International Journal of Pharmacy
Journal Homepage: http://www.pharmascholars.com

Research Article **CODEN: IJPNL6**

AN IMPACT OF EDUCATIONAL INTERVENTIONS ON REPORTING OF ADVERSE DRUG REACTIONS

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ABSTRACT

The main objective of the present study was to evaluate the impact of educational interventions (IT) on adverse drug reaction reporting (AR). Randomly selected prescribers were assigned to group A (n= 84) or B (n= 85). Three months each of Pre (Pre- IP), Intervention – I (IP- I), IP- II and Post – IP were applied in sequence. IT included Pharmacovigilance Awareness Programme, posters, written and verbal reminders during IP-I & II. Inter-group and inter-phase change in the rate and quality of AR (score of 0-50) was estimated. Data was analyzed using Chi Square and Student's "t" test. P<0.05 was considered as statistically significant. Improvement in AR rate (154% increase) and quality (Pre- IP: 34; IP-I: 35.6; IP-II: 36.3) of ADR reports was observed during IP- II as compared to Pre- IP. Group A showed significant improvement in the rate (62.6%) and quality of reports as compared to group B during both IP- I & II (p<0.01). However, upon withdrawal of IT, the impact attenuated with time. A positive impact of IT on rate and quality of AR was observed, albeit temporarily. Hence, administration of IT on a regular basis is recommended for a sustainable impact.

Key words: ADR reporting, educational interventions, adverse drug reactions

INTRODUCTION

The World Health Organization defines an Adverse Drug Reaction (ADR) as "a response to a drug which is noxious and unintended, which occurs at doses normally used in man for treatment, prophylaxis, diagnosis and for the modification of physiological function" [1]. Around 6% of hospital admissions are estimated to be due to ADRs and about 6-15% of hospitalized patients experience a serious ADR [2]. India being third largest producer and user of drugs in the world, [3], post-marketing surveillance of medicines and the use of generated information for effective drug regulation are of paramount importance. Spontaneous ADR reporting by healthcare professionals, intensive ADR monitoring, pharmaco-epidemiological studies and computer assisted methods are some of the methods for monitoring drug safety after approval of a drug for marketing[4,5]. As health care professionals are important stakeholders in patient safety, spontaneous reporting is an important method from both the regulatory and economic perspective [6]. The signal detection of serious, yet unrecognized, drug associated events and benefit risk assessment related activities requires good quality ADR reports that allow a meaningful causality assessment [7].

However, under reporting is a major drawback of this method as literature shows that only 6-10% of all ADRs are reported worldwide [8,9]. Important factors that might discourage reporting are ignorance, lethargy, doubtful diagnosis of ADR, lack of financial benefits, patient confidentiality and professional liability issues, lack of access to ADR reporting forms, etc [10]. Educational and non-educational interventions have been globally suggested to improve spontaneous reporting which may have varying impact on the actual rate of reporting. These include increasing availability to ADR reporting forms, frequent reminders to health care professionals, poster display, introducing ADR reporting training as a part of undergraduate

curriculum, facility of online reporting, sending feedback and acknowledgement to reporters, conducting face-to-face interviews or meetings, structured questionnaires, training courses/lectures, giving economic incentives or credits for reporting etc [12-21].

While working at a large, tertiary care, teaching hospital and operating an ADR monitoring centre under the national Pharmacovigilance programme of India, it was observed that only a small population of prescribers report ADRs. With the hope that the educational intervention(s) (IT) would help foster the culture of ADR reporting in our hospital, the present study was undertaken to analyze the impact of various IT on ADR reporting (rate and quality)by prescribers.

MATERIALS AND METHODS

This was a prospective, comparative, interventional study carried out for a period of 12 months at a 2500 bedded tertiary care, public sector, teaching hospital (TH) in India (Figure 1). The study was approved by the Institutional Ethics Committee of the hospital. A situation analysis showed that the whole population of 486 prescribers at the hospital was distributed amongst various clinical departments [i.e. strata]. Each of the clinical department was further divided amongst various units. Each unit consisted of 3-6 residents, 2-3 assistant professors, 1-2 associate professors and 1 professor. A total of 40 such units existed in the hospital.

