SHORT COMMUNICATION

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Promoting Spontaneous Adverse Drug Reaction Reporting in Hospitals Using a Hyperlink to the Online Reporting Form

An Ecological Study in Portugal

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Abstract

Background: Spontaneous adverse drug reaction (ADR) reporting has been described as an efficient method to detect drug safety signals. However, under-reporting is a major issue undermining the effectiveness of spontaneous reports. Among hospitalized patients, ADRs are a particularly serious problem because these patients are often treated with more than one drug, and these drugs are often new and aggressive.

Objective: To promote spontaneous ADR reporting by healthcare professionals working in hospitals in the northern regions of Portugal, we propose the inclusion of a hyperlink to an online ADR reporting form on hospitals' electronic patient records (EPRs). The main aim of this study was to evaluate the impact of these hyperlinks on the number of spontaneous ADR reports to the Northern Pharmacovigilance Centre (UFN – Unidade de Farmacovigilância do Norte). We also assess the number of daily UFN website visits before and after the inclusion of the hyperlinks.

Methods: An ecological study was performed in northern Portuguese hospitals from 2006 to 2010. The hyperlinks were included in either EPRs or on computer desktops. The median of spontaneous ADR reports (total and online) per month and the respective ranges were presented before and after the intervention in all hospitals in this study. The comparisons were performed using the Mann-Whitney U-test.

Results: Sixteen hospital centres were involved in the study (27 hospitals). Eleven centres (18 hospitals) included the hyperlinks. Considering the hospitals with hyperlink access to the EPRs, the median ADR reports per month significantly increased, from two (range 0–12) to five reports (range 1–17). The median of ADR reports per month using the online form also increased

significantly, from one (range 0–5) before the intervention to four (range 1–17) after it. Moreover, serious ADRs increased 3-fold, and non-previously described ADRs increased 4.5-fold. None of these significant increases were observed in the hospitals where the hyperlink was not installed. We also found a significant increase in daily UFN website visits, from ten before the intervention to 27 after it ($p < 0.001$).

Conclusion: The increase in ADR reporting shows that the inclusion of hyperlinks to online ADR reporting forms is an easy and cost-effective way to change health professional behaviours with regard to spontaneous ADR reports.

Introduction

Adverse drug reactions (ADRs) are a well recognized public health problem worldwide and a major cause of death and hospitalization in developed countries.[1] In fact, rare and long-term ADRs are difficult to detect during the drug development stage. Only when the drugs begin to be used by a large population after marketing authorization is it possible to detect new ADRs not previously identified during clinical trials. In reality, the safety of a new drug cannot be established until it has been on the market for several years.[2] As such, it is essential to keep reactions to drugs under close surveillance, especially after marketing, through a pharmacovigilance system.

In Portugal, this system is based on spontaneous ADR reports made by healthcare professionals.[3] These reports can be made using paper, telephone, e-mail or through an online form,[4] and they consist of a description of an adverse event supposedly caused by a medicine. Spontaneous ADR reporting has been described as an efficient method for detecting drug safety signals.[5] However, under-reporting is a major issue undermining the effectiveness of spontaneous reporting. Several studies suggest that less than 10% of detected ADRs are effectively reported to medicine regulatory authorities.[6,7] In addition, the spontaneous ADR report rate in northern Portugal was 90 reports/million inhabitants in 2009, which is highly unsatisfactory according to the WHO recommendations (200 reports/million inhabitants[8]).

Worldwide, systems using informatics to promote ADR reporting or to detect ADRs that have occurred in healthcare institutions have been tested and are currently being used. Computer programs that allow voluntary and automated detection of ADRs,[9,10] informatics tools created to analyse clinical databases,[11] or websites that actively inform healthcare professionals[12] are examples of such systems.

Among hospitalized patients, ADRs are a particularly serious problem. In fact, these patients are often treated with more than one drug, and these drugs are often new and aggressive. Despite these treatments, there is currently no specific system for monitoring or reporting ADRs in Portuguese hospitals. We believe that making the reporting system easier would considerably increase the number of reported ADRs.

