Asian Journal of Pharmaceutical and Health Sciences
www.ajphs.com

Effect of educational interventions in improving spontaneous adverse drug reaction reporting in a tertiary care setting

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ARTICLE HISTORY

Received: 08.11.2013

Accepted: 15.12.2013

Available online: 10.02.2014

Keywords:

ADR, educational intervention based approach, spontaneous reporting

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ABSTRACT

Spontaneous reporting remains one of the most effective methods to detect new, rare and serious adverse drug reactions (ADRs). Although Health Care Professionals (HCPs) play a key role in early detection and reporting of ADRs, underreporting is common. This study was thus carried out to assess the effect of educational interventions on HCPs in improving spontaneous ADR reporting at our hospital. A longitudinal study with two periods, the first period before the interventions from 2008 to 2009 and the second period after implementation of the interventions from 2011 to 2012, was carried out in a tertiary care teaching hospital. Educational interventions were developed and implemented in 2010. A greater than fourfold increase in the number of ADR reports (340.2%) was seen in the second period as compared to the first period. During the second period 832 ADRs were reported as compared to 189 ADRs in the first period. Before the interventions, a maximum 15 ADRs were reported in a month while in post intervention period, 71 ADRs were reported. In both periods of the study, cutaneous reactions were the most frequently reported ADRs. Antimicrobial agents were the most common therapeutic subgroups involved in ADRs. An education interventions, was associated with an increase in spontaneous ADR reporting by hospital physicians.

INTRODUCTION

Adverse drug reactions (ADRs) cause important public health problems in terms of morbidity, mortality and cost. Thus it is imperative to have a post marketing surveillance program or Pharmacovigilance program, wherein ADRs seen in everyday clinical practice can be reported without fail. However the effectiveness of such a programme is directly dependent on the active participation of health care professionals (HCP) like physicians, nurses and pharmacists as they are in the best position to report suspected ADRs observed in their routine patient care. [1, 2]

Although spontaneous reporting has been commonly used as a method of ADR detection in hospitals, underreporting is a major flaw. [2-5] A systematic review about the determinants of under-reporting found that a large proportion of physicians did not report ADRs because they felt that these were either well known or too trivial to report. [6] The estimated median underreporting rate (defined as percentage of ADRs detected from intensive data collection that were not reported to relevant spontaneous reporting systems) was 94% [7] which occurs frequently even for serious and unlabeled reactions [8-9]

Educational interventions have been shown to influence reporting rates. [10-12] A 10-fold increase in the rate of ADR reports was observed following an educational intervention in a cluster-randomized controlled study carried out in Portugal. [10] Hence, the present study was conducted to evaluate the effect of educational interventions in improving spontaneous ADR reporting in a tertiary care hospital setting.

MATERIALS AND METHODS

Study Design

A longitudinal study over a period of 5 years (2008 to 2012) in two periods was conducted at a tertiary care, teaching hospital in India, which has an ADR Monitoring Centre (AMC) under the Pharmacovigilance Program of India (PvPI). The duration of both periods was 2 years, with the first period (prior to the educational

interventions) being from January 2008 to December 2009, while the second period (post intervention) was from January 2011 to December 2012. In both these periods, the trends in spontaneous ADR reporting were assessed. In the interim year i.e. 2010, different educational interventions were developed and implemented.

Ethics

This study was initiated following administrative and ethical approvals. Informed consent waiver was obtained from the Ethics Committee, as analysis of ADR reports did not reveal patient's identity.

Study population

ADR reports of patients from all age groups suspected to be due to medications from the inpatient or outpatient departments of the hospital were included. ADR reports with over dosage, or excess consumption and medication errors were excluded from the study.

Study instrument:

The Central Drug Standard Control Organization (CDSCO) ADR reporting forms were used for the collection of data. The forms comprised of patient demographic details, medication details (name, dose, frequency and route of administration of drug) including non-prescription drugs, alternative treatments and concomitant medications, comprehensive adverse reaction details including description of the reaction, time of onset and duration of the reaction and treatment given with relevant investigation reports.

Educational Interventions

The major reasons for underreporting identified at our hospital following discussions with the hospital physicians were lack of time to report ADRs due to patient overload, lack of suspicion of occurrence of ADRs & lack of awareness of the need and where to report. Thus, in the interim year (i.e. 2010) between the 2 periods, interactive discussions were held with the physicians & nurses and Departmental staff members associated with the AMC of our hospital. During these discussions, they were first made aware of the importance of reporting ADRs, the objectives of the National Pharmacovigilance Program, presence of an AMC within the hospital, how to report ADRs, types of ADRs that need to be reported with emphasis on serious ADRs, unexpected ADRs and those associated with new drugs, details that need to be captured in the ADR reporting form, etc. A small presentation of the various ADR reports collected from different departments till date and the various activities carried out by the Pharmacovigilance Centre was also made.