In a behavior modifying study of this kind, confounding factors such as age, gender, clinical specialty and experience of the prescribers may have a bearing on ADR reporting. Therefore, it was ensured that both groups had equitable distribution of clinical departments and these included prescribers of similar experience/cadre (i.e. equal proportion of residents, assistant professor, associate professor and professors). In order to accomplish this, proportionate stratified random sampling technique was employed i.e. from each of the strata/ clinical department, a simple random sample was selected by draw of lots. The number of units drawn from each of the strata therefore became proportional to their respective strata size. Hence, 4 out of 10 units each of medicine and surgery, 2 out of 5 units of obstetrics & gynecology, 2 out of 2 units each of dermatology and venereal diseases and psychiatry, 2 out of 3 units of orthopedics, 2 out of 4 units of pediatrics, 2 out of 3 units of otorhinolaryngology and 1 out of 1 unit of anesthesiology were sampled. Therefore, a sample constituting of 169 prescribers that belonged to 21 units was derived, representing nearly one third of the prescribing population at TH (34.7%).

In the next step, the prescribers of this sample were subdivided into 2 groups i.e. group A (n = 84) and group B (n = 85). The proportionate stratified random sampling technique was repeated i.e. 2 out of 4 selected units each of medicine and surgery and 1 out of 2 selected units of rest of the departments were obtained by draw of lots. The prescribers belonging to this subsample of 10 units (medicine – 2, surgery – 2, obstetrics & gynecology- 1, dermatology and venereal diseases – 1, psychiatry – 1, orthopedics – 1, pediatrics – 1 and Otorhinolaryngology – 1) were allotted to group A. And the prescribers belonging to the remaining subsample of 10 units (medicine – 2, surgery – 2, obstetrics & gynecology- 1, dermatology and venereal diseases – 1, psychiatry – 1, orthopedics – 1, pediatrics – 1 and Otorhinolaryngology – 1) were allotted to group B.

Department of anesthesiology functioned as a single unit in the TH, therefore, 1 professor, 1 associate professor, 1 assistant professor, 1 tutor and 2 residents from anesthesiology were selected by draw of lots and allotted to group A ; similar process was repeated for group B Prescribers were enrolled after obtaining a written, informed, valid consent.

ADR reporting forms of CDSCO (Central Drugs Standard Control Organization) were made available to all participants throughout the study period. Two cross-sectional KAP surveys were conducted (before and after the IT). During Pre–Intervention Phase (Pre IP) of 3 months, a KAP (knowledge, attitude and practice) questionnaire analysis on ADR reporting was conducted. The questionnaire was adapted from a previous study (which was validated and tested by the authors) [10]. In the beginning of 3 months of intervention phase–I (IP- I), an interactive pharmacovigilance awareness program (PAP) for 60 minutes was conducted for all the participants. Information regarding pharmacovigilance (PV) and ADR reporting, importance of spontaneous reporting, the logistics of reporting (i.e. how, when and where to report ADRs), and the role of department of pharmacology in this activity was briefly communicated during the session. Throughout the IP-I, written reminders (once a month) via Short Messaging Services (SMS) to prescribers of group A and e-mails to prescribers of group B were sent. These reminders contained information on interesting case reports, emerging drug safety concerns, warnings and alerts issued by different regulatory authorities and spontaneous reporting. During the next 3 months of intervention phase –II (IP- II), in addition to the above mentioned IT, prescribers in group A were exposed to verbal reminder in the form of a personal briefing (i.e. 10 minutes of short meeting). The meetings were held in all clinical departments (so as to target each of the prescriber