With the intention of promoting spontaneous ADR reporting by healthcare professionals working in hospitals, we proposed the inclusion of a hyperlink to an online ADR reporting form (part of the Northern Pharmacovigilance Centre [UFN] website) on the electronic patient records (EPRs) or on the desktops of hospital computers. With this system, we expected to reach not only the physicians but also the pharmacists and nurses working at these hospitals. In Portuguese hospitals, pharmacists have an important role in ADR detection and reporting because physicians discuss with them the adverse events that occurred during medical treatment, asking for alternative drugs available at the pharmacy. In addition, some pharmacists are part of the clinical visit and frequently detect ADRs themselves.

Aim

Our main aim was to evaluate the impact of the hyperlinks installed in Portuguese hospitals on the number of ADRs reported by these hospitals using the hyperlink versus those that did not, and we also evaluated the number of visits to the UFN website.

Methods

Intervention

Hyperlinks to the ADR online reporting UFN form were proposed to the 18 northern Portuguese hospitals. The hyperlinks can be included either in healthcare professional-specific software (typically EPRs or pharmacy-specific applications used by doctors, nurses and pharmacists) or on hospital computer desktops (see figure 1 for examples of both situations). Notably, most of the Portuguese EPRs are web-based, so the hyperlink automatically opens the UFN form in a new browser window.

The online reporting UFN form requires the health professional to log in with their personal account. Patient data are collected in an anonymous way (only the initials of the patient name are required, aiming to help the health professional identify each case) and are secured in an Oracle database with appropriate access restrictions.

In the beginning of October 2007, a letter was sent to the chief physicians of these 18 northern Portuguese hospitals suggesting the inclusion of the hyperlink. If there was no response within 2 weeks, clinical administration boards were reminded by telephone. Thirteen centres forwarded this announcement to the respective computer departments, and only one hospital forwarded it to the pharmaceutical department. Five of the centres failed to respond by the end of 2010. After approval by the hospital board and after being forwarded to the respective departments, UFN made a third contact to explain technical specifications and to send the specific hyperlink for each hospital.

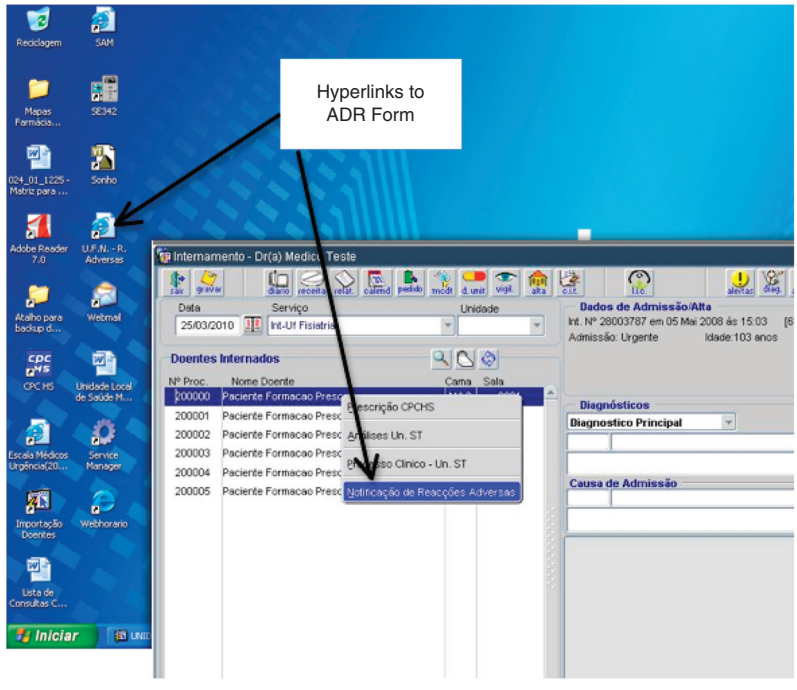

Fig. 1. Examples of hyperlinks on a computer desktop (back image) and in an electronic patient record (front image).