In addition to these discussions that were held twice in that year, 'Dear Doctor' letters were also distributed to all Departments at 3 monthly intervals giving feedback on the number of ADRs collected and thanking the Department/s that submitted the highest number of ADRs. Posters were also distributed to the various clinical departments with a request that these posters be put up in the different wards. The posters highlighted the need for ADR reporting and also gave contact details for reporting. Provisions were made to either call or send Short Message Service (SMS) or emails to our Department to report ADRs and/or seek opinion regarding causality assessment of suspected ADRs or any other drug related information. Medical House Officers from the Department too took rounds in the OPDs/wards, emergency departments, Anti Retro viral Therapy (ART) centres and Directly Observed Therapy Short course (DOTS) centres daily so as to identify and collect ADRs. The reminder letters to the clinical departments and rounds by the Medical House Officers continued throughout the second period.

Table 1. ADRs classified by organ or system affected

Organ/ System	First period		Second period	
	2008-2009		2011-2012	
	N	%	N	%
Cutaneous reactions	144	76.2	314	37.7
Neurological reactions	24	12.7	223	26.8
Gastrointestinal reactions	19	10.1	96	11.5
Hematological reactions	00	00	150	18.1
Others (Weight gain, blurred vision, hyperlipidemia etc.)	02	1.1	49	5.9
Total	189	100	832	100

Differences in the rate of ADR reporting between the two periods was then analysed for variables like number of ADRs reported before and after the educational interventions, the organ/system affected and suspected drugs involved in the ADRs.

Statistical *analysis*

The number of spontaneous ADR reports and their characteristics were analyzed using descriptive statistics. To assess the changes in reporting rate, the median number of ADR reports and inter-quartile range (IQR) were calculated per month before and after the educational intervention. Data was tested for normality using Kolmogorov-Smirnov test. Numerical data was compared using Mann Whitney U-test. The level of statistical significance was set at $P < 0.05$.

RESULTS

Number of spontaneous ADR reports

The total number of ADR reports rose from 189 (111 in 2008 and 78 in 2009) to 832 (239 in 2011 and 593 in 2012) after the educational interventions ($p < 0.0001$), which correspond to an increase of 340.2%. The monthly reporting rate was significantly higher in the post-intervention period compared to the pre-intervention period (median and IQR, 29.5 [20, 53] vs. 8.5 [4, 11]; $p<0.0001$). The results are summarized in Figure 1.

Details of the ADRs reported:

In both the study periods, cutaneous reactions (76.2% in the 1st period vs. 37.7% in the 2nd period) were the most frequently reported ADRs followed by neurological (12.7% vs. 26.8%) reactions. In first period, gastrointestinal reactions were the third highest reported ADRs (10.1%) followed by other reactions (1.6%). In the second period, hematological (18.1%) and gastrointestinal (11.5%) reactions were the next highest reported ADRs followed by other reactions (5.9%). (Table 1)

Details of suspected drugs involved in the ADRs

In both periods, the most common therapeutic subgroups involved in the ADR were antimicrobial agents. They accounted for 50.3% and 28.2% of the total suspected pharmacological exposures in the 1st and 2nd period, respectively. (Table 2) Regarding the remaining therapeutic subgroups, the biggest difference between the 2 periods was an increase in the proportion of reports due to anti-retroviral and antiepileptic drugs in the second period.

DISCUSSION

Our study was an attempt to assess the effect of educational interventions in improving the rate of spontaneous reporting of ADRs at a tertiary care hospital in India. A fourfold increase in spontaneous reporting was observed after implementation of educational interventions based on activities like periodic meetings with the physicians and nurses, reminder letters and posters, daily visit to the wards and OPDs. There was an initial lag before the effect of the interventions were seen with the maximum impact seen in the second year of the 2nd period (i.e. 2012) This could be because of the continuous reinforcement by means of the 'Dear Doctor' letters and presence of the Medical House Officers in the wards/OPDs.

