intervention group or a control group. It was expected that each unit reported ADRs to varying extents. In addition, a small number of the units were participating in a contemporary educational intervention during the study period. Consequently, the allocation was stratified according to number of ADR reports in 2006 and whether or not the unit had received the educational intervention. A person not involved in the study and without any knowledge of the study protocol performed the randomization procedure.

The intervention consisted of repeated e-mails with attachments during 2007. These followed the established system for e-mails on drug news and included one page with (1) the heading “Every ADR report is important”, (2) a current case report of an ADR and (3) instructions on how to report. The e-mails were distributed three times during 2007, in January, May and September, with each including a new current case report of an ADR.

The number of reports from each primary care unit run by the same head was registered, as was the quality of the report. The quality was defined as high if the ADR undoubtedly should have been reported, i.e. was (1) serious, (2) unexpected or (3) related to the use of new drugs and not labeled as common in the SPC. All other reports were regarded as low-quality reports.

Statistics

Statistical analyses were conducted using SPSS ver. 14.0 (SPSS, Chicago, IL). The Wilcoxon signed rank test was used for comparisons within groups, and the Mann–Whitney test was used for comparisons between groups. A P value < 0.05 was considered to be significant.

Results

Before the intervention (2006), a total of 89 reports from the primary health care units were registered, with the number of reports per unit ranging from zero to 12 (intervention group) and zero to five (control group). The

Table 1 Number and quality of reports in the primary health care units in 2007

Reports	Intervention units ($n=59$)	Control units ($n=58$)
Total	56	55
Serious	10 (18)	9 (16)
Previously not known ADR	16 (29)	11 (20)
New drug	4 (7)	1 (2)

ADR, Adverse drug reaction

Values are given as the number (n) with the percentage in parenthesis

proportion of high-quality reports did not differ between the groups—36 and 40% in the intervention and control group, respectively ($P=0.38$).

The total number of reports increased to 111 in 2007, which is a 25% increase in the number of reports per unit compared to 2006 ($P=0.037$). Of these, 56 were in the intervention group (range zero to six reports per unit) and 55 were in the control group (range zero to eight reports per unit). The proportion of units reporting ADRs in 2007 did not differ between the intervention and the control group (49 vs. 52%, $P=0.78$). The proportion of high-quality reports before and after the intervention was 36 and 48%, respectively, in the intervention group ($P=0.11$) and 40 and 36%, respectively, in the control group ($P=0.55$). However, the proportion of high-quality reports did not differ between the groups ($P=0.53$). The number and quality of reports are shown in Table 1.

In the intervention group, 16 reports concerned ADRs not mentioned in the SPC. The corresponding figure in the control group was 11. These reports are described in Table 2.

Discussion

The number of ADR reports per primary health care unit increased from 2006 to 2007. However, an isolated effect of the intervention could not be detected, since neither the number of reports nor the proportion of units reporting ADRs differed between the intervention and the control units. One explanation for the results of our study may be an increased attention to patient safety in general and, therefore, also a focus on ADR reporting. The intervention may also have spilled over to the control units. Doctors may work in more than one primary health care unit, i.e. both in the intervention group and in the control group. Also, the units all belong to the same organization, and information may easily be passed on from one unit to another. Also, given the available number of health care units in the region, the study had a power of >80% to detect a doubling of the reporting in the intervention group. Thus, the results indicate that repeated e-mails may not affect the reporting rate to a major extent. Indeed, the intervention could be of importance even with a smaller effect, since it

Table 2 Description of ADRs not mentioned in the SPC reported by the primary health care units

Randomization group ^a	Age (years)	Gender ^b	ADR diagnosis/es	Suspected drug(s)	Serious	New drug
I	25	F	Leg pain	Mirtazapine	No	No
I	33	F	Hyperprolactinemia	Lithium	No	No
I	35	M	Paraesthesia	Terbinafine	No	No
I	47	F	Syncope	Etoricoxib	No	No
I	49	F	Bradycardia, apathy	Varenicline	No	Yes
I	50	F	Nightmares	Loratadine	No	No
I	59	F	Photosensitivity	Buprenorphine	No	No
I	61	M	Hyperpigmentation	Warfarin	No	No
I	65	F	Confusion	Nitrofurantoin	No	No
I	73	F	Taste alteration, parosmia	Amoxicillin	Yes	No
I	74	M	Melaena	Ketoprofen	No	No
I	74	F	Syncope	Varenicline	Yes	Yes
I	79	M	Erythema multiforme	Propiomazine, paracetamol, zopiclone	Yes	No
I	81	M	Petechiae	Dexibuprofen, ketoprofen	Yes	No
I	81	M	Prothrombin decreased	Warfarin, nabumetone	No	No
I	82	F	Nightmares	Simvastatin	No	No
C	29	F	Galactorrhea, nasal congestion	Citalopram	No	No
C	31	F	Palpitations	Ketoprofen	No	No
C	32	M	Pulmonary embolism	Venlafaxine	Yes	No
C	36	F	Hemorrhage nos	Pregabalin	No	No
C	40	F	Vasodilatation	Amitriptyline	No	No
C	45	F	Skin discoloration	Hydroxocobalamin	No	No
C	47	F	Angioedema	Solifenacin	Yes	Yes
C	52	F	Rash pustular, psoriasis aggravated	Chloroquine phosphate	No	No
C	54	F	Chest pain	Ramipril	No	No
C	76	F	Insomnia	Simvastatin	No	No
C	82	F	Stomatitis	Codeine+paracetamol	No	No

SPC, Summary of product characteristics

^a C, Control; I, intervention

^b F, Female; M, male

is neither costly nor time-consuming. To investigate this possibility would require an expanded “e-mail attachment” system that includes more than the 117 heads of our region.

The number of high-quality reports increased numerically in the intervention group, but not in the control group. However, the power of the study to detect significant differences regarding this aspect was low. A previous study has shown that an educational program may increase the quality of the reports [10]. Further evaluation of a combination of an educational program and repeated e-mails for increased quality of reports may be of interest.

One major limitation of the study is that an individual doctor’s interest in ADRs may have a great impact on the reporting rate; for example, a total of 12 reports were registered from one primary care unit, all of which came from the same doctor. Another limitation of the study is that we do not know whether the intervention actually reached the target population. However, the “e-mail attachment” system has been on-going for several years and has been shown to influence the sales of prescribed drugs, indicating that the system seems to be working properly [15]. On the other hand, heads of primary health care units could be more inclined to push their doctors to prescribe cost-effective drugs according to producer-independent drug information, thus improving the local budget of the unit, rather than to push their doctors to report ADRs, an action which does not directly benefit the unit, but is of worldwide interest for safe drug use.

In conclusion, no apparent effect of repeated ADR e-mails on the reporting of ADRs could be detected. However, an increase in the reporting rate in general was found.

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Conflict of interest statement No conflicts of interests exist.

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