personally) and information regarding ongoing PV activities of the hospital was given. The prescribers were encouraged to resolve their doubts or concerns during the meeting. Three attempts were made to contact the individual. Similarly, group B prescribers received an additional written reminder i.e. an information leaflet on PV during IP-II. The leaflet contained news regarding recently banned drugs in India and commonly encountered ADRs in clinical practice, in addition to fostering spontaneous reporting. To further reinforce the reporting practices, posters with PV messages (one new poster every 2 months) were displayed in the areas most visited by the prescribers during both the intervention phases consistently. To facilitate the reporting, all the reminders included the contact details (telephone numbers and email addresses) of the PV team of the hospital. All of the IT were withdrawn during the post- intervention phase (Post- IP) for next 3 months. A post- intervention KAP questionnaire, similar to the pre IP phase was administered at the end of the study period. Knowledge based questions were evaluated with the help of an internally validated scoring system, whereby differentiated scores were allotted to each five of such questions (0- 1, 0-2, 0-3,0-6 and 0-8 respectively), with a resultant maximum score of 20. The response of attitude and practice based questions was evaluated qualitatively. ADR reports were collected from participating prescriber community during the entire study period and analyzed. The rate of ADR reporting during each phase of intervention, number of serious ADRs reported and quality (tested in terms of mean completeness score) of all the ADR reports was inferred. An ADR was assessed as serious if the outcome of the event is death, the event is life threatening, it led to hospitalization (initial or prolonged) caused disability, caused a congenital anomaly, required intervention to prevent permanent impairment/damage and for any other medically significant condition. A scoring criterion was devised and internally validated to ascertain the quality of report. As per the items of the CDSCO ADR reporting form, information regarding patient details, date of start of ADR, description of ADR, details of suspect drug(s), details of concomitant drug(s), outcomes of ADRs, reporter details and the date of report are essential. The information regarding other items of the form like date of recovery, diagnosis of ADR, action(s) taken, treatment (if any), dechallenge (reaction abated after the drug is stopped), rechallenge (reaction reappeared after reintroduction of the drug), relevant tests/ vital data/lab data including dates (if any), other items of relevant history (pre-existing medical conditions if any), alternate causes of reaction (if any) and seriousness of reaction are considered as voluntary. Accordingly, for analysis, each sub-item of the obligatory item (eg., patient initials under patient details) of the ADR report was scored from 0- 2 depending on the completeness of information provided and presence of voluntary information was given the score as 0 or 1. Total score thus varied from 0 to 50. Data obtained from the study was analyzed by Student's paired "t" and Chi-square tests using new Graph pad software version 3 (INSTAT 3); $p<0.05$ was considered as statistically significant.

RESULTS

The mean age of the prescribers in group A (29.51 years ± 7.4 SD) and group B (27.71 years ± 4.5 SD) was comparable (p= 0.09). Gender distribution in both groups was also similar (p= 0.66) (male: female ratio of 1.4 and 1.2 respectively in group A and B). A total of 94/169 KAP questionnaires (response rate 55.6%) and 125/169 KAP questionnaires (response rate 73.9%) were returned Pre IP and Post IP respectively, the response rate being higher Post IP as compared to Pre IP (p = 0.0006). The difference in the response rate between the two interventional groups was not significant (p = 0.31) during the Pre IP; whereas during post IP, a significantly higher (p = 0.025) number of prescribers from group A responded as compared to group B. A significant increase in response rate of group A was observed Post IP (response rate 82.1%) as compared to Pre IP (response rate 51.1%)(p <0.0001).As illustrated in Figure 2, the baseline mean KAP questionnaire scores were similar in both the groups (p = 0.35), whereas the score of KAP questionnaire after the interventions was significantly higher in group A (14.95 ± 2.81) as compared to group B (11. 85 ± 1.97) (p <0.0001). The improvement in attitude and practices were also noted. Ignorance about method and logistics of ADR reporting was considered to be an obstacle to ADR reporting before IT, while Post-IP, lack of time and doubtful diagnosis were cited as the reasons that discouraged reporting. PAP was actually attended by 71% of the participating prescribers. Seventy-nine prescribers of Group A were available for personal briefing. A total of 190 ADR reports (119 from group A and 71 from group B) were submitted during the study period which contained 221 ADRs. The majority of these reports were submitted during IP I (n= 48) and IP II (n = 57) (Figure 3). A 154% increase in ADR reporting during IP- II was observed as compared to Pre- IP (n = 37) (p< 0.001). However, the improvement was not sustained during Post- IP (n= 48) (p = 0.00). The reporting rate between the two groups was similar during Pre IP (p = 0.23). However, prescribers of group A reported significantly higher number of

