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Attitude survey of spontaneous adverse drug-reaction reporting by general practitioners in Sicily

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Summary

Spontaneous adverse drug reaction (ADR) reporting is fundamental for drug safety surveillance. However, under-reporting is one of the main limitations of the pharmacovigilance system and may cause bias for data interpretation. The purpose of the present study was to assess the general practitioners'(GPs) knowledge about Pharmacovigilance in Sicily (Italy) and their spontaneous reporting attitude, in order to identify the reasons for under-reporting, and to determine which steps to pursue to increase the reporting rates. A self-administered questionnaire has been sent to a sample of 440 GPs in Sicily. After two weeks, the same questionnaire was administered by telephone to non-responders. When the response rate was significantly high ($>$ 40%), data were evaluated. Four-hundred-and-forty GPs were contacted, but only 41.3% of them completed the interviews. Reasons for under-reporting included 'lack of time', 'lack of adequate feed-back by the Pharmacovigilance's Service', 'fear of legal liability or appearing foolish', 'reluctance to admit that harm had been caused to a patient'. These results showed that there is a scope for further development of such techniques and their use on a wider basis in Italy.

Keywords: *Adverse drug-reaction, Spontaneous reporting system, General Practitioners, Under-reporting.*

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Riassunto

Indagine attitudinale sulle segnalazioni spontanee di reazioni avverse da farmaci da parte dei medici di medicina generale in Sicilia

Il sistema di segnalazione spontanea delle reazioni avverse è fondamentale per la sorveglianza della sicurezza dei medicinali. Tuttavia, la sotto-segnalazione rappresenta uno dei principali limiti del sistema di farmacovigilanza e può causare distorsioni nell'interpretazione dei dati. Scopo di questo studio è stato quello di valutare le conoscenze dei medici di medicina generale (MMG) sulla farmacovigilanza in Sicilia (Italia) e la loro attitudine alla segnalazione spontanea, al fine di identificare le ragioni della sotto-segnalazione e determinare le misure da adottare per aumentare i tassi di segnalazione. Un questionario è stato inviato ad un campione di MMG in Sicilia. Dopo due settimane, lo stesso questionario è stato somministrato per telefono a chi non aveva risposto. I dati sono stati valutati quando il tasso di risposta era significativamente alto ($>$ 40%). Sono stati contattati 440 MMG, ma solo il 41.3% di essi ha completato il questionario. Tra le ragioni della mancata segnalazione figurano la 'mancanza di tempo', la 'mancanza di un'adeguata risposta da parte del servizio di farmacovigilanza', il 'timore di responsabilità legale o l'apparire sciocchi' e la 'riluttanza ad ammettere che un paziente è stato danneggiato'. Questi risultati hanno dimostrato che in Italia vi è la possibilità di un ulteriore sviluppo di tali metodiche e del loro uso su una base più ampia.

Parole chiave: *Reazioni avverse, Sistema di segnalazione spontanea, Medici di medicina generale, Sotto-segnalazione.*

1 Introduction

It is universally accepted that medicines might produce adverse drug reactions (ADRs) during their normal therapeutic use. Most developed countries have, therefore, established formal procedures to enable healthcare professionals to report suspected ADRs, encounter in their clinical practice, to their national drug regulatory authority or to the appropriate pharmaceutical manufacturer (Belton, 1997).

These schemes are of established value in the identification of previously unknown ADRs, in the identification of factors predisposing to ADRs, and in monitoring the safety of pharmaceutical products throughout the duration of their use in clinical practice and following their extension to new indications (Rawlins *et al.*, 1992; Rawlins, 1988).

Therefore, the spontaneous ADRs reporting is fundamental for the definition of drug's safety profile in the post-marketing surveillance. However, only 10% of already existing ADRs is correctly reported (Rawlins, 1995). Being a spontaneous activity, which depends on the attitude of the healthcare professionals, a high level of "under-reporting" exists, and this tendency results into a limitation of the system (Hazell and Shakir, 2006). Most reports come from hospital

professionals; on the contrary, general practitioners (GPs) are less familiar with ADRs reporting (Cosentino *et al.*, 1997).

Main purpose of the study was to collect data on the knowledge of GPs about Pharmacovigilance and on their attitude to report spontaneous ADRs. Secondary purposes were to evaluate the efficiency of the territorial Pharmacovigilance Service examined and to make the Doctors more aware of ADRs signal.

2 Methods

The attitude of GPs in Sicily to national ADR reporting schemes was assessed by means of a self-administered postal questionnaire. The names of GPs involved in this research were given by SIMG (Italian Society of General Medicine) and by FIMMG (Italian Federation of General Practitioners) of Sicily.

