Reporting of adverse drug reactions: predictors of under-reporting in Malaysia

Zoriah Aziz PhD*, Tan Ching Siang BPharm and Nurul Suhaida Badarudin BPharm

Department of Pharmacy, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia

SUMMARY

Background Malaysia like many other countries worldwide uses spontaneous reporting systems as a means of collecting data on suspected adverse drug reaction (ADR). However, compared to other countries, which use the system, the reporting rate in Malaysia is very low. Why some physicians do not report ADRs is not well understood.

Objective To identify factors, which would predict physicians' failure to send ADR reports.

Design and Setting Face-to-face interview using a structured questionnaire involving physicians working at the University of Malaya Medical Centre, Malaysia.

Results About a third of the physicians in the Centre participated. Sixty-five of the 415 approached refused to participate. A high proportion of the respondents (81.4%) indicated that they had suspected an ADR but did not report it, while about 40% of the respondents were not aware of the existence of the national reporting system in Malaysia. Logistic regression modelling identified the variable 'ADR considered to be too trivial or too well known to report' as the strongest predictor of not reporting, followed by physicians' category and uncertainty that the reaction had been definitely caused by a drug.

Conclusion Important predictor variables, which limit physicians from reporting ADR in Malaysia, were related to uncertainty of types of reaction to report, lack of awareness about the existence, function and purpose of national ADR reporting. The findings could be useful for planning strategies to improve the reporting rate. Copyright © 2006 John Wiley & Sons, Ltd.

INTRODUCTION

Many reasons have been given as to why health care professionals do not report adverse drug reactions (ADRs). Factors commonly identified are: the reluctance to send reports based on mere suspicion, lack of time, unawareness of the reporting system and ignorance of reporting requirements. Fear of involvement in litigation and lack of information on how to report have also been cited.

Malaysia like many other countries worldwide uses a spontaneous reporting system as a means of collecting suspected ADRs. The Malaysian Adverse Drug Reaction Advisory Committee (MADRAC) is responsible for collecting ADRs reports in Malaysia. The monitoring system, which was established in 1987, has now been operating for 18 years but the number of reports received by MADRAC remains low compared to other countries.

Since MADRAC's establishment, there have been no studies examining the reasons for under-reporting...
of ADRs by physicians in Malaysia. Some physicians are less likely to send ADR reports than others. However, little is known about factors, which are predictive of their likelihood of not reporting an ADR. The aim of this study was to identify variables, which predicted physician’s failure to send ADR reports. Findings of this study should enable national monitoring centers to take steps to improve ADR reporting. It is important to improve ADR reporting rates because it is the only system of post-marketing surveillance available in many countries, including Malaysia and is therefore the only way of detecting specific in-use drug problems. Even though the setting for this study is Malaysia, many of the issues discussed are relevant for national monitoring centres worldwide.

METHODS

Design and sample

The design of the study was a proportionately large convenience sample of physicians working in University Malaya Medical Centre (UMMC). This is a teaching hospital with 875 beds in the capital of Malaysia. Physicians across all specialities were represented in the survey. Two trained interviewers conducted face-to-face interviews using a structured questionnaire over a month period in January 2005.

The first draft of the questionnaire was tested on 20 physicians from the UMMC. Slight modifications to the wordings of the questionnaire were made based on the comments received during the pilot testing. Data from the pilot study was not included in the final analysis. The director of UMMC approved the study protocol.

Survey instrument

The questionnaire used was based on The Attitudinal Survey II Questionnaire of the European Pharmacovigilance Research Group (AS2QEPRG) with some slight modifications on the demographic sections to adapt it to the Malaysian setting.

The final questionnaire has five sections; (a) personal history of reporting ADRs, (b) reasons for not reporting, (c) responses to several hypothetical ADR situations, (d) understanding of expressions of risk that are commonly used to describe the frequency of ADR and (e) demographic characteristics. Demographic data collected were age, gender, race, country they received their medical qualifications, the number of years they have been practising and their employment category (consultants, medical officers, house officers).

Only responses from section (a), (b) and (e) were used for this paper.