ADRs as compared to group B during IP I (p = 0.02) and IP- II (p = 0.01); the difference being insignificant during Post IP (p = 0.31).

Sixty-six (35 from group A and 31 from group B) serious ADRs were reported (Figure 4). A significant increase in reporting of serious ADRs reported was observed during IP–I (22) and IP II (25) as compared to Pre- IP (8) (p < 0.05). The difference in reporting rate of serious ADRs between the two groups was not significant (p>0.05) during the pre IP and IP- I. However, during IP- II, prescribers of group B reported significantly higher number of serious ADRs as compared to group A (p = 0.03). The number of serious ADRs reported decreased during Post IP (11) as compared to IP- II (p = 0.04).

The quality of ADR reports i.e. mean completeness score was comparable between the groups(Group A- 34.5 and Group B- 33.2) during pre IP (p = 0.23). While an overall improvement in the quality of ADR reports was observed during both the intervention phases i.e. IP- I (35.6) and II (36.3), a statistically significant (p= 0.0003) difference was observed during IP II as compared to Pre- IP (34). However, this improvement was not sustained during Post IP (33.8) (Figure 5). The mean score of ADR reports collected from prescribers of group A was significantly higher as compared to group B (p<0.01) during IP-I (Group A- 36.34 and Group B- 34.05) and IP-II (Group A- 37.08 and Group B- 34.9). We observed that after the IT, an overall increase in awareness and inquisitiveness about ADRs took place. It also became evident that prescribers from Group A not only reported significantly higher number (62.6% of reports than Group B (37.4%), the quality was also better in group A than Group B during both the intervention phases (p<0.01). Group A also demonstrated significant improvement in KAP scores post-IT as compared to group B (Group A- 14.9 and Group B- 11.8). During the Post-IP, 2 prescriber from Group A (both the prescribers had left the institution) and 3 from Group B (2 had left the institution and 1had did not wish to continue in the study) were lost to follow up, however were included in the analysis.

DISCUSSION

Out of all conventional methods for PV, spontaneous ADR reporting is one of the most cost effective and time tested method and it remains as the cornerstone of any successful PV program. Unfortunately, under-reporting is a major drawback inherent with it. The effect of educational and other interventions on ADR reporting has been studied in the past [12-22]. However, the effectiveness of such interventions is highly variable and is confounded by several factors. To our knowledge, our study is one of the first in India to assess the impact of some of the globally suggested IT on the quantum and quality of ADR reporting. Since the applicability and suitability of some of the proposed interventions in an Indian context may differ, the present study was designed to evaluate the effects of a few of the suggested IT on ADR reporting in a tertiary care hospital (TH).The prescribers working in major clinical specialties of the TH were exposed to periodic written and verbal reminders (i.e. SMS, emails, educational leaflet, personal briefing), pharmacovigilance awareness programme and posters. A quantitative and qualitative analysis of the impact of these IT on ADR reporting and KAP of the prescribers was performed.

Following the IT, the improvement in prescribers' knowledge, attitudes and ADR reporting practices was noted in parallel to an increase in rate and quality of reporting. We also observed that while all the IT were useful, a combination of verbal and written reminders i.e. SMS and personal briefing was more effective than only written reminders in the form of e-mails and information leaflet. Therefore, the present study demonstrated a positive impact of IT on ADR reporting, albeit temporarily.

