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Research Article

A Study on the Effectiveness of Acarbose in combination with other Hypoglycemic Agents in Reducing Blood Glucose Values in Type 2 Diabetes

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ABSTRACT

Objective - To obtain data on efficacy and safety of Acarbose combination therapy during daily life treatment. **Methods**- It's a prospective study done for a period of 7 months in a south Indian hospital. Out of 74 Type II diabetic patients 40 patients were on Acarbose therapy and 34 patients were in another group taking oral hypoglycemics alone. After a period of three months in the Acarbose group 35 patients came for review and in the other group 26 patients came for review. The reduction in blood glucose profile in both groups were done. Based on body mass index (BMI) the patients were classified as obese and non obese and the significant reduction in post prandial blood glucose level (PPBS) and glycosylated hemoglobin (HbA_{1C}) in each group were determined. **Results**- Among the study population 42 (56.7%) were male and 59 (43.2%) were female. The different doses of Acarbose prescribed were 25mg (48.64%), 50mg (37.83%) and 100mg (13.51%). The percentage reduction in blood glucose values in Acarbose group was found to be higher than oral hypoglycemics alone. The p value of PPBS and HbA1C in Acarbose group was found to be (p=0.002) and (p=0.043). Based on BMI they were classified as 27 (77.14) obese and 8 (22.8) as non obese. The p value of PPBS and HbA1C was highly significant in obese patients (p=0.0006) and (p<0.0001). **Conclusion**- Acarbose therapy was efficacious and well tolerated in daily life in patients with type II diabetes mellitus.

Keywords: Type II diabetes, Acarbose, Obesity.

1) INTRODUCTION

Type II Diabetes Mellitus

Diabetes mellitus is one of the most common endocrine disorders affecting almost 6% of the world's population, with the majority having Type II diabetes. The global prevalence of diabetes is estimated to rise substantially, with an accompanying increase in diabetes-related morbidity and mortality[1] The different factors which may contribute to type II DM are greater longevity, obesity, unsatisfactory diet, sedentary life style and increasing urbanization[2] Obesity is a disorder which results from a complex interplay of environmental and genetic factors and is associated with significant morbidity and mortality[3].

Acarbose

Results of recent evidence-based clinical studies, indicate that an acarbose has a beneficial effect on glycemic control without weight gain effect in Type II diabetes mellitus.[4] It delays the digestion of complex carbohydrates and disaccharides by competitive α-glucosidase inhibition at the ciliated border of the small intestine[5]. It has been estimated that 86% of those with type 2 diabetes are overweight or obese. It is associated with significantly worse cardiovascular risk factors in these patients[6].

Chunlin Li et al (2011) in their study suggested that Acarbose can be used as a first-line therapy or in combination with other glucose-lowering agents for type 2 DM and it was found to be associated with improvement in glycemic parameters, and was safe and well tolerated. In addition, it will maintain glycemic control and a good tolerability profile over the long term in diabetic patients[1].

L. Sangiorgio et al (2000) suggested that addition of acarbose was effective in improving glycemic control in overweight elderly Type II diabetic patients with poor glycemic control on OHA or

insulin regimes. It is an inhibitor of α-glucosidase and acts directly at the gastrointestinal level slowing down the absorption of glucose and eventually reduce the rapid increase in glycemia induced by a meal rich in carbohydrates[7].

2) METHODS

The prospective observational study was conducted at a multidisciplinary superspeciality hospital in India over a period of 7 months between June 2011 and December 2011. The study was conducted in the department of Diabetology and ethical committee clearance was obtained from the institutional ethical committee. Both male and female patients diagnosed as Type II diabetes and having HbA1C value above 6.5% were included in the study. Patients with Type I diabetes taking Insulin as sole therapy and patients with chronic intestinal diseases were excluded.