The questionnaire was formulated by the Maternal-Fetal Pharmacovigilance Center of Catania and modified in order to make it in accordance with the international standards used in previous studies (Bateman *et al.*, 1992). The questionnaire and an accompanying letter of invitation to participate were submitted by email to a sample of 440 GPs in Sicily. After two weeks, the same questionnaire was administered, by phone, to those who had not answered by email, warranting the data confidentiality.

Non-responders were sent a reminder letter and a further copy of the questionnaire after 4 weeks. Ten weeks after the date of distribution of the first questionnaire was deemed to be the deadline of the study and questionnaires received after this date were excluded from the analysis. When the percentage of answers reached the 40% of the sample, data were elaborated.

Question 1: Do you know, even not in detail, the actual law on Pharmacovigilance? ($N = 245$)
- Yes: 233 (95%)
- No: 12 (5%)

Question 2: Have you ever sent an adverse drug reaction (ADR) report to your national reporting agency or to a pharmaceutical company? ($N = 245$)
- Yes: 126 (51.4%)
- No: 119 (48.6%)

Question 3: If yes, how many reports have you made in the last three years? ($N = 126$)
- < 5: 112 (89.1%)
- > 5: 14 (10.9%)

Question 4: Did you receive an adequate feedback from the Head of Pharmacovigilance of your Local Sanitary Unit? ($N = 126$)
- Yes: 52 (41.3%)
- No: 74 (58.7%)

Question 5: In general, are you satisfied from your local Pharmacovigilance Service? ($N = 245$)
- Yes: 131 (53.6%)
- No: 86 (35.2%)
- I don't know: 28 (11,2%)

Question 6: What is the reason for which you have never made a report of a suspected ADR? ($N = 119$)
- lack of a clinical event requiring it: 78 (65%)
- lack of time: 16 (13%)
- lack of faith in the sanitary authority: 2 (2%)
- legal reasons: 2 (2%)
- lack of interest: 0 (0%)
- other reasons: 21 (18%)

Question 7: In your opinion, which are the possible relapses of a Pharmacovigilance report? (many answers are possible) ($N = 245$)
- an increment of our knowledge about the risk/benefit drug profile: 53%
- an increment of the cases of a kind of medical phenomena that may be used for a scientific publication: 22%
- the risk, for the doctor, to be involved in a legal procedure for an eventual therapeutic error: 13%
- the fastidious event, for the doctor, to be called for further information about the reported case: 12%

Question 8: Do you think that reporting an ADR of a prescribed drug may elicit legal consequences (for instance, a legal action of the patient)? ($N = 245$)
- Yes: 75 (30.7%)
- No: 170 (69.3%)

Question 9: In your opinion, the reasons for a suspected ADR are (many answers are possible) ($N = 245$)
- a therapeutic error: 32 (13%)
- predisposition of the patient: 110 (45%)
- intrinsic drug toxicity: 103 (42%)

Question 10: If you think that the therapeutic error could be a possible cause of ADR, could it be possible that iatrogenic diseases are due to therapeutic errors? ($N = 245$)
- Yes: 32 (12.9%)
- No: 213 (87.1%)

Table 1: Questionnaire. The total number N of answers is given in parentheses after each question.

3 Results

We contacted 440 physicians, while 245 of them completed the interview (41.3% of the total sample). Results are reported in Table 1.

Question 1: Knowledge of law on pharmacovigilance.

95% of the sample (233 out of 245 physicians) answered to know, although not in detail, the law on Pharmacovigilance.

Question 2: Have you ever sent an adverse drug reaction (ADR) report to your national reporting agency or to a pharmaceutical company?

51.4% of the sample (126 out of 245) made at least one ADR report, while 48.6% (119 out of 245) have never reported a ADR.

The results also suggest that practitioners report ADR, predominantly, to national agencies rather than to pharmaceutical manufacturers.

Question 3: If yes, how many reports have you made in the last three years?

The 89.1% (112 out of 126 physicians) who declares to report, made less than five reports in the last three years.

Question 4: Guidance on reporting

The 41.3% of the sample (52 out of 126 physicians) states to have received an adequate feedback from the Head of Pharmacovigilance of the Local Sanitary Unit, while the 58.7% (74 out of 126 physicians) answered negatively.

Respondents were asked whether it would be useful if the national agency produced more detailed guidelines on the type of reactions to be reported and products of special interest. Overall, “never” reporters appeared more likely to want further advice on reporting criteria than “ever” reporters.

Question 5: In general, are you satisfied from your local Pharmacovigilance Service?

53.6% (131 out of 245 physicians) gave a positive answer; the 35.2% (86 out of 245 physicians) declared not to be satisfied; 11.2% (28 out of 245 physicians) declared to be unable to give an answer.

Question 6: Factors which may discourage reporting.