The better response observed in the group intervened with both verbal (personal briefing) and written (SMS) reminders could be because of the possibility that a direct briefing gave the better chance to build personal rapport and gave the prescribers a chance to solve their doubts and apprehensions about reporting. In addition, owing to the busy schedules, it is possible that many of the prescribers of Group B did not read their emails regularly while a higher number of prescribers in Group A did read SMS. Obviously, PAP and posters could have complemented these IT in both the groups.

The findings of the present study are supported by most of the published literature concerning ADR reporting [12-19]. The varied intervention(s) utilized in these studies led to considerable improvement in rate and/or quality of the reports, although the benefit attenuated with time. In a cluster-randomized controlled trial in Portugal the rate of ADR reporting increased 10-fold after targeted outreach visits but the effect was significant only for a year [12]. Similarly, in another randomized clinical trial the 4th year medical students underwent a 15 minute lecture on ADR reporting. An overall quality scores for intervention group were significantly higher than the nonintervention group but again the long term effect could not be observed [13]. It has been shown that ADR reporting can be increased by providing detailed and specific feedback to the healthcare provider and the contents of the feedback may influence the reporting rates [14]. Among doctors exposed to questionnaire containing ADR reporting

information along with verbal and written reminders and yellow cards placement in drug chart, a four-fold increase in reporting rates has been demonstrated but rates reverted to baseline once the interventions were stopped [15]. In another study, reporting rates have been reported to rise after sending quarterly adverse drug reaction bulletins to physicians and after introducing yellow cards in prescription pads [16]. However, others have reported no significant improvement in ADR reporting rate and quality even after distribution of ADR information letters to prescribers and nurses [20] and sending repeated e-mail reminders [21].

Our study had some limitations, chiefly the short duration of study period and lack of control group. Also, since the combination of various interventions was administered; the single best intervention could not be ascertained. Confounding factors like seasonal variation in ADR incidence, personal interests of prescribers, patient flow during festivals etc were not evaluated. Additionally, we could not ascertain that all the prescribers had actually read the written reminders given to them.

Thus, based on the findings of this study, it is suggested that regular implementation of a combination of IT (posters and PV awareness program), and verbal (personal briefing) and written reminders (SMS, emails and leaflet) can improve spontaneous ADR reporting. Cost, organizational support and feasibility should be taken into account while implementing these interventions on a long term basis.

ACKNOWLEDGEMENTS

The authors would like to thank the hospital physicians who participated in this study. No external source of funding was obtained for this study. The authors have no conflict of interest to declare relevant to the contents of this study.