Different methods identify different types of ADRs and drugs. Moreover, the type of suspect drugs, their rank order and the types of ADRs identified vary widely among studies. The traditional methods and systems to detect ADRs in hospitals have been

Table 2. Suspect drugs by therapeutic subgroup

Therapeutic subgroup	First period		Second period	
	2008-2009		2011-2012	
	N	%	N	%
Anti-microbial	95	50.3	234	28.2
NSAIDs	28	14.8	80	9.7
Anti epileptic	33	17.5	182	21.8
Antipsychotic	06	3.1	39	4.7
Anti retro viral (ART)	05	2.7	228	27.4
Other drugs (anti cancer drugs, vaccines, radio contrast dye, blood products etc.)	12	6.3	63	7.5
Unknown drugs	10	5.3	06	0.7
Total	189	100	832	100

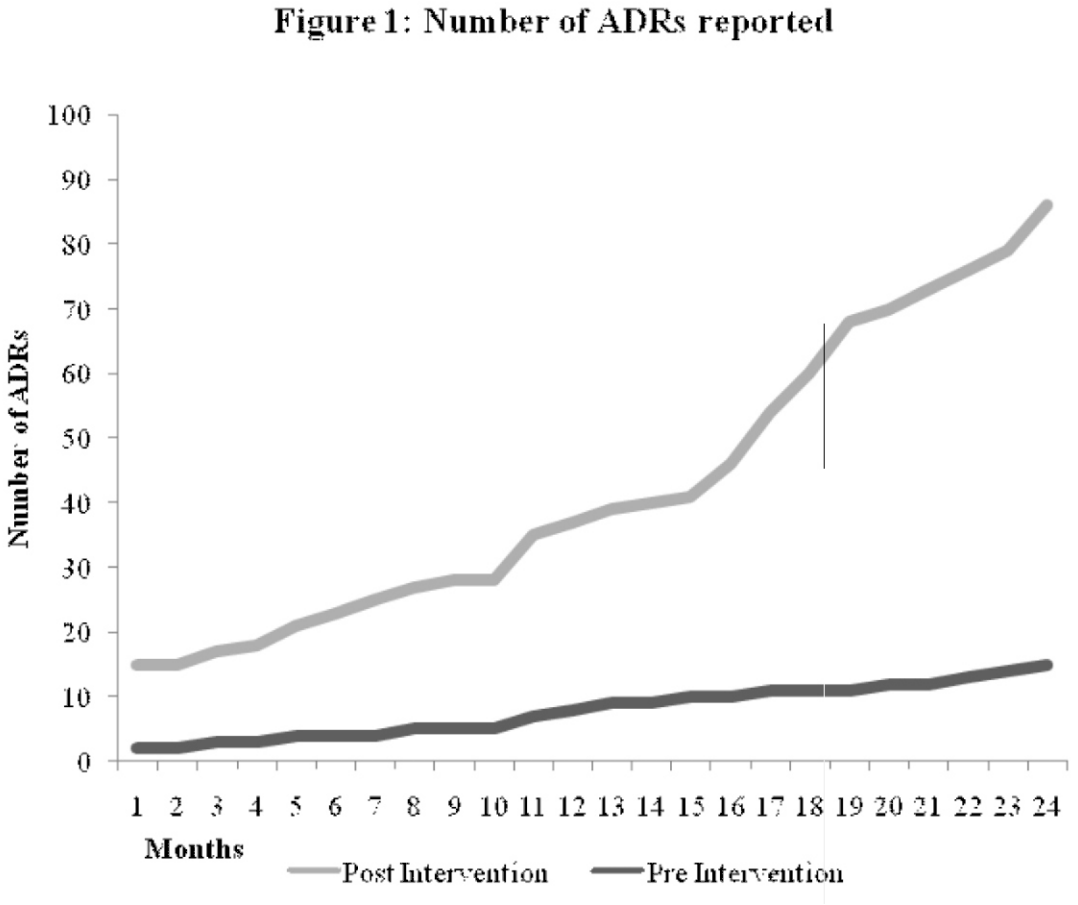

Fig 1. Monthly ADRs reported to AMC in pre and post intervention period

spontaneous reporting, intensive surveillance of hospital admissions and more recently, computer-assisted approaches using routine data from hospital information systems. [3]

The poor reporting by hospital physicians is a major problem because only a third of reports come from them, despite the fact that serious reactions are most likely to be seen in hospitals. [4] It is necessary to clear doubts and misconceptions regarding ADR reporting that lie in the minds of the physicians. For example, many physicians believe that it is necessary to first confirm the causality of an ADR rather than report even suspicions. The reason for this is not known; lack of time and other clinical work load have been argued as potential problems to the spontaneous reporting of ADRs by the physicians at our hospital.

