RESEARCH ARTICLE

An analytical quantification clinical research, and an observational descriptive qualitative pharmacological research analysis on pharmacovigilance assessments of metformin monotherapy and combination therapies: A mixed-method study

Moumita Hazra

Department of Pharmacology, Mamata Medical College and Hospitals, Khammam, Telangana, India

Correspondence to: Moumita Hazra, E-mail: drmoumitahazra.198017thjune@gmail.com

Received: March 22, 2022; Accepted: May 18, 2022

ABSTRACT

Background: The anti-diabetic mono- as well as combination pharmacotherapy with metformin, for the routine healthcare treatment of type II diabetic patients, is sufficiently efficacious, with an adequately safe glycemic stabilization rate. This pharmacotherapeutic property of metformin has resulted in metformin being a widely used first-line oral hypoglycemic drug, among different types of diabetic patients. Aims and Objectives: The objective of this mixed-method research study was an analytical quantification clinical research, and an observational descriptive qualitative pharmacological research analysis, on the pharmacovigilance assessments of metformin. Materials and Methods: This study procedure was a multivariate, observational, descriptive, retrospective, qualitative, pharmacological research analysis study, and, a multivariate, multicenter, analytical quantification of global clinical research study literature databases on pharmacovigilance assessments of metformin, among type II anti-diabetic patients. A multivariate evidence-based pharmacological research study was done, for a comparative quantification analysis between the qualitative pharmacovigilance studies on metformin monotherapy and combination therapies, and the quantitative pharmacovigilance studies on metformin monotherapy and combination therapies, conducted within a span of the past 5 years. This study was conducted, by recording, calculating, statistically deriving the percentage of the differential quantitative analysis, retrieved from the medical study literature database, along with a statistical interpretative analysis and the subsequent graphical representation of the deduced study results. Results: In this mixed method quantitative and qualitative research study, it was deduced from these study results, that slightly more qualitative pharmacovigilance assessment studies, that is 53%, were conducted on metformin monotherapy and combination therapies, than quantitative pharmacovigilance assessment studies, that is 47%, on metformin monotherapy and combination therapies; and both were analyzed with evidence-based details. Conclusion: This research study provided a comprehensive pharmacovigilance assessment of metformin monotherapy and combination therapies.

KEY WORDS: Metformin; Pharmacology; Clinical Research; Pharmacovigilance

INTRODUCTION

The anti-diabetic mono- as well as combination pharmacotherapy with metformin, for the routine healthcare treatment of type II diabetic patients, is sufficiently efficacious, with an adequately safe glycemic stabilization rate. This pharmacotherapeutic property of metformin
has resulted in metformin being a widely used first-line oral hypoglycemic drug, among different types of diabetic patients.

Pharmacovigilance assessments are conducted for assessing, continuous monitoring, preventing as well as treating the occurrence of any manifested adverse drug reaction. In accordance with the World Health Organization Global Benchmarking Tool, the global pharmacovigilance systems range from being suboptimal to highly effective resource-optimized systems. This pharmacovigilance appraisal of different and wide-ranged clinical research studies on metformin was performed, for a better comprehension of the various intricate pharmacovigilance aspects in regular anti-diabetic mono- and combination therapies prescribed to type II diabetic patients.

Metformin, the oral biguanide hypoglycemic drug, causes gradual overwhelming of insulin resistance and hypoglycemia, by activating the enzyme 5’ adenosine monophosphate, which catalyses the activation of protein kinase. Metformin also stabilizes the HbA1c levels, along with a reduction in weight, among the patients affected with diabetes associated obesity. Metformin also lessen the type II diabetes mellitus associated cardiovascular and neuropathological co-morbidities, and malignancies, and also enhances the blood glucose stabilized life-span among these patients. Even among critically ill hospitalized type II diabetic patients, metformin reduces their mortality rate.1-[5]

There is ample pharmacologically oriented clinical research on the oral hypoglycemic drug, metformin and the several pharmacovigilance perspectives of metformin. To further supplement these clinical research studies, with an emphasis on the qualitative and quantitative interpretations of the pharmacovigilance aspects of metformin, this research study was conducted.

The objective of this mixed-method research study was an analytical quantification clinical research, and an observational descriptive qualitative pharmacological research analysis, on the pharmacovigilance assessments of metformin.