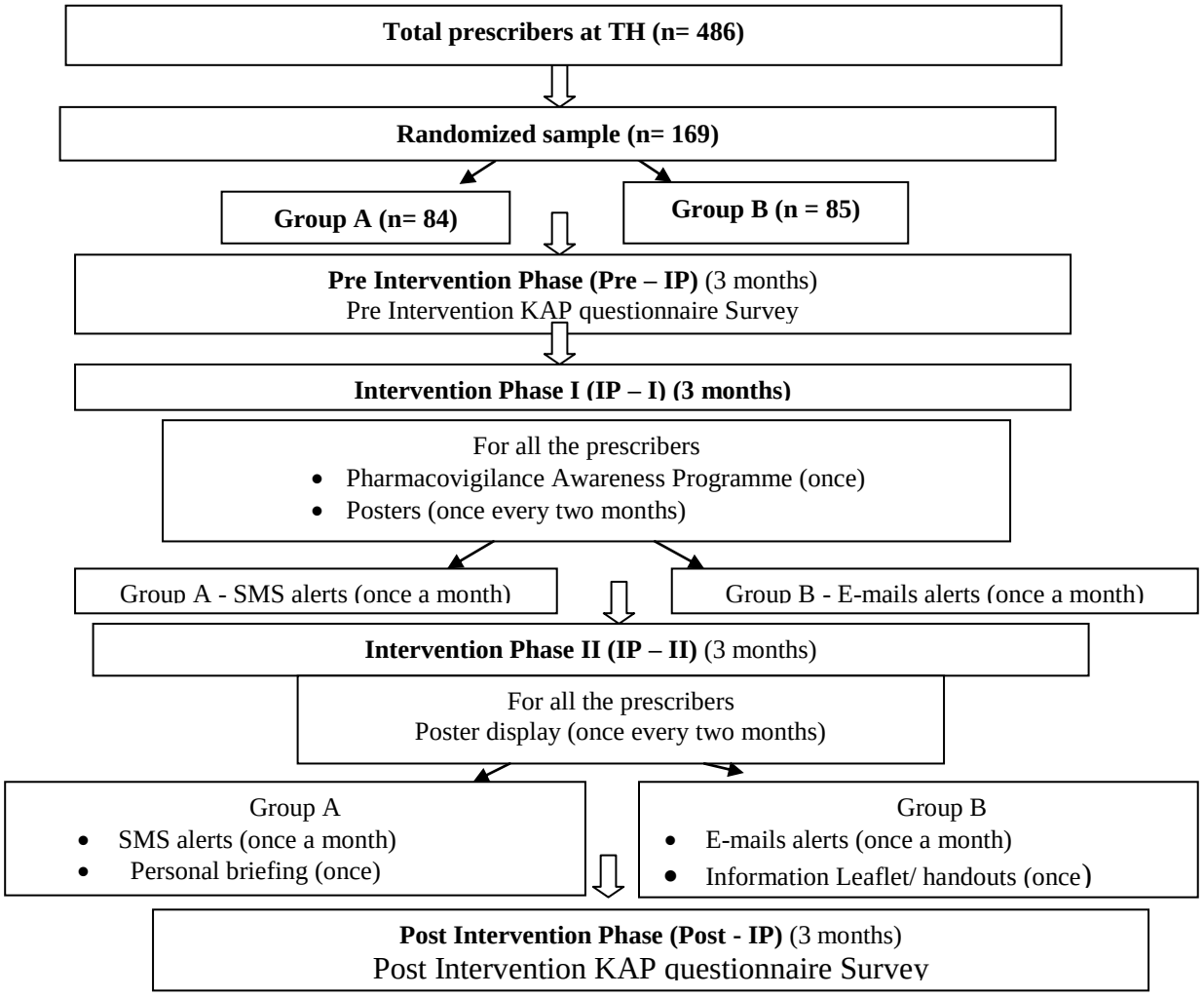

Figure 1: Study design

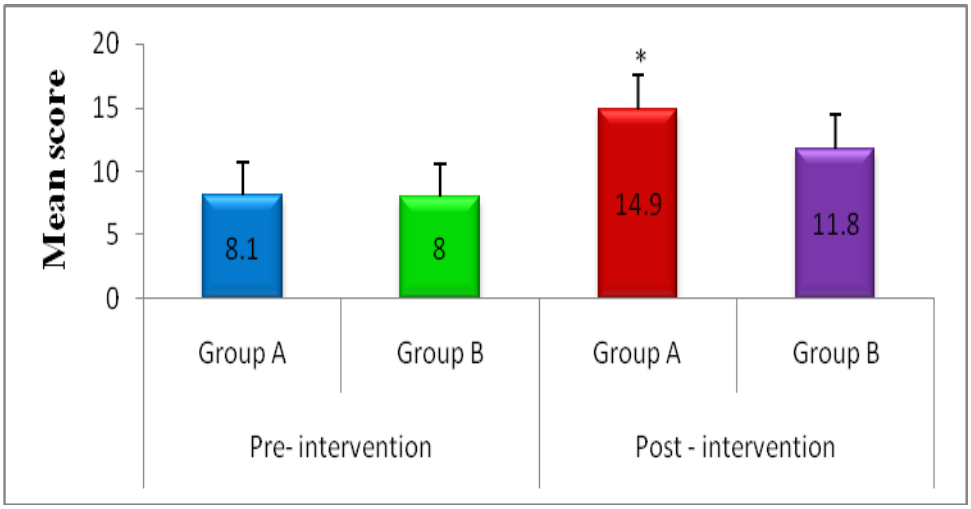

Figure 2: Impact of interventions on KAP about ADR reporting among prescribers at TH (n=169)

