ORIGINAL RESEARCH ARTICLE

Drug Saf 2011; 34 (9): 755-762
0114-5916/11/0009-0755/$49.95/0

Effectiveness of Pharmacovigilance Training of General Practitioners

A Retrospective Cohort Study in the Netherlands Comparing Two Methods

Roald Gerritsen,[1] *Hans Faddegon,*[2] *Fred Dijkers,*[3] *Kees van Grootheest*[1,4] and *Eugène van Puijenbroek*[1]

1 Netherlands Pharmacovigilance Centre Lareb, 's-Hertogenbosch, the Netherlands
2 Department of General Practice, Erasmus MC, University Medical Centre Rotterdam, Rotterdam, the Netherlands
3 Department of Public Health and Primary Care, Leiden University Medical Center, Leiden, the Netherlands
4 Department of Pharmacy, Division of Pharmacotherapy and Pharmaceutical Care, University of Groningen, Groningen, the Netherlands

Abstract

Background: Spontaneous reporting is a cornerstone of pharmacovigilance. Unfamiliarity with the reporting of suspected adverse drug reactions (ADRs) is a major factor leading to not reporting these events. Medical education may promote more effective reporting. Numerous changes have been implemented in medical education over the last decade, with a shift in training methods from those aimed predominantly at the transfer of knowledge towards those that are more practice based and skill oriented. It is conceivable that these changes have an impact on pharmacovigilance training in vocational training programmes. Therefore, this study compares the effectiveness of a skill-oriented, practice-based pharmacovigilance training method, with a traditional, lecture-based pharmacovigilance training method in the vocational training of general practitioners (GPs). The traditional, lecture-based method is common practice in the Netherlands.

Objective: The purpose of this study was to establish whether the use of a practice-based, skill-oriented method in pharmacovigilance training during GP traineeship leads to an increase of reported ADRs after completion of this traineeship, compared with a lecture-based method. We also investigated whether the applied training method has an impact on the documentation level of the reports and on the number of unlabelled events reported.

Study Design: A retrospective cohort study. The number of ADR reports submitted to the Netherlands Pharmacovigilance Centre Lareb (between January 2006 and October 2010) after completion of GP vocational training was compared between the two groups. Documentation level of the reports and the number of labelled/unlabelled events reported were also compared.

Results: The practice-based cohort reported 32 times after completion of training (124 subjects, 6.8 reports per 1000 months of follow-up; total follow-up of 4704 months). The lecture-based cohort reported 12 times after training (135 subjects, 2.1 reports per 1000 months of follow-up; total follow-up of 5824 months) [odds ratio 2.9; 95% CI 1.4, 6.1]. Reports from GPs with practice-based training had a better documentation grade than those from GPs with lecture-based training, and more often concerned unlabelled events.
Conclusions: The practice-based method resulted in significantly more and better-documented reports and more often concerned unlabelled events than the lecture-based method. This effect persisted and did not appear to diminish over time.

Background

When a new drug is licensed, data on the drug's safety are incomplete. The information acquired from preclinical trials is limited because of small sizes and short study periods. In addition, the characteristics of study subjects differ from real-life users with respect to age and drug use. Reporting of adverse drug reactions (ADRs) is one of the main instruments for filling this gap. Healthcare professionals and patients report their experiences in everyday conditions as opposed to the artificial settings of preregistration trials. Unfortunately, the reporting rate is low, with unfamiliarity with ADRs and the basic principles of the reporting process being one of the main reasons given for this low reporting rate.[1-3] There is considerable potential for improvement of reporting rates. In the late 1980s, structuring of the reporting process, case confirmation and the sending of feedback resulted in a more than 15-fold increase of reports from physicians in one study.[4] Since then, more specific strategies to increase awareness of ADRs have included increased attention to education, improved accessibility of information and improved communication regarding ADRs.[5] In a number of studies, a positive effect of incentives,[6,7] distant learning modules[7] or educational outreach visits[8] for reporting ADRs have been demonstrated, but all tended to have a short follow-up or the effects diminished over time. Because of the need for increasingly comprehensive reporting of suspected ADRs in the postmarketing surveillance of drugs, targeted education on reporting suspected ADRs is essential.