Data analysis

Data from the paper-based survey were first entered into spreadsheets (Microsoft Office Excel®) and then imported into a Statistical Package for the Social Sciences (SPSS), version 11.5. Chi-square was used to evaluate the relationships between reporter status (reporter vs. non-reporter) and all the independent variables. When the expected cell number was lower than five in the contingency table, we used Fisher’s exact test. Logistic regression modelling was used to assess the significance of variables, which predicted the likelihood of not reporting suspected ADRs.

Predictor variables. The following factors are implicitly hypothesised as predictors of the likelihood of not sending ADR reports in the AS2QEPRG:

1. Lack of awareness on the function and purpose of ADR monitoring. This variable was assessed using three items; unaware of the existence of a national ADRs reporting scheme; unaware of the need to report ADRs; reporting of an ADR has no effect at all.
2. Uncertainty that the reaction was definitely caused by a drug.
3. ADR considered to be too trivial or too well known to report or both.
4. Did not know how to report or reporting an ADR is considered too complicated a process or both.
5. Did not have enough time to report ADR.
6. Physicians’ category (categorised as consultants, medical officers, house officers).

However, to avoid over-parameterisation, we analysed the data qualitatively, to exclude some of the factors.

Strong correlations and associations were found among the demographic variables, ‘length of time in practice’, ‘age’ and ‘physicians’ category’. Given the practical importance of the variable ‘physicians’ category’, the other two variables were dropped from the model. We did not force the demographic variable, gender into the model because a previous study showed that male and female physicians did not differ in their attitudes towards ADR reporting.

We excluded the variable ‘no financial compensation for the time spent for reporting’ because of the
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difficulty in separating socially desirable responses from reliable answers. Additionally, two studies suggest that financial compensation did not affect reporting.

Data by Hasford suggested that fear of litigation is not a major reason for not reporting. Additionally, in Malaysia the threat of litigation is insignificant. We therefore excluded the variable ‘concerned that report could be used in a legal case for damages by the patient’ so as not to over-parameterise the model.

Possible predictor variables. Following the qualitative and univariate analyses, the following independent variables were considered as possible predictors of not reporting ADR in our model:

1. Lack of awareness on the function and purpose of ADR monitoring.
2. Uncertainty that the reaction was definitely caused by a drug.
3. ADR considered to be too trivial and well-known to report.
4. Did not know how to report and reporting was considered as too complicated a process.
5. Did not have enough time to report ADR.
6. Physician’s category.

Logistic regression. A binary logistic regression analysis was performed with ‘not reporting a suspected ADR’ as a dependent variable and the above six possible predictors as independent variables.

Non-ordered categorical data with more than two levels, ‘physicians’ category’ were entered as $k - 1$ dummy variables with consultants as the reference group ($k = 2$). All the other variables were regarded as dichotomous variables and coded 0 = ‘No’ response and 1 = ‘Yes’ response.

RESULTS

Demographic

Of the 415 physicians approached for the face-to-face interview using the structured questionnaire, 350 (84.3%) agreed to participate. Slightly more of the sample was male (55%) than female (45%). Race (Malay) made up 36% of the respondents, followed by Chinese (32%), Indian (27%) and the others (5%). About 42% of the respondents obtained their medical degree outside of Malaysia. A high proportion of our respondents (81.4%) indicated that they have suspected an ADR but not reported it, while about 40% of the respondents were not aware of the existence of the national reporting system in Malaysia.

Comparison of reporters and non-reporter on reasons for not sending reports

Physicians who responded ‘yes’ to the question ‘Have you ever suspected an adverse drug reaction but not reported it?’ was classified as non-reporters. Of the 350 respondents, 285 have suspected an ADR but not reported it.

Table 1 shows that there is statistically significant relationship between status of reporters (reporters vs. non-reporters) and all the variables assessed, except for two variables ‘there is no financial compensation for the time spent for reporting’ and ‘reporting of an ADR has no effect at all.’

