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Original Article

A Qualitative Study of Published Case Reports of Adverse Drug Reactions

Rajesh Kumar G[1*], Manikandan[1], Kavitha V[1], Soundarapandian[1], Ramachandra Bhat C[1], Stalin C[2]

[1]Department of Pharmacology; [2]Senior Pharmacovigilance Associate (PVPI), Adverse events Monitoring Centre, Govt Kilpauk Medical College, Chennai-10.

ABSTRACT

Background: *To study whether the case reports published in the past and present are meaningful and useful, this study was undertaken. Case reports about adverse drug reactions published in the journals were randomly selected and analyzed by using a questionnaire.* ***Methods:*** *Twenty Case reports reporting the adverse effects to drugs were selected from different journals. They were thoroughly analysed for their completeness, reason for publication, quality of presentation and ability to highlight the main features to the readers. Salient features mentioned in the case reports were noted.* ***Results:*** *Most of the case reports were the reports of rare ADRs. Most of them adequately described the onset of ADR, dechallenge result and application of causality assessment scales. Areas needing improvement in writing case reports have been identified in this study.* ***Conclusion:*** *Most rare ADRs reported as case reports have to be followed up further to identify any potential signal by pharmacovigilance staff. Case reports can follow a common format which includes the critical aspects like causality assessment, mechanism of ADR, treatment of ADR, dose which causes the ADR, review of relevant literature, details of reporting to nearby Pharmacovigilance centre, PVPI report number, photos wherever applicable, reason for publication and known or new nature of the ADR, and future recommendations by the author of the case report.*

Keywords: *Case Reports, Pharmacovigilance, Adverse Drug Reactions.*

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Corresponding Author

Dr. Rajesh Kumar
Assistant Professor,
Department of Pharmacology,
Govt Kilpauk Medical College,
Chennai-10.
Mail ID: grkumar.ich@gmail.com

INTRODUCTION

Medical literature mainly consists of reputed indexed journals, non-indexed journals and recently edited textbooks. Case reports are published in most of the journals. They include interesting case presentations, novel diagnostic aspects and clinical presentations of rare diseases besides adverse drug effects. Adverse drug effects reported as case reports draw the attention of many medical practitioners. It is a type of Pharmacovigilance activity. In this regard, it is to be ensured that the case reports are properly presented so as to enable to convey the right interpretation on the part of the readers. To study whether the case reports published in the past and present are meaningful and useful, this study was undertaken. Case reports published in the journals were randomly selected and analysed using a questionnaire.

METHODS

Twenty Case reports reporting the adverse effects to drugs were selected from different journals. They were thoroughly analysed using a questionnaire (Table-1) for their completeness, reason for publication, presentation quality and ability to highlight the main features to the readers. Salient features mentioned in the case reports were noted.

RESULTS

Selected case reports were found to be published during the years ranging from 1995 to 2017.They reported ADRs pertaining to the following drugs:

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Ticlopidine, Ciprofloxacin, Carbamazepine, Dapsone, Celecoxib, Topiramate, Fluorouracil, Venlafaxine, Cefotaxime, Fluconazole, Clozapine, Olanzapine, Lithium, Phenytoin, Piroxicam, Ibuprofen, Isotretinoin, Etoricoxib, Montelukast, Oxcarbazepine

Table 1. Questionnaire used

1. Reason for reporting the case?
2. Is causality assessment done?
3. Whether Dechallenge was done?
4. Degree of ADR?
5. Route of administration?
6. Seriousness of the ADR?
7. Therapeutic dose or Toxic dose?
8. Duration of ADR
9. Age group involved?
10. Suspected drug?
11. PK reaction or PD reaction?
12. Whether Rechallenge was tried?
13. Acute use of the drug or chronic use of the drug?
14. Whether earlier reports were discussed?
15. Use of WHO scale or NARANJO scale?
16. Reported to PVPI?
17. Photos related to ADR'S were attached?
18. Outcome of treatment mentioned?
19. Concomitant drug mentioned?
20. Whether future recommendations given?

Table 2. The ADRs caused by the above drugs are shown as Drug-ADR pairs

DRUGS	ADVERSE REACTION
Ticlopidine	Agranulocytosis
Ciprofloxacin	Bradycardia
Carbamazepine	Erythema
Dapsone	Blood dyscrasia
Celecoxib	Edema
Topiramate	Ocular ADRs
Flurouracil	Encephalopathy
Venlafaxine	Akathisia
Cefotaxime	Near fatal anaphylaxis
Fluconazole	Fixed drug eruption
Clozapine	Akathisia
Olanzapine	Restless leg syndrome
Lithium	Persistent cerebellar dysfunction
Phenytoin	Adenoma
Phenytoin	Seizures
Piroxicam	Pustulosis
Ibuprofen	Nephritis
Isotretinoin	Myopathy
Etoricoxib	Epidermal necrolysis
Oxcarbazepine	Epidermal necrolysis

Most of the case reports were the reports of rare ADRs. Most of them adequately described the onset of ADR, dechallenge results and application of causality assessment scales.