Figueiras *et al* had examined the effectiveness of educational outreach visits for improving ADR reporting by physicians. They found maximal effect of the interventions during the first four months after the intervention, and the differences remained statistically significant for 12 months. [10] A study by Cereza *et al* has shown an effect of specific intervention on reporting of spontaneous ADRs in hospital setting based on educational activities and economic incentives which allowed them to detect some drug related problems and to identify several signals. [13] In Spain, Pedros *et al*. observed that, continuous interventions like periodic educational meetings and economic incentives was associated with four fold increase in spontaneous reporting of ADRs as well as in reported serious reactions. They also found an increase in the absolute number of suspected pharmacological exposures to new drugs and in the number of different new drugs causing ADRs. [14] Tabali *et al*. found more gain in the knowledge of physicians from face-to-face training with an increase in the completeness of ADR reports from 80.3% to 90.7% after the intervention. [15] Radhakrishnan *et al* have shown that, an educational intervention can increase awareness of pharmacovigilance among the health care professionals who then incorporated this knowledge into their every day clinical practice. [16] In a similar interventional program in pharmacists, Herdeiro *et al*. showed that educational outreach visits improved ADR reporting in terms of quantity and relevance. [17]

In our study the most frequently reported ADRs were similar in both periods, although some types of ADRs that were hardly reported in the first period increased in the second one. Cutaneous reactions were the most frequently reported ADRs in both periods. These findings were similar to studies carried out by Kushwaha *et al* [18] and Naina *et al* [19] and in our study this can be due to active involvement of the Dermatology staff in detecting and reporting ADRs.

Other ADRs commonly reported during both periods were neurological, hematological and gastrointestinal reactions. However, an increase in hematological reactions was observed in second period which could be the outcome of our interventions. Further studies should be carried out to analyze the effect of different interventions on the features of the spontaneously reported ADRs.

In our study the drug class list associated with ADRs was headed by antimicrobial agents (AMA) and anti inflammatory

drugs. This finding is consistent with the study reported by Murphy *et al.* [20] We found that the major change between the two periods in our study was an increase in the proportion of anti-retroviral and antiepileptic drugs. In addition, anti neoplastic drugs, a therapeutic subgroup highly reported in other studies, also increased after the intervention. [21-23]

The therapeutic subgroups most commonly involved in the spontaneously reported ADRs were drugs frequently used in our hospital setting. Nevertheless, taking into account the differences in the pattern of suspect drugs in the two periods, it is likely that the intervention allowed us to identify during the second period some suspect drugs involved in ADRs that were infrequently reported in the first one.

Our interventions comprised mainly of repeated interaction with the physicians and nurses, through letters and physical presence in the wards & OPDs. Other interventions like periodic training sessions, motivation of the physicians and other HCPs, economic incentives etc. are other interventions that have been utilized to promote spontaneous reporting. [13] [14] It would be interesting to investigate the effect of these other types of interventions on the type of suspected drugs in spontaneously reported ADRs.

Limitations

Although we found good improvement in the ADR reporting rate following implementation of the educational interventions, the issue of sustainability of the reporting rate over time needs to be discussed. Some of our interventions were continued in the second period which could have influenced the reporting rate in our study. Whether the same reporting trend will continue once the effect of these interventions wane needs to be assessed, which was not done in our study. Another study limitation was that we did not assess the improvement in the quality and completeness of the ADR reports.

CONCLUSION

The problem of underreporting still exists in our country. Only the good will of reporters, who are mostly HCPs and their good knowledge about PvPI, can sustain & promote the system. Our study was useful as a preliminary study in understanding whether educational interventions can improve the rate of spontaneous ADR reporting of PvPI among HCPs in India. Bridges need to be built linking Pharmacovigilance centers and HCPs in order to strengthen the ADR reporting rate which will enhance patient safety. This study shows that, an intervention based approach may help to consolidate the Pharmacovigilance Program in India.