Group A - Poster, pharmacovigilance programme, SMS and personal communication;
Group B - Poster, pharmacovigilance programme, emails and information leaflet; Statistical significance was determined by Student's paired and unpaired "t" test *p<0.0001 Group A Post intervention scores as compared to Pre intervention scores #p<0.0001 Post intervention scores of Group A as compared to Group B. All data are mean ± SD

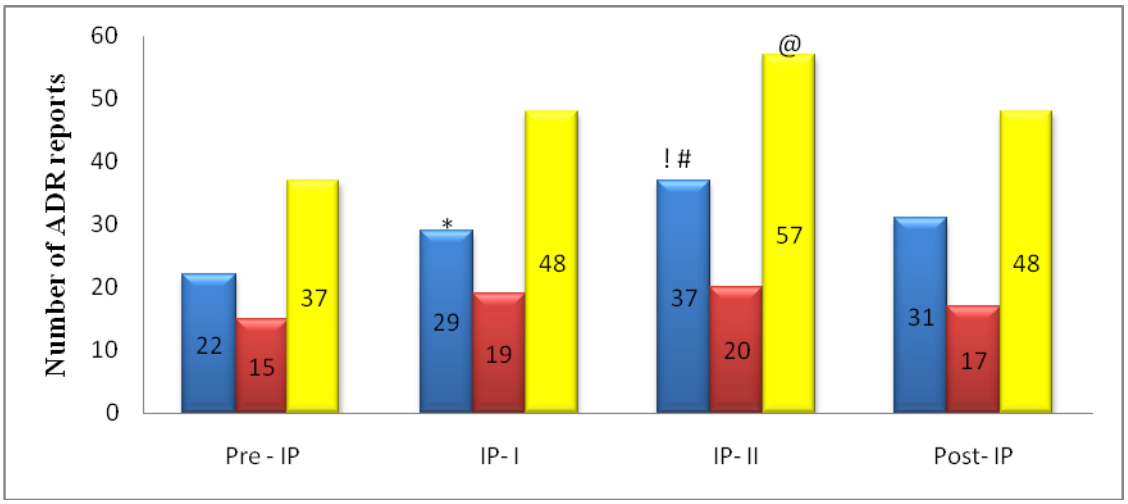

Figure 3: Impact of educational interventions on ADR reporting rate by prescribers (n=169)

Group A - poster, pharmacovigilance programme, SMS and personal communication;
Group B - poster, pharmacovigilance programme, emails and information leaflet
Statistical significance was determined by Student's paired and unpaired "t" test; p<0.05 was considered as statistically significant; *p= 0.02 ADR reporting rate of Group A during IP- I as compared with Group B; @p<0.001 ADR reporting rate during IP- II as compared with Pre IP; #p= 0.02 ADR reporting rate of Group A during IP- II as compared with Group B;! p= 0.01 ADR reporting rate of Group A during IP- II as compared with Pre-IP