Logistic regression analysis

With 350 cases analysed, the logistic regression full model was significant ($\chi^2 = 173.88, df = 7, p < 0.05$). Using the model, 92.3% of predictions were correct. Except for the variable, ‘lack of time’ all the other variables were found to contribute significantly to the

Table 1. Percentage of responders and non-responders responding ‘yes’ to the questions probing the reasons for not sending reports

<table>
<thead>
<tr>
<th>Variables</th>
<th>Non-reporter, $n = 285$</th>
<th>Reporter, $n = 65$</th>
<th>$p$-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>You were uncertain that the reaction had been definitely caused by a drug?</td>
<td>74.0</td>
<td>22.7</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>You considered the adverse drug reaction to be too trivial to report?</td>
<td>43.9</td>
<td>16.9</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>You considered the adverse drug reaction to be too well known to report?</td>
<td>41.4</td>
<td>4.6</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>You were unaware of the existence of a national adverse drug reaction reporting scheme?</td>
<td>44.9</td>
<td>0</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>You were unaware of the need to report adverse drug reactions?</td>
<td>39.3</td>
<td>0.2</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>You did not know how to report adverse drug reactions?</td>
<td>54.4</td>
<td>9.2</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Reporting an adverse drug reaction is too complicated a process?</td>
<td>16.8</td>
<td>6.2</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>You do not have enough time to report adverse drug reactions?</td>
<td>17.2</td>
<td>6.2</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>You were concerned that your report could be used in a legal case for damages by the patient?</td>
<td>9.1</td>
<td>0</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>You did not have enough time to report adverse drug reactions?</td>
<td>4.2</td>
<td>0</td>
<td>0.09</td>
</tr>
<tr>
<td>Reporting an ADR has no effect at all?</td>
<td>13.7</td>
<td>1.5</td>
<td>0.05</td>
</tr>
</tbody>
</table>

Table 2. Predictors of not reporting suspected ADR in the multivariate logistic regression model

<table>
<thead>
<tr>
<th>Variables</th>
<th>Beta</th>
<th>SE (Beta)</th>
<th>Wald</th>
<th>Odds ratio</th>
<th>95%CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lack of awareness on the function and purpose of ADR monitoring</td>
<td>1.62</td>
<td>0.48</td>
<td>11.55</td>
<td>5.06</td>
<td>1.99-112.87</td>
</tr>
<tr>
<td>Uncertainty that the reaction had been definitely caused by a drug</td>
<td>2.11</td>
<td>0.43</td>
<td>24.04</td>
<td>8.22</td>
<td>3.54-19.07</td>
</tr>
<tr>
<td>ADR considered to be too trivial and well known to report</td>
<td>3.32</td>
<td>0.68</td>
<td>23.98</td>
<td>27.59</td>
<td>7.31-104.08</td>
</tr>
<tr>
<td>Did not know how to report and reporting an ADR is considered too complicated a process</td>
<td>1.71</td>
<td>0.52</td>
<td>10.89</td>
<td>5.50</td>
<td>2.00-15.15</td>
</tr>
<tr>
<td>Lack of time</td>
<td>1.14</td>
<td>0.70</td>
<td>2.62</td>
<td>3.13</td>
<td>0.79-12.42</td>
</tr>
<tr>
<td>Physicians' category (Medical officers)</td>
<td>2.16</td>
<td>0.77</td>
<td>7.96</td>
<td>8.717</td>
<td>1.94-39.15</td>
</tr>
<tr>
<td>physicians' category (House officers)</td>
<td>1.34</td>
<td>0.48</td>
<td>7.84</td>
<td>3.82</td>
<td>1.50-9.77</td>
</tr>
<tr>
<td>Constant</td>
<td>-3.78</td>
<td>0.93</td>
<td>16.40</td>
<td>0.02</td>
<td></td>
</tr>
</tbody>
</table>

predictive ability of the model. Table 2 gives coefficients, SE, Wald statistics, odds ratio and the confidence intervals values for all the variables forced into the model. Variable for Physicians’ category used ‘Consultants’ as the reference group.

The strongest predictor was the variable relating to ADR considered to be too trivial or too well known to report. The odds ratio is 27.59. This suggests that physicians who considered the ADR to be too trivial or too well known were about 28 times more likely not to report suspected ADR than those who did not feel the same way. Similarly, physicians who were uncertain that the reaction had been definitely caused by a drug were eight times more likely not to report than those who were certain. Physicians who lack awareness on the function and purpose of ADR monitoring were predicted to be five times more likely not to send ADRs reports than those who were aware of the system.