ACKNOWLEDGEMENTS:

None

REFERENCES

1. Ahmad SR. Adverse drug event monitoring at the Food and Drug Administration. J Gen Intern Med 2003;18:57-60
2. Wysowski DK, Swartz L. Adverse drug event surveillance and drug withdrawals in the United States, 1969-2002: the importance of reporting suspected reactions. Arch Intern Med 2005;165:1363-9
3. Thürmann PA. Methods and systems to detect adverse drug reactions in hospitals. Drug Saf 2001;24:961-8
4. Rawlins MD. Pharmacovigilance; paradise lost, regained or postponed? The William Withering Lecture 1994. J R Coll Physicians Lond 1995;29:41-9
5. Vallano A, Cereza G, Pedros C, Agusti A, Danes I, Aguilera C, *et al*. Obstacles and solutions for spontaneous reporting of adverse drug reactions in the hospital. Br J Clin Pharmacol 2005;60: 653-8
6. Lopez-Gonzalez E, Herdeiro MT, Figueiras A. Determinants of under-reporting of adverse drug reactions: a systematic review. *Drug Saf* 2009;32:19-31
7. Hazell L, Shakir SA. Under-reporting of adverse drug reactions: a systematic review. Drug Saf 2006;29:385-96
8. Moride Y, Haramburu F, Requejo AA, Begaud B. Under-reporting of adverse drug reactions in general practice. Br J Clin Pharmacol 1997;43:177-81
9. Heeley E, Riley J, Layton D, Wilton LV, Shakir SAW. Prescription-event monitoring and reporting of adverse drug reactions. Lancet 2001;358:1872-3
10. Figueiras A, Herdeiro MT, Polonia J, Gestal-Otero JJ. An educational intervention to improve physician reporting of adverse drug reactions: a cluster-randomized controlled trial. *JAMA* 2006;296:1086-93
11. Bracchi RC, Houghton J, Woods FJ, Thomas S, Smail SA, Routledge PA. A distance-learning programme in pharmacovigilance linked to educational credits is associated with improved reporting of suspected adverse drug reactions via the UK yellow card scheme. *Br J Clin Pharmacol* 2005;60:221-3
12. Cosentino M, Leoni O, Banfi F, Lecchini S, Frigo G. Attitudes to adverse drug reaction reporting by medical practitioners in a Northern Italian district. *Pharmacol Res* 1997;35:85-8
13. Cereza G, Agustí A, Pedrós C, Vallano A, Aguilera C, Danés I, *et al*. Effect of an intervention on the features of adverse drug reactions spontaneously reported in a hospital. Eur J Clin Pharmacol 2010 Sep;66:937-45
14. Pedros C, Vallano A, Cereza G, Mendoza-Aran G, Agusti A, Aguilera C, et al. An Intervention to Improve Spontaneous Adverse Drug Reaction Reporting by Hospital Physicians: A Time Series Analysis in Spain. Drug Saf 2009;32:77-83
15. Tabali M, Jeschke E, Bockelbrink A, Witt CM, Willich SN, Ostermann T. Educational intervention to improve physician reporting of adverse drug reactions (ADRs) in a primary care setting in complementary and alternative medicine. *BMC Public Health* 2009;9:274
16. Radhakrishnan R, Vidyasagar S, Varma DM. An Educational Intervention to assess Knowledge Attitude Practice of pharmacovigilance among Health care professionals in an Indian tertiary care teaching hospital. Int. J. Pharm Tech Res 2011;3:678- 92
17. Herdeiro MT, Polonia J, Gestal-Otero JJ, Figueiras A. Improving the reporting of adverse drug reactions: a cluster-randomized trial among pharmacists in Portugal. *Drug Saf* 2008;31:335-44
18. Kushwaha KP, Verma RB, Singh YD, Rathi AK. Surveillance of drug induced diseases in children Indian J. Pediatr 1994;61:357-65

19. Naina HH, Philip AN, Dennis PW. In: Dipiro, T.J. Editor. Pharmacotherapy; A Pathophysiologic Approach. 4th Edition. Appleton and Lange: Stamford Cannecticut; 1999. p.1505

20. Murphy BM, Frigo LC. Development, implementation and results of a successful multi disciplinary adverse drug reactions reporting program in a University teaching hospital. *Hosp Phar* 1993;28:11991204

21. Jose J, Rao PGM. Pattern of adverse drug reactions notified by spontaneous reporting in an Indian tertiary care teaching hospital. *Pharmacol Res* 2006;54:226-33

22. Baniasadi S, Fahimi F, Shalviri G. Developing an adverse drug reaction reporting system at a teaching hospital. Basic & Clinical Pharmacology & Toxicology 2008;102:408-11

23. Uppal R, Jhaj R, Malhotra S. Adverse drug reactions among inpatients in a north Indian referral hospital. Nat Med J India 2000;13:16-8