Research Article

Medication Adherence and Clinical Outcomes towards Oral Hypoglycemic Agents among Type II Diabetic Cohort

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ABSTRACT

Introduction: Clinical outcomes are measurable clinical parameter which predicts the glycemic control of the disease. Poor adherence to oral hypoglycemic agents remains as one of the main reasons for poor metabolic control. Poor self-management of drug therapy may increase the burden of diabetes to the patient. **Materials and Methods:** The current prospective observational study of six months duration was performed to assess the adherence of oral hypoglycemic agents and clinical outcomes with reference to patient's glycemic level in diabetic outpatients of both genders, age greater than 18 years; in a secondary referral hospital of south India. **Results:** Out of 90 diabetics, 47.78% were male and 52.22% were female; and 37.8% of patients were aged between 61 - 70 years; and 63.31% were prescribed with combination of metformin and glibenclamide, when compared to 22.2% of monotherapy with metformin and the same was directly proportional to their mean medication possession ratio. Our study observed 83.3% of patients were non-adherent to therapy based on their medication possession ratio value, the results also showed that there is significant difference between clinical outcomes in patients based on medication compliance. It was observed that for every 10% increase in medication possession ratio there was improved glycemic control and also significant difference of charlson comorbidity index among patients who are adherent and non-adherent. **Conclusion:** In conclusion, correlating adherence towards medication use could be a tool to improve and maintain healthoutcomes and quality of life in diabetic cohort populations.

Key words: Adherence, Charlson comorbidity index, Medication possession ratio, Oral hypoglycemic agents, Outcomes.

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INTRODUCTION

Nonadherence to medications is a common problem in clinical practice, especially among patients with asymptomatic chronic conditions such as diabetes, hypertension and hypercholesterolemia.[1-3] Nonadherence to medication is associated with increased hospitalization, progression of disease and higher mortality.[4-5] However, only about 50% of patients with chronic conditions take their medications as prescribed.[6-7]

Adherence to diabetes medications is generally poor.[8-9] Several studies have demonstrated a link between adherence

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and diabetes-related outcomes, including A1C levels.[10-12] A recent meta-analysis has showed that the average adherence in patients with diabetes is 67.5%, which is lower than that found among many conditions.[13] Also, recently, a specific systematic review on adherence to medications for diabetes showed that average adherence to oral hypoglycemic agents ranged from 36 to 93%.[14]

Studies in India indicates that more than 50% of people with diabetes have poor glycemic control (HbA1c > 8%), uncontrolled hypertension and dyslipidemia and a percentage have diabetic vascular complications.[15]

Research has demonstrated that adherence can lead to lower health care utilization and total costs,[16-17] and is associated with better health outcomes and decreased risk of hospitalization.[17-18]

Oral hypoglycemic agents (OHAs) are the major treatment options for T2DM patients and these drugs helps to improve glycemic control and decrease disease progression towards complications such as nephropathy and retinopathy. Medication non-adherence may explain the suboptimal achievement of therapeutic targets.[5]

However, poor adherence to OHAs remains as one of the main reasons for poor metabolic control. Poor self-management of drug therapy may increase the burden of diabetes to the patient.[19-20] Only 37.7 % of the patients treated with OHAs have glycosylated hemoglobin (HbA1c) < 7%.[21]

Adherence to medications is not routinely measured in clinical practice and a gold standard that can be easily implemented, even for research purposes, does not exist.[22]

Adherence may be measured indirectly or directly. Two indirect adherence metrics used in research and administrative work are the medication possession ratio (MPR) and the proportion of days covered (PDC). MPR is calculated as the total number of days supplied, divided by the number of days between the first and last refills; while PDC is calculated as the total number of days supplied during an interval, divided by the total number of days during that interval.[23] An MPR of 80% is often used as the cut off between adherence and nonadherence based on its ability to predict hospitalizations across selected high prevalence chronic diseases.[24]

The MPR is calculated by dividing the total days' supply of the medication by the total number of days within the period of analysis.[25] This calculation is used to evaluate how much medication a patient received over a period of observation, compared to the amount the patient should have ideally obtained.[25] A MPR equal to one represents absolute adherence and serves as a benchmark.[26]

Clinical outcomes are measurable clinical parameter which predicts the glycemic control of the disease. In this study we considered FBS, PPBS and RBS as clinical outcome parameters. For instance, prescription refill adherence to diabetes medications correlates with improved hemoglobin A1C results. Similarly, adherence to blood sugar self-monitoring is also associated with lower HbA1c levels as is adherence to diet and lifestyle change.[27]

Not many studies on medication adherence among diabetic patients have been documented in rural Indian healthcare settings. Hence, the current research study was designed to assess the adherence of OHAs and clinical outcomes with reference to patient's glycemic level.

