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IMPACT OF METFORMIN AMONG PREDIABETIC PATIENTS WITH ISCHEMIC HEART DISEASE

Medicine

Dr. Lakhan Kumar* Resident Department Of Medicine , Saraswathi Institute Of Medical Sciences, Hapur. *Corresponding Author

Dr. Anil Kem Prof & HOD Department Of Medicine , Saraswathi Institute Of Medical Sciences, Hapur.

Dr. Subhash Chandra Jha

ABSTRACT

Prediabetes is an intermediate metabolic state between normoglycemia and diabetes. 1 Pre- diabetes includes patients with impaired glucose tolerance and impaired fasting glucose and hemoglobin A1c (HbA1c) values between 5.7% and 6.5% (49–56 mmol/mol).Metformin, in addi- tion to its hypoglycemic effects, appears to have a preventive impact on coronary arteries, according to growing research.Present randomised clinical trials was conducted to know the impact of Metformin among prediabetic patients.

KEYWORDS

INTRODUCTION

Prediabetes is an intermediate metabolic state between normoglycemia and diabetes [1] Prediabetes includes patients with impaired glucose tolerance and impaired fasting glucose and haemoglobin A1c (HbA1c) values between 5.7% and 6.5% (49–56 mmol/mol)[1]

With the global burden of coronary artery disease (CAD) rising, early detection and treatment of risk factors are crucial to lower morbidity and mortality in these patients. [2]

Diabetes mellitus (DM) is a known risk factor for coronary artery disease (CAD) [3] Metformin, an anti-diabetic medicine, has been proven to reduce cardiovascular events in diabetes individuals in preclinical and clinical investigations. [4,5]

Metformin, in addition to its hypoglycemic effects, appears to have a preventive impact on coronary arteries, according to growing research. [5]

Metformin is an alternative/additional treatment option for primary and secondary prevention of CAD in diabetics and non-diabetics alike, due to its global availability, method of administration, and cost.

Although clinical trials conducted on diabetic patients clearly demonstrated the therapeutic potential of metformin in reducing cardiovascular mortality and morbidity in DM patients [4], their beneficial effects in non-diabetic patients remain unclear.Present randomised clinical trials was conducted to know the impact of Metformin among prediabetic patients.

Objectives:

1. To determine the impact of metformin in terms of their survival rate.
2. To study effect of metformin to maintain inflammatory markers in blood.

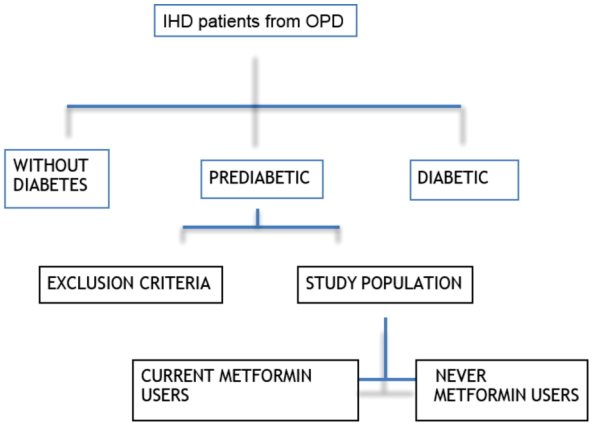
METHODOLOGY:

- Current cohort was conducted among known of IHD patients in department of Medicine, From Sep 2020 to Sep 2021, we have screened patients using WHO criteria to lable patient as prediabetic.
- The World Health Organization (WHO) has defined prediabetes as a state of intermediate hyperglycemia using two specific parameters, impaired fasting glucose (IFG) defined as fasting plasma glucose (FPG) of 6.1-6.9 mmol/L (110 to 125 mg/dL). [6]

Exclusion Criteria:

1. Patients with no coronary disease detected by left ventricular ejection fraction <50%, previous myocardial infarction, previous percutaneous coronary intervention and/or coronary bypass grafting, Takotsubo cardiomyopathy, myocarditis, pregnancy, impaired renal function, or stroke.
2. Patients treated with metformin for <6 months were instead excluded from the study. Information on the duration of treatment was available for all current users.

SAMPLE SELECTION:



Furthermore, patients with prediabetes answered a specific questionnaire about metformin treatment before the beginning of the study, the dates of beginning and end of treatment, and the duration of use. Information from the medicine inventory during the study and this specific questionnaire were used to classify the subjects.