In order to increase awareness, the Netherlands Pharmacovigilance Centre Lareb is active in the vocational training of general practitioners (GPs). Traditionally, this training in pharmacovigilance is lecture based. Lareb is invited by most vocational training centres to present a twice-yearly lecture as part of their regular education programmes. This 2-hour lecture is given by an experienced collaborator and addresses key themes in pharmacovigilance and spontaneous reporting. Information is provided on reporting ADRs, including an explanation of the process and on the pharmacovigilance system in the Netherlands. This lecture is offered to GP registrars in their third (final) year of vocational training. GP trainees are invited to present cases of suspected ADRs encountered in clinical practice for discussion in the session. Those reporting an ADR receive feedback, as is common practice at the Netherlands Pharmacovigilance Centre Lareb. The main aims of this training are the transfer of knowledge and for trainees to become acquainted with the process of reporting suspected ADRs in the Netherlands. This lecture-based method is used at Leiden University Medical Centre. Reporting is encouraged, but is neither mandatory nor rewarded in this training.

Since 2006, a new, practice-based pharmacovigilance training method has been offered to GP trainees at Erasmus MC, University Medical

Centre Rotterdam. This method is based on incentive-stimulated active reporting of ADRs through a reporting assignment. This reporting assignment is incorporated into a practice-based vocational training programme, aimed at changing the behaviour of future GPs. The training method is based on the principle that doctors learn most when they are motivated enough to identify their own learning needs and meet those needs at their own workplace.[9,10] Over 20 systematic reviews of interventions[11-13] to change practitioner behaviour suggest that such interventions should be multifaceted, have a focused and active educational outreach component, include skills development and be congruent with clinicians' values.[14,15] Therefore, the education programme needs to contain feedback elements and have a clear clinical significance. Furthermore, the trainee needs to participate in educational activities in the practice he or she is working in. A practical assignment allows GP trainees to turn workplace experience into realistic learning objectives.[16]

In practice, this reporting assignment is incorporated into a series of assignments in the third (final) year of their vocational training. The main objective of these assignments is to incorporate predefined desired skills and competences in daily practice, thus encompassing more than the transfer of knowledge alone. Although no specific assignments are mandatory, a minimum of 14 credit points must be acquired during this training year. As repetition is assumed to improve the integration of these skills, trainees are encouraged to perform these assignments repeatedly. In the reporting assignment, one or two credit points are awarded for reporting one ADR (one for reporting the ADR, one for processing the ADR in the patient's medical record) and the reporting of an additional ADR is rewarded with one extra credit point. Reporting more repeatedly is encouraged; however, this is not rewarded with additional credit points. Any suspected ADR can be reported as this serves to improve familiarity with the reporting process; however, reporting of clinically relevant or unknown ADRs or to address a learning need for the reporting GP trainee is encouraged.

In the skill-oriented, practice-based programme, the input of both the training centre and the pharmacovigilance centre is limited. The GP trainees do not receive a lecture; rather, they receive only an information folder with basic instruction from the training centre on how to report an ADR and how to process an ADR in the information system of their monitoring GP. After reporting, GP trainees receive feedback from the Netherlands Pharmacovigilance Centre Lareb, as is common practice. Additionally, GP trainees are encouraged to explore the Netherlands Pharmacovigilance Centre Lareb website, which provides both basic and detailed information on pharmacovigilance. It is expected that this element increases awareness regarding pharmacovigilance and is an additional incentive to report unexpected ADRs after completion of vocational training. GP trainees are instructed to discuss the reported ADRs and the feedback received (as well as relevant information obtained from the website) with the GPs at their training practice.

It is hypothesized that the practice-based approach performs better than the lecture-based method; however, this needs to be demonstrated. Therefore, this study compares the number and quality of ADR reports made by GPs after completion of their vocational training by GPs trained using the practice-based method (at Erasmus MC, University Medical Centre Rotterdam) with those made by GPs trained at a comparable centre that uses the lecture-based method (Leiden University Medical Center).

Methods

This study compares the lecture-based pharmacovigilance training method with the practice-based method by analysing the number and quality of reports sent in by graduate GPs who had been offered one of both approaches during their vocational training. The first group consisted of GPs who completed their vocational training at Leiden University Medical Center from January 2006 to December 2007 and had been offered lecture-based training. The second group consisted of GPs from Erasmus MC, University Medical Centre Rotterdam, who had been offered practice-based training between January 2006 and

December 2007 in the final year of their vocational training.