MATERIALS AND METHODS

Study design

Prospective observational study.

Study site

Department of general medicine of a secondary referral healthcare setting in south India.

Study duration

Six months (January – June 2016).

Study criteria

Outpatients of general medicine department of both genders, age greater than 18 years; diagnosed with type II diabetes mellitus (with or without complications), who are on OHAs were included and patients on insulin for glycemic control and who have not refilled the prescription for at least once during the study period and pregnant women were excluded from the study.

Study population

A total of 90 diabetic subjects satisfying the inclusion criteria's were enrolled in the study.

Ethical approval

The ethical approval was obtained from the Ethical Committee before the commencement of study.

Study procedure

The current prospective, observational study of six months duration was performed in Type II diabetic out-patients attending general medicine department for refill of prescriptions (only with OHAs) of a secondary care referral hospital in south India.

A structured process was followed in obtaining permission from hospital authority by submitting a detailed profoma of the study, which includes protocol of study, evidence of critically evaluated biomedical literatures, data collection form, patient informed consent form. After the initial acceptance from hospital authority, study was registered in the institutional review board (IRB) of the institution for ethical approval (RIPER/IRB/2016/009) and institutional ethics committee of hospital.

A total of 90 diabetic subjects satisfying the inclusion criteria's and showing willingness were enrolled in the study. A documentation form (data collection form) was designed to collect the individual patient demographic particulars, laboratory parameters of glycemic control (FBS, RBS and PPBS) and treatment regimen which were kept confidential, information from patients were collected only after explaining and making them understand about the merits and demerits of the study, consent from patients was obtained before their recruitment and the consent was further documented.

Statistical and Data Analysis

The data's obtained from patients were thoroughly analyzed to evaluate the adherence towards oral antidiabetics and clinical outcomes through medication possession ratio (MPR).[25]

Student *t* test was used to determine significant difference between clinical outcomes of adherent and non-adherent patients. Furthermore, the Charlson Comorbidity Index (CCI)[28] expressing the degree of comorbidity at any time during follow-up, was also assessed.

RESULTS

The study was based on evaluating the adherence of OHAs and clinical outcomes with reference to glycemic level in 90 patients attending the outpatient department of general medicine of a secondary referral healthcare setting in south India.

Demographic details of study participants

In our study, out of 90 patients 43 (47.78%) were male and 47 (52.22%) were female; and 33 (37.8%) of patients were aged between 61 - 70 years, results of which are thoroughly analyzed and reported in Figure 1 Demographic distribution of study participants.

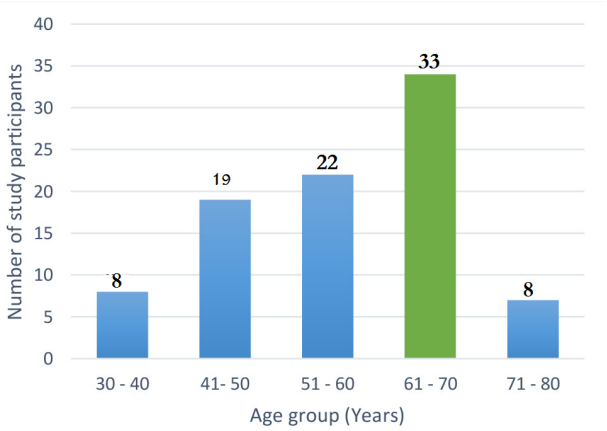

Figure 1: Demographic distribution of study participants.