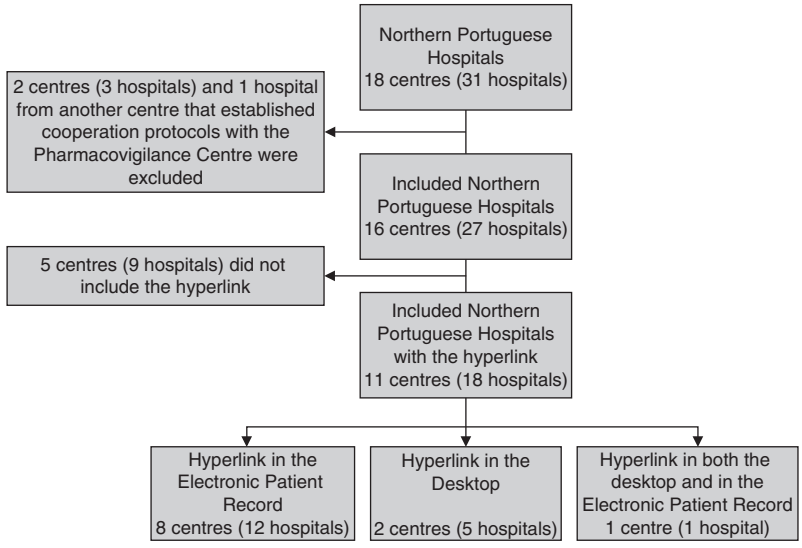

Fig. 2. Diagrammatic representation of the hospitals and hospital centres of northern Portugal that were included and excluded from the study.

Study Design and Data Collection

An ecological study was carried out in northern Portuguese hospitals from 2006 to 2010. The number of spontaneous ADR reports and online spontaneous ADR reports originating from hospitals were analysed before and after the above-mentioned intervention, without a control group. Five hospital centres implemented the hyperlink in December 2007, and the other six implemented it over the course of the next 5 months. We looked at the 23 months before and the 31 months after implementation in each hospital.

The UFN website uses an Apache web-server and has a record of the web logs related to the site visits since January 2006. These logs were initially processed using Webalizer software (www.webalizer.org) to calculate site hits, user logins and visits.

Telephone interviews with the computer departments of each hospital were performed to collect where each institution installed the hyperlink to the UFN website, and screen-shots illustrating the interventions were taken.

Variables

The main variables collected for analysis were as follows:

- Date – date and time of the ADR report.
- Hospital – institution where the ADR was detected.
- Health professional – type of health professional that reported the ADR (doctor, nurse, pharmacist or other).
- Seriousness – seriousness of the ADR, grouped as 'Serious' or 'Non-serious' according to the WHO criteria.
- Previous knowledge – whether the ADR was previously described in the Summary of Product Characteristics for the drug or not.

Bias

From the initial 18 centres (31 hospitals) we excluded four hospitals that established other cooperation protocols with UFN to avoid a possible confounder bias (see figure 2). For the other 16 centres, we believe that there were no external interventions that could potentially explain the observed results.

Statistical Methods

The number of spontaneous ADR reports and online spontaneous ADR reports per month were compared between the two periods (before and after the intervention). The number of ADR reports per quarter, before and after the installation

of the hyperlinks, is presented graphically (see figure 3). The number of ADR reports per quarter in the excluded hospitals and in the hospitals that did not participate (those that did not install the hyperlinks) is presented in figure 4.

Median values of the number of daily UFN website visits were reported because of the skewed distribution of the data. The number of daily UFN website visits was compared before and after the intervention using the Mann-Whitney U-test. The significance level was set at $p < 0.05$.

Results

Participants

Of the 16 centres involved in the study, 11 centres (18 hospitals) included the hyperlinks. Eight centres included the hyperlink only in the EPRs, two centres included the hyperlink on the computer desktops, and one included it both on the desktops and in the EPRs (see figure 2). Of the 18 hospitals involved, one is a university hospital, and three are specialized hospitals

Main Results

Considering the 16 centres that implemented the project, the median number of ADR reports per month significantly increased after project implementation. In fact, before the intervention the median of total ADR reports per month was 2, ranging from 0 to 12, and 31 months after the intervention the median was 5, ranging from 1 to 17 ($p = 0.043$). Four months after the project was implemented the median number of reports per month was 4.

Considering only the reports using the online form, before the project was implemented the median total online ADR reports per month was 1, ranging from 0 to 5, and after the intervention, this number was 4, ranging from 1 to 17 ($p = 0.009$).