Number and Timing of Reports

The database of the Netherlands Pharmacovigilance Centre Lareb was searched for ADR reports with a reporting date between 1 January 2006 and 1 October 2010, submitted by GPs after completion of their vocational training, who had followed either training approach. The names of the reporting GPs were checked against the list of names of GPs who graduated from both universities. To improve identification, a match of the person's initials and e-mail address was required. Where there was doubt, the reporting GP was contacted. A report was included in the analysis when submitted after the graduation date of the GP involved. The period of time after graduation in which reports could have been submitted (time available for follow-up) was determined for both training methods, as well as the total number of reports and the number of GPs who actually submitted reports. The number of reports received per 1000 months of GP follow-up time for both approaches was calculated.

The aim of both training programs is to induce a long-lasting effect on the reporting of ADRs. For this reason, the period between graduation and submission of the most recent ADR report was determined for every GP. Differences between the two training groups were analysed using Cox proportional hazard survival regression. It is possible that in the years following graduation, the effect of the training method diminishes, and GPs may become less willing to report ADRs. To compare the sustainability of both methods, the hazard functions for the time of submission of the most recent ADR report over time were compared graphically.

Characteristics of Reports

To compare the characteristics of the reports, both the quality of the reports and whether or not individual ADRs were mentioned in the Summary of Product Characteristics (SPC) were investigated. With respect to the quality of the reports, the level of documentation of the reports was compared for both approaches. This level is routinely assessed (independent of this study, by assessors unaware of its existence) using a predefined algorithm once a report is submitted to the pharmacovigilance centre (see table I). Possible differences between both approaches were examined using logistic regression analysis to calculate odds ratios (ORs) with a corresponding 95% confidence interval.

Table I. Criteria for assessing report documentation quality[a]

'A' criteria
Clear indication of a latency is provided (either explicitly or through start dates for both drug use and presentation of the reported event)
Sex and age of patient and detailed information on reported event is provided
Information on clinical course and outcome of the reported event is provided
'B' criteria
Are other factors that potentially cause or influence the reported event excluded?
Is information on effects of a rechallenge provided?
Is information on the indication of the suspect drug and the use of concomitant information provided?

a The report was rated as well documented if three 'A' criteria were present, moderately documented if two 'A' criteria and at least one 'B' criterion were present, and poorly documented for all remaining combinations.

A report may refer to one or more individual possible ADRs. For the various ADRs mentioned in the reports, it is routinely assessed whether or not they are mentioned in the SPC of the products involved and thus whether they could be a potential new ADR. Logistic regression analysis was used to study possible differences between both approaches.

Statistical Analysis

Statistical analyses were carried out using SPSS software, version 16.0 (IBM, Armonk, NY, USA). A p-value <0.05 was considered to be statistically significant.

Results

Number of Reports

The lecture-based training was attended by 135 GP registrars, which corresponds to 93.8% of

the trainee capacity of this centre. Five GP trainees (3.7%) reported an ADR during their vocational training. The total time for follow-up after graduation for this group was 5824 months, i.e. 43.1 (range 32–56) months per GP.

In total, 12 reports were received from this group, submitted by ten GPs (8.1%), which corresponds to an average of 1.2 (range 1–2) reports per reporting GP. The number of reports received from those who followed the lecture-based training method was 2.1 per 1000 months of follow-up.

The practice-based training was followed by 124 GP registrars. In total, 109 GP trainees (87.9%) actually reported as part of this training, corresponding to 86.1% of the training capacity. The total time for follow-up after graduation in this group was 4704 months, i.e. 37.9 (range 25–51) months per GP.

In total, 32 reports were received from this group, submitted by 24 GPs (19.3%), which corresponds to an average of 1.33 (range 1–3) reports per GP. The number of reports received from those who followed the practice-based training method was 6.8 per 1000 months of follow-up.

Cox regression analysis showed a statistically significant difference between practice-based and lecture-based training (hazard ratio 2.9; 95% CI 1.4, 6.1). A one minus log plot shows the hazard is constant over time, which is a prerequisite for applying Cox's regression analysis (figure 1).