- All study participants were assigned in two Groups.
- Group A: The patients with prediabetes who never used metformin were classified as "never metformin users."
- Group B: The patients with prediabetes who had already used metformin were classified as "current metformin users," and they had been treated with metformin for at least 6 months.
- The analyses of echocardiography were performed by the cardiologist, blinded to patient categorization, who reviewed selected cases.
- The study end points were biomarker and the assessment of number of hospitalization at12 months of follow-up.
- All patients were informed about the study nature and gave their written informed and signed consent to participate in the study..

Analysis:

SPSS Statistics, version 23.0 (IBM), was used for all statistical analyses. Categorical variables were presented as number and percentage and continuous variables as mean ± SD. Level of confidence interval and level of significance were consider 95% and 5% set respectively to re- ject null hypothesis to compare quantitative data unpaired test was used, Two-tailed P values <0.05 were considered statistically significant.

RESULT:

- A total of 869 IHD patients were consulted Out patient department of

Medicine between Sept 2020 and Sept 2021. Of these, 187 presented without diabetes, 294 pre- diabetics and 388 with diabetes.
• Among 294 prediabetic patients 46 did not meet inclusion criteria. Therefore, the final study population comprised 248 patients.
• Among patients with prediabetes, 52 were never metformin users (Group A) and 196 were current metformin users (Group B).

Table 1: General Characteristics

Clinical variables	Group A	Group B	P
Age (years)	65.5 ± 5.7	64.9 ± 6.1	n.s.
BMI(kg/m^2)	29.7 ± 1.9	26.5 ± 1.88	n.s.
Systolic blood pressure (mmHg)	132± 10	126 ± 12	n.s.
Diastolic blood pressure (mmHg)	82 ± 6	78± 6	n.s.
Heart rate	86 ± 9	88 ± 8	n.s.

There was no significant difference in both study group in terms of their Age, BMI, Blood pres- sure and heart rate. There is no selection bias or any confounding factor present in any group so, both the groups are statistically comparable for result.

Table 2: Biochemical Measurements

Clinical variables	Group A	Group B	P
HbA_{1c}(%)	6.1 ± 0.54	5.41 ± 0.66	<0.0001
Cholesterol (mmol/L)	5.31 ± 0.5	5.30 ± 0.6	n.s.
HDL (mmol/L)	0.96 ± 0.09	0.95 ± 0.07	n.s.
LDL (mmol/L)	3.42 ± 0.50	3.39 ± 0.48	n.s.
Triglycerides (mmol/L)	2.05 ± 0.25	2.05 ± 0.21	n.s.
Creatinine (µmol/L)	87.1 ± 14.1	88.2 ± 14.3	n.s.

As per Table 2, There was no significant difference in cholesterol, HDL, LDL triglycerides and creatinine among two groups except HbA1c as metformin helps to maintain blood glucose.

Table 3: Inflammatory Marker

Clinical variables	Group A	Group B	P
CRP (mg/L)	3.69 ± 1.72	3.26 ± 0.63	<0.004*
IL1 (pg/dL)	381.8 ± 92.8	318.5 ± 64.2	<0.0001*
IL6 (pg/dL)	262.4 ± 34.2	212.6 ± 22.1	<0.0001*
D-dimer	5.58 ± 0.78	4.46 ± 0.93	<0.0001*
Platelets(10^9/L)	278 ± 24	276 ± 25	n.s.

Table 3 suggests metformin help to control inflammatory markers in blood. There was significant difference found in Mean level of CRP , IL1, IL6 and D-dimer among two groups.

Metformin did no affect platelets count in blood.

Outcome	Survived	Death	Total
Group A	185 (94%)	11(6%)	196
Group B	43(83%)	9(17%)	52
Total	228	20	248

Out of total 196 metformin users, 11 were died due to Ischemic heart related course of death and 185 were survived at 12 month follow up. Among non metformin users, 43 out of 52 were survived. Survival rate is higher among metformin using group (94%) than non metformin users (83%). The difference in their survival found to b statistically Significant at $p < .05$. The chi-square statistic is 7.5819. The p-value is .005896.

CONCLUSION:

- In prediabetic patients metformin helps to decrease risk of conversion from prediabetic stage to diabetic by maintaining HbA1c.
- Metformin therapy reduces Morbidity and mortality among prediabetic CAD patients. Metformin may reduce high risk of cardiovascular events in pre-DM patients by reducing coronary endothelial dysfunction by controlling CRP level, IL1, IL6, D-dimer.

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