Following features were noted on close study of the case reports and is shown in Figure 1.

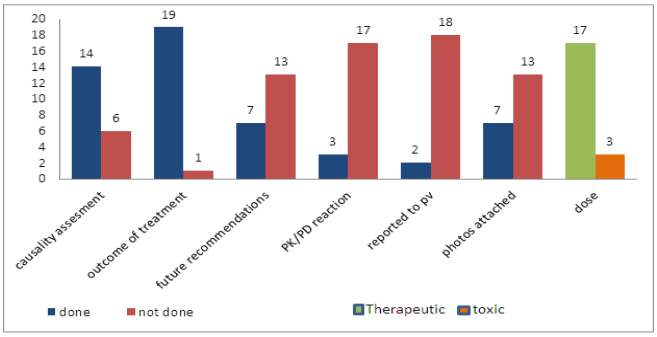

Fig 1: Features noted on close study of the case reports

Causation was adequately analysed in many reports (70%). Uniform format was not followed in many case reports. Treatment of ADRs wasnot described in many case reports. Toxic dose effects instead of ADRs to therapeutic dose range were included in three case reports. That the ADR was due to toxic dose and not routine dose was not highlighted. Review of relevant literature was found wanting in many case reports. Reporting to pharmacovigilance centre was found only in two reports. i.e in recently published case reports. Pvpi number was mentioned in only one case report. i.e in recently published case report. Photos were given only in seven reports. New ADR was given in one case report. Future recommendations were given only in seven out of twenty case reports. Nature of reaction viz pharmacokinetic /pharmacodynamics was discussed only in three out of twenty case reports. However, causality assessment scale was used in 14 reports out of 20 case reports. Type of Causality assessment scale used is shown in Figure-2.

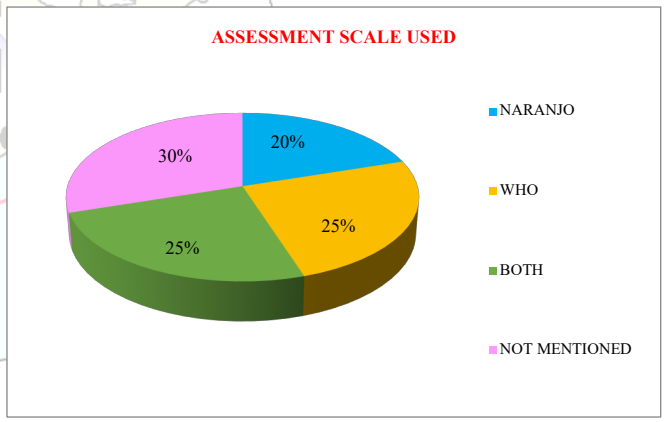

Fig 2: Outcome of treatment of adverse effects was mentioned in 19 case reports out of 20 case reports.

DISCUSSION

Case reports form a good source for pharmacovigilance. They could yield good signals too. This was examined in a study earlier which found case reports are not followed up further and they don't end in any signal or information change in the drug literature.[1]

Hence, there is always a need for proper follow up of any case report or case series. This is more important as these case reports throw light on rarer adverse effects unlike clinical trials.[2]

In an earlier analysis of case reports, need for improvement in the manner of case reporting has been stressed to make the reports more meaningful for the readers.[3]

In another study, it was found that case reports formed the basis of regulatory actions in a number of instances.[4]

In yet another unique study of case reports, more steps to prevent ADR s have been recognized viz dosing care, tailoring therapy for elderly in a special manner, taking family history and past ADR history.[5]

Considering the importance of utility and importance of case reports, guidelines on reporting adverse drug effects as case reports have been developed. But, these are not yet popularly disseminated.[6]

Proper way of reporting case reports, their review by reviewers and editors' considerations are also brought out in another interesting article.

It seems there is an urgent need to develop a format for case reports of adverse drug effects. This is specifically obvious in this study of case reports also. Most of the case reports were in individual styles and not following any common format. This issue has to be addressed fresh by editors of various journals. At the same time, case reports have to necessarily mention some aspects of the ADRs, in keeping tune with the modern advancements, especially in pharmacovigilance field.

CONCLUSION

Most rare ADRs reported as case reports have to be followed up further to identify any potential signal by pharmacovigilance staff. Case reports can follow a common format which includes the critical aspects like causality assessment, mechanism of ADR, treatment of ADR, dose which causes the ADR, review of relevant literature, details of reporting to nearby pharmacovigilance centre, Pvpi report number, photos wherever applicable, reason for publication and known or new nature of the ADR, and future recommendations by the author of the case report.

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