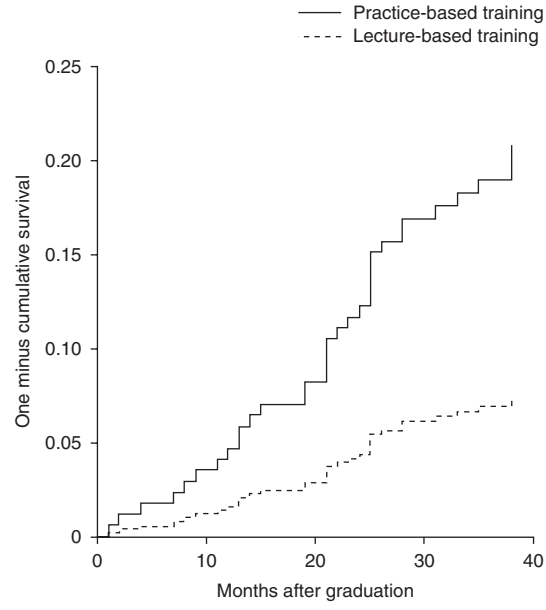

Fig. 1. One minus cumulative survival curve showing the difference between submitting reports after practice-based training and lecture-based training.

Quality of Reports

Reports from GPs who received lecture-based training were considered 'well documented' in seven cases and 'poorly/moderately documented' in five cases. Reports from GPs who received practice-based training were considered 'well documented' in 28 cases and 'poorly/moderately documented' in four cases. There was a significant difference in the quality of reports from the two approaches (OR 5.0; 95% CI 1.1, 23.6).

The total number of reports submitted by the GPs (44) referred to 90 separate ADRs. Of the ADRs reported by GPs who received lecture-based training, in 12 cases they were not labelled in the SPC and in 10 cases they were labelled. Of the ADRs reported by GPs who received practice-based training, in 45 cases they were unlabelled and in 23 cases they were labelled.

GPs who received practice-based training reported more unlabelled ADRs than those who received lecture-based training (OR 3.3; 95% CI 1.1, 10.1).

Discussion

This study compares two different pharmacovigilance training methods for GP registrars in reporting ADRs. It shows that the practice-based method is superior to the traditional, lecture-based method. GPs given skill-oriented, practice-based pharmacovigilance training reported significantly more often than GPs given lecture-based pharmacovigilance training. Moreover, reports were better documented and more often concerned unlabelled events.

The group trained by the practice-based method reported three times more often per 1000 months of follow-up than the group trained by the lecture-based method. The increase in reports stems from more GPs reporting similar numbers of ADRs.

The effects of the practice-based method persisted throughout the follow-up period, without indication of a diminishing effect. Because the practice-based method fits well into daily practice at pharmacovigilance centres and costs the centres little additional effort, this method is preferable.

As far as we know, no comparable studies have examined the incorporation of pharmacovigilance training in vocational training. Since most pharmacovigilance training is offered in vocational training and in other settings by means of lectures, the results of this study are highly relevant for increasing reporting tendencies and general awareness of ADRs.

This study investigates the effects of education and training for registrars. This group is of particular interest since GP trainees are still in a formative phase of their professional life. An intervention aimed at this 'younger' group may have more profound effects on attitude than interventions introduced later in medical careers. The positive effects of incentives (educational credits and other forms such as financial incentives) have been demonstrated in the literature.[4,6-8] Education aimed at prescribers was shown to have a positive effect on increasing the number of ADR reports. Our study corroborates these findings.

A positive feature of our study is that practice-based training led to reporting of more unlabelled events, whereas other studies either have not specified this aspect or have shown an increase in reports of well known ADRs.[6-8] Although in the present study the time available for follow-up was limited (32–56 months for the group trained by the lecture-based method and 25–51 months for the group trained by the practice-based method), no indication of a diminishing effect has yet emerged (figure 1). This is in contrast to other studies aimed at increasing the number of ADR reports within shorter periods for follow-up.[6-8] Figueiras et al.[8] found no effect after 12 months, whereas the total duration of the other studies was limited to 1 year[6] or less.[5]

Although we found a clear increase in the number of ADR reports in the group trained by the practice-based method compared with the group trained by the lecture-based method, absolute numbers of reports on ADRs are modest (32 practice-based reports vs 12 lecture-based reports). However, a many-year, nationwide implementation of the practice-based method in all eight GP training centres in the Netherlands may yield significant improvement in reporting rates. We consider this training method as a long-term investment towards increasing awareness of ADRs among this professional group that plays an important role in the Dutch healthcare system. Moreover, this method can also be applied for physicians training in other medical specialties as well as for pharmacist training.