Figure 3 shows the number of ADR reports per quarter before and after the intervention. Figure 4 presents the number of ADR reports per quarter in the excluded hospitals and in the hospitals that did not install the hyperlinks.

The 11 centres included reported 17 serious ADRs in 23 months using the online form before the intervention, and 69 in 31 months (a 3-fold increase) after the intervention. These centres reported seven non-previously described ADRs using the online form before the intervention and 42 after (increase of 4.5-fold).

The hospital with the largest increase in ADR reports submitted online was the one that included the hyperlink both in the EPRs and on the computer desktops, with a mean of three online reports per year before the intervention and 18 after. The three hospitals that included the hyperlink on

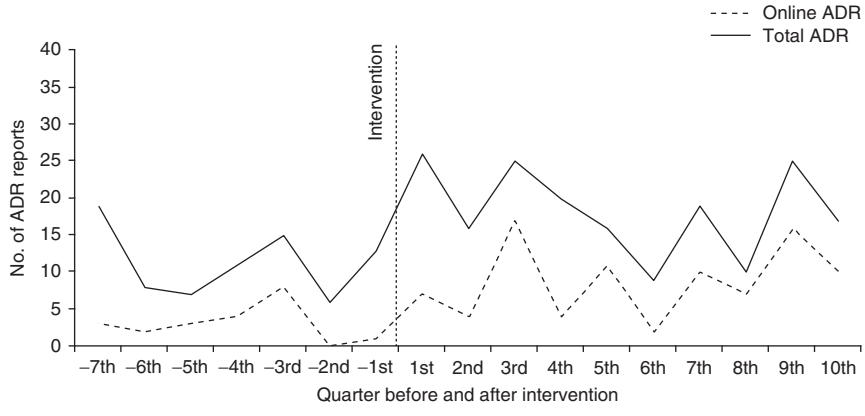

Fig. 3. Evolution of adverse drug reaction (ADR) reports (total and only online) in hospitals with the intervention. The quarters were adjusted for the time of intervention. Five hospital centres implemented the hyperlink in December 2007, two in January 2008, one in February, one in March, one in April and one in May.

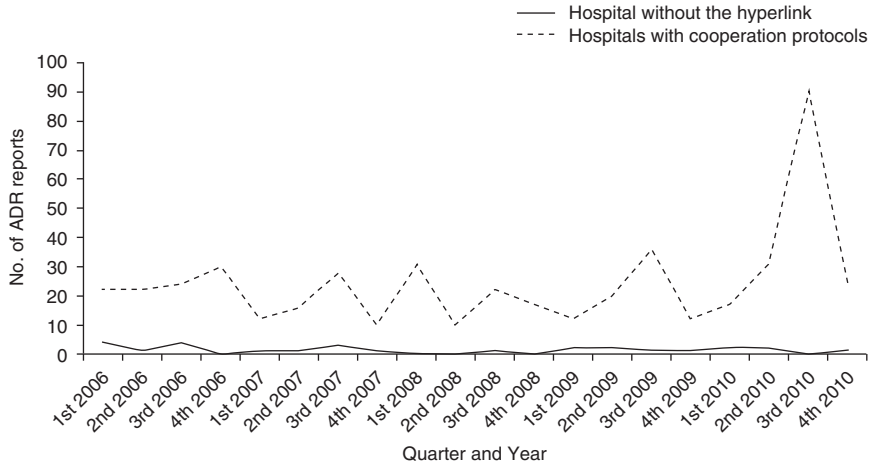

Fig. 4. Evolution of adverse drug reaction (ADR) reports in the excluded hospitals (with cooperation protocols) and in the hospitals that did not install the hyperlinks.

the desktops (including the one that simultaneously included it in the EPRs) were in the top five of the hospitals with higher increases in ADR reports submitted online.

There were no ADR reports sent in both paper and online formats by the same professional.

Other Analysis

There was a significant increase in daily UFN website visits after the intervention ($p < 0.001$). Before the intervention there was a median of ten daily UFN website visits, and after the intervention, the median increased to 27 visits.