**MATERIALS AND METHODS**

**Ethical Approval**

The study did not involve any human or animal subjects; therefore, it did not require any ethical approval, and could be exempted from ethics review. Yet, the ethical approval was obtained, to initiate the study with a confirmed ethical review.

At first, the Institutional Ethics Committee clearance and approval was taken for conducting this study. The study was conducted in accordance with the ethical principles of Declaration of Helsinki and Good Clinical Practices contained within the International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH-E6 and ICH-E17), and in compliance with the global regulatory requirements.

**Study Type**

This mixed method study type consisted of a multivariate, observational, descriptive, retrospective, qualitative, pharmacological research analysis study, and, a multivariate, multicenter, analytical quantification of global clinical research study literature databases on pharmacovigilance assessments of metformin, among type II anti-diabetic patients.

**Study Population**

The study population was global type II anti-diabetic patients, and the pharmacological clinical research database was the global heterogenous research analyses and similar study literature on the pharmacovigilance assessments of metformin.

**Study Period**

The study period for this research project and the compilation of the study literature was 1 year, from February 2021 to April 2022.

**Place of Study**

This research study and the compilation of the study literature were conducted in the Departments of Pharmacology, Clinical Pharmacology, Molecular Pharmacology, Rational Pharmacotherapeutics, Pharmacoepidemiology, Pharmacovigilance, Pharmacogenomics, Evidence-Based Medicine, Clinical Pathology, Molecular Diagnostics, Medical and Reproductive Endocrinology and Diabetology, Clinical Medicine and Clinical Research, at Dr. Moumita Hazra’s Polyclinic And Diagnostic Centre, Hazra Nursing Home, Hazra Polyclinic and Diagnostic Centre, Rama Medical College Hospital and Research Centre, Rama University, and Mamata Medical College and Hospitals.

**Study Procedure**

This study procedure was a was a multivariate, observational, descriptive, retrospective, qualitative, pharmacological research analysis study, and, a multivariate, multicenter, analytical quantification of global clinical research study literature databases on pharmacovigilance assessments of metformin, among type II anti-diabetic patients. A qualitative multivariate analysis of the retrieved study literature derived from a thorough pharmacological clinical
A mixed-method quantitative and qualitative research study on pharmacovigilance assessments of metformin

Research study literature database search from various available research study literature databases was performed, to record, thoroughly analyze and explore the various pharmacovigilance aspects of metformin monotherapy and combination therapy in the treatment of global type II diabetic patients. This pharmacovigilance analytical assessment was performed from a wide-ranged medical study literature containing pharmacovigilance researches, reviews, case studies, experimental databases, systematic reviews, meta-analyses, and varied similar pharmacological research databases about the different aspects of pharmacovigilance evaluations of metformin.

After that, a multivariate evidence-based pharmacological research study was done, for a comparative quantification analysis between the qualitative pharmacovigilance studies on metformin monotherapy and combination therapies, and the quantitative pharmacovigilance studies on metformin monotherapy and combination therapies, conducted within a span of the last 5 years. This study was conducted, by recording, calculating, statistically deriving the percentage of the differential quantitative analysis, retrieved from the medical study literature database, along with a statistical interpretative analysis and the subsequent graphical representation of the deduced study results.

To elaborate the study procedure, at first, based on the exploratory topic, the relevant medical research study literature was identified through database searching. Apart from these, the additional medical research study literature was identified through other sources. Then, any or all types of original research studies, systematic reviews, meta-analyses, case reports, case series, narrative reviews, study series, parallel studies and similar kind of studies or reviews, which are either qualitative, or quantitative, or both qualitative as well as quantitative, in their description of the investigative topic, were thoroughly analyzed, with statistical interpretations. The studies which were both qualitative as well as quantitative, were included within the qualitative studies or within the quantitative studies, based on their greater inclination of the analytical expanse toward either qualitative or quantitative studies. After examining the relevance of the full articles, the medical data and evidences were independently obtained, using forms containing different determinant criteria of analyses, based on well-defined objectives, which were subsequently reviewed, to refine the medical databases and evidences, after elaborate multidirectional processing of medical study literature database. After that, the medical research study literature was screened, and the studies which were not appropriate and relevant according to the investigative topic, were removed. Then the selected studies were included and thoroughly analyzed, for the final analytical quantification clinical research on pharmacovigilance assessments of metformin. The medical data and evidences were extracted from the study resources, of heterogenous qualitative or quantitative nature, or both.