Limitations of the Study

A number of factors may have led to an underestimation of the actual number of reports. Hence, the number of reports received from the study cohorts is more indicative of an effect rather than being a precise representation.

For practical reasons, inclusion criteria differed slightly between the two groups. All GPs in the lecture-based cohort completed their vocational training from January 2006 to December 2007, whereas the practice-based cohort included GPs who performed the reporting assignment between January 2006 and December 2007 in the final year of their vocational training. Thus, the actual time of graduation for GPs in the practice-based cohort may have been later than that for GPs in the lecture-based cohort. Actual time available for follow-up was therefore shorter for the GPs with practice-based training.

In the database search, reporter surnames were screened for matches with surnames used by GPs during their training. This may imply some loss to follow-up due to female trainees who could have later married and changed their surname. Other causes of underestimation may stem from GPs working as locums and, to warrant continuity of care, reporting under the name of the GP they replaced, as well as time lost for follow up after completion of GP training during the period of applying for a GP position, during pregnancy or maternity leave, or extended vacation. However, it is unlikely that underestimated reporting rates due to the latter reasons will differ

between the two groups of GPs, and thus affect the general results of our study.

The present study was conducted in two university medical centres that applied different pharmacovigilance training methods: Leiden University Medical Center employed the lecture-based method and Erasmus MC, University Medical Centre Rotterdam, employed the practice-based method. Given the Dutch system of state universities, no differences in admission of GP trainees are likely. Both training centres cover adjacent areas with similar sociodemographic characteristics. Traditionally, Leiden University Medical Center has a somewhat more conservative image, but it is unclear whether this would have any impact on admission policy in their general practice department. For this reason, selection bias cannot be excluded but is unlikely to have occurred. Given the different education methods, it is difficult to differentiate between the isolated effect of the two training methods and the differences in curriculum-related aspects.

Our results indicate a long-lasting effect; however, studies with a longer follow-up period are needed to confirm this. Also, an additional study may allow specific characteristics of the training programme that lead to increased reporting to be determined.

This study presents a valuable collaboration between a pharmacovigilance centre and a general practice vocational training centre, which can serve as a model for other pharmacovigilance centres. We present a superior pharmacovigilance training method that requires little additional effort from pharmacovigilance centres and which can be extended to different settings such as medical specialist or pharmacist training.

Conclusions

Skill-oriented, practice-based pharmacovigilance training of GP trainees resulted in a significantly higher number of ADR reports after completion of vocational training than a more traditional, lecture-based pharmacovigilance training method. Reports from GPs trained by the practice-based method were better documented and more often concerned unlabelled events. Positive differences persisted over a follow-up period of up to 56 months.

Acknowledgements

The cases described in this study have been reported to the Netherlands Pharmacovigilance Centre Lareb. We would like to acknowledge Marinella Langendoen-Roel, working at Leiden University Medical Centre, for providing data concerning Leiden-trained GPs. Furthermore, we would like to express our gratitude to Hans van der Woude (Erasmus MC, University Medical Centre Rotterdam) and Tina van der Velde for their critical contribution to this article, Monique Beekman-Eevers (Erasmus MC, University Medical Centre Rotterdam) for her advice on the educational background of the presented training method, Sonja van de Koppel for her role in analysing the data, and Laraine Vissers-Isles for revising the English used in this paper. No sources of funding were used to assist in the preparation of this study. The authors have no conflicts of interest directly relevant to the content of this study.

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Correspondence: Dr *R.F. Gerritsen*, MD, Netherlands Pharmacovigilance Centre Lareb, Goudsbloemvallei 7, 5237 MH 's-Hertogenbosch, the Netherlands.
E-mail: r.gerritsen@lareb.nl