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Assessment Of Frequency Of Hypoglycemia Due To Metformin Therapy In Patients With Type-2 Diabetes Mellitus, Polycystic Ovarian Disease: A Prospective Observational Study.

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ABSTRACT

To evaluate the incidence of hypoglycaemia in metformin users in diabetic and PCOD patients. Patients with Diabetes who are taking metformin alone(n=160) and polycystic ovarian disease, who are euglycemic taking metformin (n=160) are recruited for the study. They were given a questionnaire regarding hypoglycaemic symptoms. They were asked to fill the questionnaire based on the symptoms they experienced while taking metformin. Data were collected and analysed by using descriptive analysis, severity assessment and WHO causality assessment scale. PCOD patients taking metformin showed higher occurrence of hypoglycaemic symptoms than Diabetic patients, whereas severity of hypoglycaemia was more in Diabetic patients. This study provided evidence that metformin causes hypoglycaemia irrespective of the glycaemic status of the patients.

Keywords: Hypoglycaemia, Metformin, Diabetes, Polycystic Ovarian Disease.

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INTRODUCTION

Hypoglycaemia is the one of the most important adverse effects of anti-diabetic drugs. It can cause severe morbidity and even sudden death. It is a true medical emergency which require immediate recognition and treatment to prevent vital organ damage [1].

The symptom depends on the severity and duration of hypoglycaemia like behaviour changes, neurological damage, cardiovascular complication leading to seizure or coma [1].

The immediate response to hypoglycaemia is decrease in insulin secretion followed by increased release of glucagon and epinephrine causing increase glucose production and hyperglycaemia [1, 2].

Frequent bouts of hypoglycaemia cause decrease release of glucagon and epinephrine leading to Hypoglycaemia Associated Autonomic Failure (HAAF). This causes a clinical syndrome of defective glucose counter-regulation and unawareness of hypoglycaemia due to attenuation of autonomic response which leads to vicious cycle of recurrent hypoglycaemia [1, 3, 4].

Metformin, a biguanide, synthetic derivative of plant *Galega officinalis* [5] is the most commonly used oral hypoglycaemic agent to treat type-II diabetes, as the first line treatment [6], as monotherapy and in combination for type II diabetes [7].

Metformin has been shown to delay the progression of diabetes in patients with impaired glucose tolerance [7, 8].

Metformin is also used in the treatment of polycystic ovarian disease, for treatment of infertility as it improves ovulation and regulates menstrual cycle by reducing circulating androgens [7, 9, 10].

The major mechanism of metformin is by reducing hepatic glucose production and increasing peripheral glucose uptake by activating AMP dependent protein kinase (AMP Kinase) [7, 11].

Metformin does not affect insulin release [11]. Therefore, it has been claimed to cause less hypoglycaemia [7] which varied between 0% to 21% only [12]. Strenuous physical activity or fasting increases the risk of hypoglycaemia [12]. Metformin has little effect on blood glucose level in normoglycemic state [7,13].

Incidence of hypoglycaemia caused by metformin in type II diabetes and polycystic ovarian disease patient has not been documented so far, even though many patients experience the effect of hypoglycaemia which affects the quality of life.

Therefore, we conducted an observational study to find out the exact incidence of hypoglycaemia among users of metformin in type-II diabetes and polycystic ovarian disease.

METHODOLOGY

This study was done to assess the occurrence of hypoglycaemia in patients receiving metformin in type-II diabetes and polycystic ovarian disease patients.

Study Design

This was a prospective observational study done in two groups of patients attending as outpatient receiving metformin.

Study Centre

Patients who are attending the Department of Diabetology, Rajiv Gandhi Govt. General Hospital, Chennai, Institute of Obstetrics and Gynaecology, Chennai and RSRM lying in Hospital, Chennai.

Study Duration

This study was carried out for 7 months.

Study Subjects

Patients attending diabetic OPD of RGGH and gynaecology OPD of IOG, RSRM, Chennai.

Sample Size

Sample size was 320. Patients in each group -160.

Selection Criteria

Inclusion Criteria

- Age between 18- 80 years
- Patients of both genders
- Patients who are willing to participate in the study
- Patients who have type-2 diabetes mellitus taking metformin alone for more than one month with no other illness
- Patients who are taking metformin for more than one month for PCOD with normal blood glucose level and no other illness

Exclusion Criteria

- Patients who are taking other anti-diabetic drugs along with metformin.
- Patients who are taking other medications for polycystic ovarian disease.
- Patients having PCOD with increased blood glucose level.

Study Procedure

Study was started after obtaining the approval and clearance from institutional ethical committee (No. 23042013). Informed consent and information sheet written in the regional language was shown to each patient and who are willing to participate in the study, consent obtained from each patient.

Questionnaire regarding hypoglycaemic symptoms was prepared in regional language was given to the patients and asked to fill the columns.

Evaluation

The collected data were analysed by WHO causality assessment scale and ADR severity assessment was done.