Studies with any or all types of study characteristics and outcomes were obtained to derive the pertinent descriptive or analytical study literature, and subsequently the exploratory and experimental elucidations were undertaken for qualitative elaboration, from the comprehensive review compilation of the published articles, to corroborate the analytical quantification clinical research on the pharmacovigilance assessments of metformin, from the refined clinical research study literature, databases and evidences on the analytical topic, which finally directed itself towards a well-structured comprehensive research interpretation of the overall study results, for the final analyses and interpretations, ultimately to deduce the final specific conclusion.

Statistical Analysis

The quantitative study findings were statistically evaluated and represented as percentage derivations, with subsequent graphical illustration of the deduced study results.

RESULTS

The comparative analytical quantification clinical research between the qualitative pharmacovigilance assessment studies on metformin monotherapy and combination therapies, and the quantitative pharmacovigilance assessment studies on metformin monotherapy and combination therapies conducted, gave the following study results:

The percentage of qualitative pharmacovigilance assessment studies on metformin monotherapy and combination therapies conducted was 53%, and the percentage of quantitative pharmacovigilance assessment studies on metformin monotherapy and combination therapies conducted was 47%, as depicted in Figure 1. Thus, it was deduced from these study results, that slightly more qualitative pharmacovigilance assessment studies were conducted on metformin monotherapy and combination therapies, than quantitative pharmacovigilance assessment studies on metformin monotherapy and combination therapies; and both were analyzed with evidence-based details, hence
elaborating the various aspects of pharmacovigilance, as observed and pharmacotherapeutically managed in routine type II anti-diabetic treatment with metformin monotherapy and combination therapies.

Exploratory and experimental elucidations derived from the observational descriptive qualitative pharmacological research analysis on pharmacovigilance assessments of metformin monotherapy and combination therapies:

From the analytical compilation of pharmacotherapeutic databases and evidences, the exploratory and experimental elucidations derived from the observational descriptive qualitative pharmacological research analysis on pharmacovigilance assessments of metformin monotherapy and combination therapies were also described, in details, to substantiate, elaborate, clarify, and complete the quantitative and qualitative details of the conducted mixed-method research study.

DISCUSSION

From this research study, it was obtained that the percentage of qualitative pharmacovigilance assessment studies on metformin monotherapy and combination therapies conducted was 53%, and the percentage of quantitative pharmacovigilance assessment studies on metformin monotherapy and combination therapies conducted was 47%. Thus, it was deduced from these study results, that slightly more qualitative pharmacovigilance assessment studies were conducted on metformin monotherapy and combination therapies, than quantitative pharmacovigilance assessment studies on metformin monotherapy and combination therapies; and both were analyzed with evidence-based details, hence elaborating the various aspects of pharmacovigilance, as observed and pharmacotherapeutically managed in routine type II anti-diabetic treatment with metformin monotherapy and combination therapies.

The exploratory and experimental elucidations and comparative analyses on the oral hypoglycemic pharmacovigilance assessments research on metformin monotherapy and combination therapies were as following:

Metformin has pleiotropic pharmacological actions, other than its main hypoglycemic effects, in treating type II diabetes mellitus. A variety of research studies had been undertaken in different clinical environments as well as with the experimental animal models to explore the innumerous beneficial effects of metformin.

Pharmacovigilance standardization guidelines are in accordance with the International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH) and the Council for International Organizations of Medical Sciences. Any valid regulatory adverse drug reactions Individual Case Safety Report (ICSR) must minimally include the criteria (ICH E2D guidance), that the reporter must be identifiable, there must be a single patient who is identifiable, there must also be a suspect medicinal product, which manifests a suspect adverse drug reaction. The national regulatory authorities members of the WHO Programme for International Drug Monitoring can appraise the national pharmacovigilance database at the online VigiFlow system initiated by the Uppsala Monitoring Center (UMC), the WHO-associated center for international drug monitoring. This can later be forwarded to the global pharmacovigilance database system, the VigiBase. VigiBase functioning also includes an UMC provided advanced online analytic tool, VigiLyze, through which foreign ICSRs can also be observed. Periodic safety reports, like, the European Union (EU) Periodic Safety Update Report gives a review on the present benefit–risk profile of any medicinal product. Multi-dimensional global pharmacovigilance data including safety, efficacy, and effectiveness data; data on the use of the medicinal product for authorized and non-authorized, “off-label” indications; and the data that are missing, like, the data in special populations, are also available in the Periodic Safety Update Report. For the Periodic Benefit Risk Evaluation Report, within minimum possible time-span, it is recommended that the reporting can be done for 15 calendar days for serious ICSRs as per ICH E2D guidance, and for 90 calendar days for non-serious ICSRs as per EU good vigilance practice.