48.6% of interviewed physicians (119 out of 245) who answered to have never made a suspected ADR, was asked the reason for this, purposing several options of answering. 65% (78 out of 119 physicians) states to have never made reports because of the lack of a clinical event requiring it; 13% (16 out of 119 physicians) for the lack of time; 2% (2 out of 119 physicians) for the lack of faith in the sanitary authority; 2% (2 out of 119 physicians) for legal reasons; 18% (21 out of 119 physicians) for other reasons; nobody declared ‘lack of interest’ as reason for not reporting suspected ADRs.

Question 7: Purpose of reporting schemes

Respondents were asked about what they regarded as the purpose of their national ADR reporting scheme. 53% (130 of 245 physicians) states that a Pharmacovigilance reporting may increase the own knowledge about the benefit/risk drug profile; 22% (54 out of 245 physicians) that an increment of the number of cases of a medical phenomena may be possible. 13% (32 out of 245 physicians) states that a report may be risky because of legal procedures linked to an eventual therapeutic error. 12% (30 out of 245 physicians) states that a report may be fastidious for the doctor, since he may be called for further information about the reported case.

Question 8: Do you think that reporting an ADR of a prescribed drug may elicit legal consequences (for instance, a legal action of the patient)?

69.3% of interviewed physicians (170 out of 245) thinks that reporting ADR of a prescribed drug couldn't elicit legal consequences.

Question 9: In your opinion, the reasons for a suspected ADR are (many answers are possible)

- a therapeutic error;
- predisposition of the patient;
- intrinsic drug toxicity.

13% (32 out of 245 physicians) answered a therapeutic error; 45% (110 out of 245 physicians) a patient predisposition; 42% (103 out of 245 physicians) an intrinsic drug toxicity.

Question 10: If you think that the therapeutic error could be a possible cause of ADR, could it be possible that iatrogenic diseases are due to therapeutic errors?

87.1% (213 out of 245 physicians) answered negatively, while the 12.9% (32 out of 245 physicians) states that iatrogenic diseases are due to therapeutic errors.

4 Discussion

This survey was conducted to assess the attitude of GPs in Sicily to national ADR reporting schemes.

Several factors, appearing to deter reporting, have been identified in this study. First of all, the lack of confidence in making an iatrogenic diagnosis and the belief that only proven ADRs should be reported strongly suggest that many physicians in Sicily are reluctant to report suspected (as opposed to proven) reactions. Second, the lack of availability (or knowledge) of the meaning of reporting suspected ADRs (report forms, telephone numbers) appears to deter reporting. Third, respondents in many cities have frequently argued that reporting of suspected ADRs was inhibited by "lack of time".

Results obtained through this survey show that the development of better Pharmacovigilance Service methods and their wide use at the local level is necessary. A permanent update represents a fundamental feature in the Pharmacovigilance field, since it is strictly related to pharmacology and to the information about drugs in commerce, in constant evolution.

The problem of under-reporting is to ascribe in part to "cultural" deficiencies. Despite the important role of the physicians in starting the Pharmacovigilance path(for example, the importance of the event, its correlation with the drug, the reporting), however, they don't receive a specific education, don't have the reporting paper available, don't know whom sending it, waste time to fill the paper, don't have the information back, and consider the Pharmacovigilance as a bureaucratic activity without direct effect on their work.

Indeed, the universities courses don't focus the attention on the iatrogenic disease, don't educate to the differential diagnosis, don't give adequate space to the ADR, so don't create solid basis for the Pharmacovigilance culture.

The under-reporting is misleading for the doctor's knowledge about the risk/benefit profile of medicines and contributes to favor the underestimation of safety issues.

It is important to know the mechanisms of drugs (i.e. drugs interactions) which can provoke adverse reactions. Some physicians state that the actual approval regulatory systems warrant that only the "safe" drugs have to be approved for the commerce and the event has to be the consequence of other causes, then has not to be reported. In addition, the sense of guilty that the patient could be damaged, or the fear of potential legal problems can obstacle the adverse events reporting. Only a few doctors think that reporting is necessary, know the legislation and how to send an ADR report to the regulatory authorities. Other inhibitory factors can be the fear of "appear foolish", reporting well known adverse events and then "to be expected", or the reporting an event which could result non attributable to the drug.

To obtain a substantial improvement some actions are needed:

- to favor educational initiatives pre- and post-degree about the Pharmacovigilance;
- to stimulate the spontaneous reporting of suspected ADRs in Italy through a GPs network;
- to involve the reporters in a permanent Pharmacovigilance web with a rapid disposition of system results;
- to furnish to GPs the instruments of permanent and continuative education about drug safety and benefits that the spontaneous reporting system may yield to the community, in terms of both a risk reduction for the patient and resources saving to cure adverse reactions.

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