Comparison of adherence and non-adherence with outcome parameters

The current study observed, twenty five patients were adherent and sixty five patients were non-adherent based on the medication possession ratio. The mean MPR observed in adherence patients was 83.3±2.8 and 53.9±3.7 in non-adherence patients which was found statistically significant (*P* value = 0.0009 and the charlson comorbidity index (CCI) for the adherent patients were found to be less in comparison to non-adherent patients which was observed statistically significant (P < 0.001); results of which are analyzed and reported in Table 1 Comparison of adherence and non-adherence with outcome parameters.

Oral Antidiabetics prescribed in study participants (n = 90)

In our study, 63.31% were prescribed with combination

Table 1: Comparison of adherence and non-adherence with outcome parameters.

Variables	Adherence	Non-adherence	P value
Number of patients	25	65	
MPR (Mean + SD)	83.3 + 2.8	53.9 + 3.7	0.0009
FBS (Mean + SD)	113.08 + 12.3	165.34 + 36.4	< 0.009
PPBS (Mean + SD)	154.69 + 40.5	260.37 + 54.55	< 0.0015
CCI (Mean + SD)	2.6 + 1.7	2.9 + 1.7	< 0.001

(P value < 0.05 is considered as statistically significant student t test)

Table 2: Oral Antidiabetics prescribed in study participants (n = 90).

Therapy	Number of patients (%)	Mean MPR (%)
Monotherapy (Metformin)	20 (22.2)	76.3
Dual therapy (Metformin + glibenclamide)	57 (63.31)	60.4
> 2 drugs	13 (14.4)	45

of metformin and glibenclamide, when compared to 22.2% of monotherapy with metformin and the same was directly proportional to their mean MPR observed, results were thoroughly assesses and reported in Table 2 Oral Antidiabetics prescribed in study participants.

DISCUSSION

In diabetes, as with other chronic conditions, successful prevention of the long term clinical manifestations of disease requires a lifetime treatment with medication. Although randomized clinical trials are keystone of clinical decision making, adherence to medication therapy is a key factor in translation of clinical trial efficacy to real world effectiveness. To this end, both clinicians and health policy decision makers could benefit from a vigorous understanding of the issues affecting the links between adherence and various outcomes. The current research represents clear evidence in diabetes, linking adherence to clinical outcomes.

Based on the literature, better adherence was found to be associated with improved glycemic control and decreased health care resource utilization.[29] In our study, for every 10% increase in MPR, glycemic control of 17.77 mg/dl (FBS) and 35.94 (PPBS) was observed; and adherence towards monotherapy (76.3%) was far better in comparison to dual therapy but not optimum. Regarding the OHAs treatment, no significant difference was observed in the glycemic control from either the single drug or two drugs or more than two drugs. Probably it is true that use of more medications is not associated with better glycemic control.[21] Similar kind of result was obtained in another study which also emphasizes that more oral medications, rather is a marker for a greater likelihood of poor control.[30] Only by increasing the number of medicines might not improve glycemic control. There are various confounding factors that have effect on the glycemic control. Our study also observed among individuals still being treated after a year, 22% were non-compliant, in whom the MPR observed was less than 80%. However, the mean MPR observed was 86.3% results of which are similar to the findings of Guenette L *et al*. 2013.[31] At the end of our study, 83% of total study participant was non-adherent with MPR less than 80%.

Additional status about clinical status confirmed that 36% of patients were re-hospitalized for diabetic ketoacidosis showing poorest adherence.

Limitations

The findings of the current research has to be reinforced and simulated, with larger sample size and regular follow-ups; to improve their external validity and the non-existence of gold standards in measuring adherence is a evident limitations.

CONCLUSION

In conclusion, treatment non-compliance is being increasingly recognized as one of the major limitations to improve healthoutcomes; and measurement of adherence is associated with improving and maintaining health outcomes and quality of life in patients with diabetes.

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CONFLICT OF INTEREST

The author declares no Conflict of Interest

ABBREVIATIONS

CCI: Charlson Comorbidity Index; FBS: Fasting Blood Sugar; HbA1c: Glycated Hemoglobin; IRB: Institutional Review Board; MPR: Medication Possession Ratio; OADs: Oral Anti Diabetics; OHAs: Oral Hypoglycemic Agents; PDC: Proportion of Days Covered; PPBS: Post Prandial Blood Sugar; RBS: Random Blood Sugar; RIPER: Raghavendra Institute of Pharmaceutical Education and Research; T2DM: Type 2 Diabetes Mellitus.

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