In a study, in which type II diabetic patients received either metformin alone, remogliflozin alone, or both as combination therapy, over 3 day treatment periods, separated by two non-treatment intervals of variable duration, it was found that concomitant administration of metformin and remogliflozin was well tolerated with minimal hypoglycemia, and no serious adverse events and no increase in lactic acid occurred. This safety analysis of the anti-diabetic drugs emphasizes the conclusion that the administration of metformin, as a monotherapy or as a combination therapy with remogliflozin showed rational pharmacovigilance results for anti-diabetic treatment with metformin monotherapy and combination therapy.

Another study on the glycemic efficacy and safety of sitagliptin initiation during metformin dose-escalation within type II diabetic patients not at glycated hemoglobin levels on sub-maximal metformin doses, showed that there was improvement in the glycemic response and HbA1c levels, with similar safety and tolerability, compared to metformin monotherapy.[1-5]

This observational descriptive qualitative pharmacological research analysis and the analytical quantification clinical research on pharmacovigilance assessments of metformin had the merits that the research was conducted with a
well-organized and meticulous quantitative systematized methodology, along with detailed qualitative analytical explanations of the medical study literature and evidences, compiled from the different analyzed studies. This comprehensively substantiated the research question of this study, regarding the pharmacovigilance assessments on metformin monotherapy and combination therapies. This mixed method quantitative and qualitative research study also provided a convenient and comprehensible methodology for the conclusive derivation and descriptive analysis, while intensifying the entire research study within a compact time-frame. This study had no limitations.

Therefore, this mixed method quantitative and qualitative research study provided a comparative quantification between the different assessment methods of pharmacovigilance assessment of metformin monotherapy and combination therapies, with well-comprehensive elaborations and interpretations, resulting in a significant progress toward research innovations in pharmacovigilance assessments of metformin monotherapy and combination therapy, as well as causing improvisation in the anti-diabetic pharmacotherapeutic modalities, for an efficacious and safe glycemic stabilization among global type II anti-diabetic patients.

CONCLUSION

Therefore, in this mixed method quantitative and qualitative research study, it was deduced from these study results, that slightly more qualitative pharmacovigilance assessment studies, that is 53%, were conducted on metformin monotherapy and combination therapies, than quantitative pharmacovigilance assessment studies, that is 47%, on metformin monotherapy and combination therapies; and both were analyzed with evidence-based details, therefore, providing a comprehensive pharmacovigilance assessment of metformin monotherapy and combination therapies.

ACKNOWLEDGMENTS

My gratitude to the Departments of Pharmacology, Clinical Pharmacology, Molecular Pharmacology, Rational Pharmacotherapeutics, Pharmacoepidemiology, Pharmacovigilance, Pharmacogenomics, Evidence-Based Medicine, Clinical Pathology, Molecular Diagnostics, Medical and Reproductive Endocrinology and Diabetology, Clinical Medicine and Clinical Research, at Dr. Moumita Hazra’s Polyclinic And Diagnostic Centre, Hazra Nursing Home, Hazra Polyclinic And Diagnostic Centre, Rama Medical College Hospital and Research Centre, Rama University, Mamata Medical College and Hospitals, and electronic medical study literature databases, for the successful completion of this research project.

REFERENCES


How to cite this article: Hazra M. An analytical quantification clinical research, and an observational descriptive qualitative pharmacological research analysis on pharmacovigilance assessments of metformin monotherapy and combination therapies: A mixed-method study. Natl J Physiol Pharm Pharmacol 2022;12(07):984-988.

Source of Support: Nil, Conflict of Interest: None declared.