The category of physicians was also a significant predictor (\(p = 0.04\)). The odds ratio for the category, medical officers and house officers are 8.71 and 3.82 respectively. This implies that medical officers were about nine times and house officers four times more likely than Consultants not to report ADRs.

DISCUSSION

This study attempted to identify variables, which predicted the likelihood of physicians not sending ADR report. The strongest predictor was the variable ‘ADR considered to be too trivial or too well known to be reported’. Other studies have also showed that this variable was a major determinant of not reporting ADR.\(^\text{1,4,7,8}\) However, our study was able to predict that physicians who considered the ADR to be too trivial or too well known were about 28 times more likely not to report suspected ADR than those who did not feel the same way.

Not sending well-known ADR, which is inconsistent with MADRAC's requirement, demonstrated that there is misconception among the physicians about the types of reactions to be reported. MADRAC required ALL ADRs to be reported so that the frequency and incidence of adverse reactions, both the well-recognised and newly discovered reactions can be established.\(^\text{16}\) However, it seems that this requirement is not clear to the physicians. We can speculate that misconception was due to inadequate explanation and information about ADR reporting from the national reporting centre. We believe the first step to minimise these misconceptions in order to improve reporting is to have regular and greater communication between the physicians and the national centre.

The reaction being certainly caused by a drug was also a predictor of not sending an ADR. This finding suggests that physicians were not clear about MADRAC’s requirement that call for all suspected ADR to be reported even though causality cannot be established.\(^\text{16}\)

About 40% of the respondents were not aware about the existence of the national reporting system in Malaysia. This is surprising, considering that MADRAC has been in existence for more than 18 years. Since our result shows that lack of awareness on the function and purpose of ADR monitoring was a significant predictor of not reporting by physicians, MADRAC need to aggressively publicise its activities. Despite efforts such as publications of bulletin articles and information sharing,\(^\text{12}\) our study shows that awareness about the reporting system among the physicians is still low. We believe the benefits of reporting to the country need to be emphasised with evidence of the usefulness of submitted reports in those publications and communications. Regulatory
decisions and feedback on a regular basis detailing what had been done with the reports for those who submit reports need to be given as proposed by Biriell and Edwards.\textsuperscript{17} Providing regular feedback and personal encouragement have been shown to be an important factor to encourage continued reporting.\textsuperscript{18}

Another significant predictor of not reporting ADR was the physicians' category. Consultants were more likely to report ADRs compared to Medical officers and House officers. This result is expected as generally consultants are more likely to diagnose ADRs.

Our result was similar to a Chinese study\textsuperscript{6} showing lack of time was not a significant predictor for not sending ADR report. This finding was in contrast to result in most Western countries such as France, UK, Netherlands, Sweden and Germany, which seem to indicate that lack of time is an important limitation to reporting.\textsuperscript{1-4,5} It would be interesting to find out whether these differences were due to the way the countries' health systems operate. For example, physicians in the West may be pressured to spend more time in actual contact with their patients and as such may find it difficult to find the time to report suspected ADRs.

More attention to the education and training on issues relating to pharmacovigilance in the undergraduate and postgraduate medical curriculum should also be initiated. Education and training in ADR reporting have been shown to increase reporting.\textsuperscript{19} Additionally, the national reporting centre could play a role in developing educational packages with universities offering medical degree courses.

Results from our study were from a single institution, and therefore may not be generalisable to other settings or even to the same institution over time. We do not claim to have identified all the variables that predicted the likelihood of not reporting suspected ADR among our physicians since other possible explanations for not reporting were not explored in this study. We could speculate that the variables we identified were correlated to the questions we asked in the questionnaire. Other factors which might have influenced their decision not to report could have been identified by exploring the physicians' thought processes. This can be the basis for further research.

CONCLUSIONS

Our survey suggests that important predictor variables, for physicians not reporting ADR in Malaysia, are related to uncertainty of types of reaction to report, lack of awareness about the existence, function and purpose of the national ADR reporting system. We believe that the results of this study could be useful for planning strategies to improve ADR reporting rate in Malaysia. The first step would be for MADRAC to have regular communications with physicians to explain reporting procedures and also for universities to incorporate the teaching of pharmacovigilance and the importance of the spontaneous reporting in medical curriculum.

REFERENCES