OBSERVATION AND RESULTS

Total of 320 patients were enrolled, and 160 in each group were analysed. Descriptive statistics were used for data analysis.

DISCUSSION

The incidence and severity of hypoglycaemia due to metformin has been assessed in two groups of patients namely type-2 Diabetes mellitus and PCOD with normal blood sugar level.

In type-II Diabetes, 94% patients reported symptoms of hypoglycaemia whereas 6% doesn't have any symptoms of hypoglycaemia. Around 38% had mild, 43% had moderate and 19% had severe degree of hypoglycaemia.

In patients with polycystic ovarian disease, 98% of patients had symptoms of hypoglycaemia. out of which 66% had mild,33% had moderate and 3% had severe degree of hypoglycaemia.

The standard textbooks say that metformin monotherapy does not cause hypoglycaemia [13] in euglycemic patients. Hypoglycaemia due to metformin was reported only in association with strenuous physical activity and fasting [12]. In this study the incidence of hypoglycaemia was more in euglycemic patients (PCOD patients) under normal condition than in type-II diabetes.

The severity of hypoglycaemia was more in type-II diabetes (19%) than in PCOD patients (3%). Recurrent attacks of hypoglycaemia can cause severe morbidity and even death due to myocardial infarction or cerebrovascular disease [1]. Therefore, the physicians and the patients should be aware of this adverse effect while using oral hypoglycaemic agents.

From this study, we have found that metformin causes hypoglycaemia irrespective of glycaemic state of the individual, which should be documented in standard textbooks and the patients should be informed about the symptoms of hypoglycaemia whenever metformin is prescribed.

CONCLUSION

From this observational study, we have concluded that metformin causes various degrees of hypoglycaemia in both diabetic and euglycemic (PCOD) patients.

Hypoglycaemia is one of the most important causes of sudden death, frequent attacks of hypoglycaemia can worsen the health condition despite of treatment.

Therefore, awareness should be created regarding the consequences of recurrent attacks of hypoglycaemia among the physicians and patients.

Hypoglycaemia can be prevented by life style modification, timely food and early recognition of symptoms while using metformin.

REFERENCES

[1] Gita Shafiee, Mohammadreza Mohajeri-Tehrani, Mohammad Pajouhi and Bagher Larijani: The importance of hypoglycaemia in diabetic patients, Journal of Diabetes & Metabolic Disorders 2012;17:1- 7.
[2] Cryer PE: Hypoglycaemia, functional brain failure, and brain death Clin Invest 2007;117:868-870.
[3] Cryer PE: Diverse causes of hypoglycaemia-associated autonomic failure in diabetes Engl J Med 2004;350:2272-2279.
[4] Dagogo-Jack SE, Craft S, Cryer PE: Hypoglycaemia-associated autonomic failure in insulin-dependent diabetes. Recent antecedent hypoglycaemia reduces autonomic responses to, symptoms of, and defence against subsequent hypoglycaemia Clin Invest 1993; 91: 819-828
[5] Stephanie A.Amiel and Melanie J.Davies: Oxford Textbook of endocrinology and Diabetes 2nd edition, page no 1783.
[6] Jolien de Jager, Adriaan Kooy, Phillppe Lehert, Michiel G Wulffele, Jan van der Kolk, Daniel Bets, Joop Verburg, Ab J M Donker, Coen D A Stehouwer: Long term treatment with metformin in patients with type 2 diabetes and risk of vitamin B-12 deficiency: randomized placebo controlled trial: BMJ 2010:340:c2181 page1-7
[7] Brunton LL, Chabner BA, and Knollmann BC, Goodman and Gilman's The Pharmacological Basis of Therapeutics, 12 th Edition page no-1258
[8] Diabetes Prevention Program Research Group: Reduction In The Incidence Of Type 2 Diabetes With Lifestyle Intervention Or Metformin. N Engl J Med 346(6):393-403.
[9] Tahira Dar, Sidra Batool, Khawaja Tahir Mahmood, Fatima Amin: Benefits of Metformin in Polycystic Ovarian Syndrome. International Journal of Pharmaceutical Sciences 2011;3 (1):118-124.
[10] BB Tripathy: Research society for the study of Diabetes in India (RSSDI) Text book of DIABETES MELLITUS 2nd edition page no-531.
[11] K D TRIPATHI: Essentials of Medical Pharmacology, 7th Edition, page no-275.

[12] Bodmer M, Meier C, Krahenbuhl S, jick SS, Meier CR: Metformin, sulfonylureas, or other antidiabetic Drugs and the risk of lactic acidosis or hypoglycaemia. Diabetes Care 2008;31(11):2086-2091.
[13] Joslin's Diabetes Mellites 14th Edition page no 698-699.
[14] Richard S Surwit, Mark S Schneider, Mark N Feinglos: Stress and Diabetes Mellitus: Diabetic Care 1992;15 (10):1413-1421.
[15] PG Sundararaman, Shweta, GR Sridhar: Psychosocial Aspects of Women with Polycystic Ovary Syndrome from South India: JAPI 2008;56:945-948.