Discussion

Our results show that the inclusion of hyperlinks to an online ADR reporting form in the EPRs does change health professional behaviours in ADR reporting. In reality, there was an increase in ADR reporting in the hospitals involved in this project, in the total number of ADR reports (more than 2-fold), in the number of ADR reports submitted online (4-fold), in serious ADRs reported online (3-fold) and in non-previously described ADRs (more than 4-fold). Additionally, daily visits to the UFN website increased approximately 3-fold after the intervention.

A similar intervention based on changing the EPRs of a hospital to facilitate ADR reporting is presented in Ortega et al.[13] Compared with our ADR reporting growth, the measured impact was higher in their study as they moved from zero to 1.6 ADRs per month in just one hospital. We argue that this difference may be due to the fact that they were able to fine-tune the EPRs to increase ADR reporting because they had more control over its application, while in our case we were limited to placing hyperlinks in existing heterogeneous EPRs. Therefore, our approach seems more easily implementable because hospitals are known to have many different information systems[14] and a national pharmacovigilance institution is probably not able to impose the changes described in Ortega et al.[13] to most commercial EPRs.

In the study by Figueiras et al.,[15] which was performed in the same region as our study, an educational intervention to improve physician reporting is described, namely by performing outreach visits to groups of health professionals. Their results present a very impressive increase (10-fold) in ADR reporting in the intervention group, and a 6-fold increase in the reporting of serious ADRs. When compared with our results, it is clear that the educational intervention has proven to be much more effective, but also requires more resources (human and financial).

Also, the effectiveness of these interventions appears to decrease through time. In the study by Pedrós et al.,[16] an educational (periodic meetings) and economic incentives-based intervention strategy was initiated in 2003. Their results present an increase of 5.6-fold in all ADRs and a 2-fold increase in serious ADR reports. Their impact is similar to our study, but again used more financial resources.

When compared with other types of interventions, such as solely educational[15] or educational combined with economic incentives,[16] our intervention seems to have less impact although it is more long lasting and less expensive.

As an additional outcome, we can see that the hospital with the highest increase in ADR reports submitted online was the one that simultaneously included the hyperlink in the EPRs and on the computer desktop. According to our results for hyperlink placement, the computer desktop is likely more efficient than the EPR homepage. It is our opinion that these improvements could also be effective in other countries because they are more related to generic usage of graphic user interfaces than to local practices.

Notably, making the ADR forms easily accessible might also promote future ADR reporting initiatives that can take advantage of the visibility of the hyperlink to the users. Therefore, we argue that our solution is cost effective, appropriate for widespread use in many healthcare institutions, and can consistently increase ADR reporting over time.

Limitations

In some hospitals, we found that although the hyperlink was included, the professionals did not know about it. In the near future, we aim to increase the knowledge of the hyperlink by more actively informing health professionals using flyers sent to the hospitals, posters and an e-mail showing specifically how to find the hyperlink. Another problem detected was the inability to use the hyperlink in some hospitals because the users did not have permission to access to the internet.

Future Work

To solve the problem of not being able to access the Internet, we are now developing Web-services[17] to be used by other systems available on hospital intranets. With this tool, it will not be necessary to access the UFN website and healthcare professionals can simply use the existing information systems as proposed in Ortega et al.[13] With this future work, we expect to eliminate all the technical obstacles to ADR reporting, further increasing the reporting rate. Meanwhile, we also aim to implement this project in northern Portugal primary-care healthcare centres and to provide the hyperlink to general practitioners and nurses.

Conclusions

The inclusion of hyperlinks on computer desktops and in EPRs to online ADR reporting forms is an easy and cost-effective way to change health professionals' behaviours with regard to spontaneous ADR reports. In fact, daily visits to the UFN website significantly increased after the inclusion of the hyperlinks, but even more importantly, the amount and relevance of ADR reports significantly increased after the inclusion of the hyperlink in the hospitals involved in this project.

Acknowledgements

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Inês Ribeiro-Vaz was responsible for most of the intervention and data collection. Cristina Santos performed the statistical analysis. Altamiro Costa-Pereira and Ricardo Cruz-Correia supervised the writing of the paper. Ricardo Cruz-Correia also conceptualized the intervention.

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