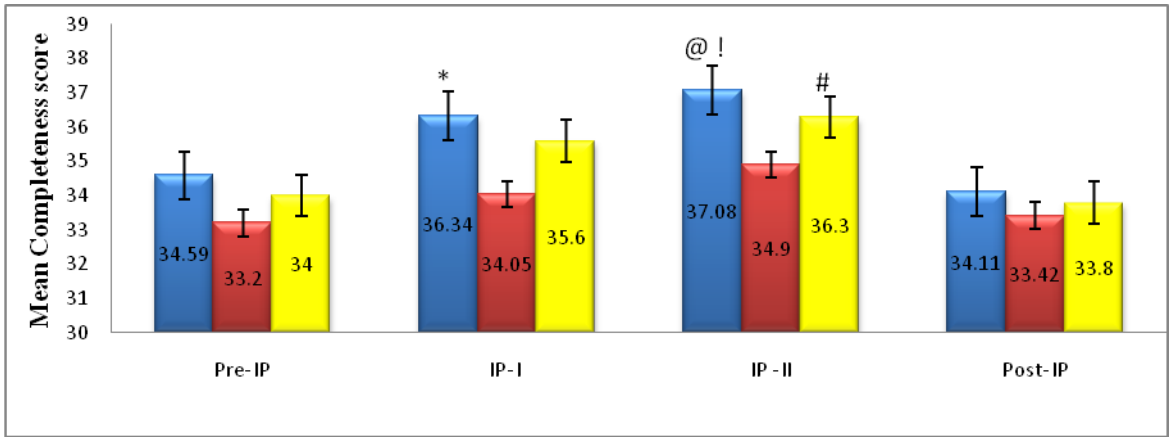

Figure 4: Impact of educational interventions on reporting rate of serious ADRs by prescribers (n = 169)

Group A - poster, pharmacovigilance programme, SMS and personal communication;
Group B - poster, pharmacovigilance programme, emails and information leaflet
Statistical significance was determined by Student's paired and unpaired "t" test; $p<0.05$ was considered as statistically significant; *p= 0.03 reporting rate of serious ADRs during IP- I as compared with Pre- IP; @ p= 0.04 reporting rate of serious ADRs during IP- II as compared with Pre- IP; # p =0.03 reporting rate of serious ADRs by prescribers of Group B as compared to Group A

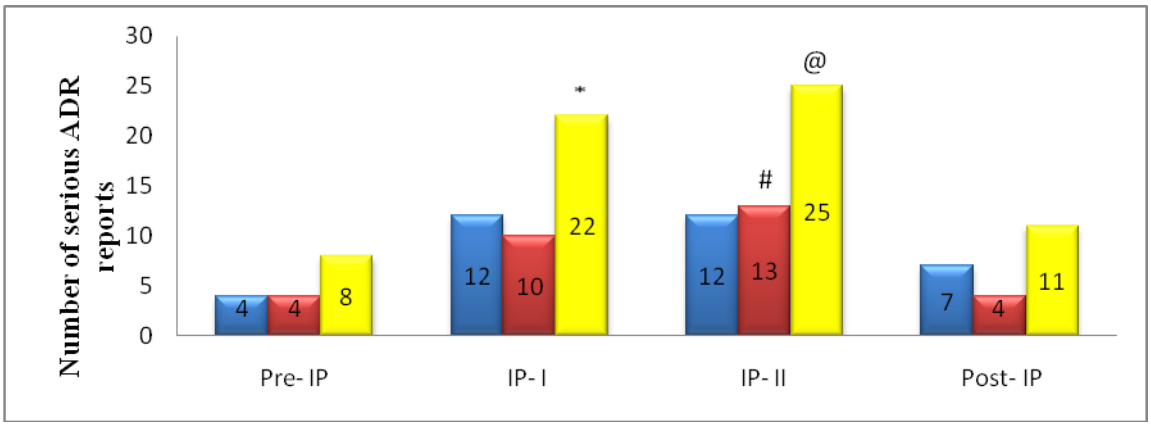

Figure 5: Impact of educational interventions on mean completeness score of ADR reports by prescribers (n = 169)

Group A - poster, pharmacovigilance programme, SMS and personal communication;
Group B - poster, pharmacovigilance programme, emails and information leaflet
Statistical analysis by Student's paired and unpaired "t" test; *p= 0.006 Completeness score of ADR reports during IP- I of Group A as compared to Group B; # p= 0.0003 Completeness score of ADR reports during IP- II as compared to Pre- IP; @ p = 0.0009 Completeness scores of ADR reports during IP- II of Group A as compared to Group B; !p = 0.03 Completeness score of ADR reports of Group A during IP- II as compared to Pre- IP; Data are expressed as mean ± SD

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