A total of 74 Type II diabetic patients were included in the study. The study population consisted of two groups where patients taking Acarbose was included in group I and patients taking other oral hypoglycemic agents were included in the group II. It was again divided into three groups where patients taking oral hypoglycemic agents except Acarbose was group I, Acarbose with oral hypoglycemic agents was group II, Acarbose with combination of oral hypoglycemic and Insulin considered as group III and the percentage reduction in FBS, PPBS and HbA1C produced in each group were calculated .

Values such as FBS, PPBS, HbA_{1C}, BMI are noted at the initial visit and the therapeutic efficacy of the drug in reducing these parameters were determined during the next review. Acarbose was usually given in addition to the current diabetes medications. Based on BMI the review patients were classified as obese and non obese. The percentage reduction in blood glucose profile in both groups were done and the therapeutic efficacy of the drug was determined.

Data were collected from the data entry form which gives values of blood glucose profile. Baseline and review values were compared by paired students 't' test. The significant reduction produced in blood glucose value was determined. Also the percentage reduction in blood glucose profile produced by Acarbose in obese and non obese patients was also calculated. The different doses of acarbose prescribed were 25mg, 50mg and 100mg and it was given orally.

Results were expressed as percentage, mean and standard deviation. The result of the study was analysed by paired 't' test. All the test were two tailed Values of $P<0.05$ and $P<0.01$ were considered statistically significant.

3) RESULTS

In our study 74 Type II diabetic patients were included, out of which 40 patients were on acarbose therapy and 34 patients were on oral hypoglycemic agents other than acarbose. Among them 42 (56.7%) were male and 59 (43.2%) were female. Family history of Type II diabetes was present in 48 (64.8%) and 26 (35.1%) had no family history. On considering the diet habits among the study population 56 (75.6%) patients were on diabetic diet and 18 (24.32%) were on non diabetic diet. Age wise distribution of patients taking Acarbose among the study group were 6 (8%) in 30-39 years, 17 (23%) in 40-49 yrs, 22 (30%) in 50-59 years and 29 (39%) patients were in the age group of 60-69 years. The percentage of patients taking other oral hypoglycemics alone were 26 (76.4%), Acarbose with oral hypoglycemics were 16 (45.7%), Insulin12 (34.2%) and combination of oral hypoglycemics and Insulin were 7 (20%) {Fig-1}. The percentage of patients using different doses of Acarbose were 25mg (48.64%), 50mg (37.83%) and 100mg (13.51%) {Fig-2}. Based on BMI the patients were classified as 27 (77.14) obese and 8 (22.8) as non obese. The p value of PPBS and HbA1C was found to be highly significant in obese patients as compared to non obese patients. It was found to be ($p=0.0006$) for PPBS and ($p<0.0001$) for HbA1C. {Table 1 &2} The percentage reduction in blood glucose values in Acarbose treated group was found to be higher than oral hypoglycemic agents alone. It showed a percentage reduction of 18.8% in FBS, 16.82% in PPBS and 17.92% in HbA1C. The p value of PPBS and HbA1C in Acarbose treated group was found to be ($p=0.002$) and ($p=0.043$). {Table 3& 4}.

4) DISCUSSION AND CONCLUSION

Efficacy of alpha glucosidase inhibitor Acarbose has been confirmed in more than 350 studies involving more than 30,000 patients. It has been shown to be efficacious and have an excellent safety profile with minimal drug drug interactions. It is currently the only oral antidiabetes agent approved for the treatment of both prediabetes and Type II diabetes[8].

Henrick Wagner et al have reported 48 of 62 type 2 diabetic patients patients (77.4%) as having cardiovascular disease in the study population.[9] We detected cardiovascular disease in thyroid disorders in 18.9% and renal disease in 29.7 % of our study population.

The study revealed that Acarbose was a safe and tolerable drug and no serious adverse events could be linked to that drug but only few gastrointestinal symptoms were related to it. It caused flatulence in (20%) diarrhea in (11.4%) and (5.7%) patients had hypoglycemia. Jean- Louis Chiasson et al has found similar results in their study that Acarbose

dose as large as 200mg had no toxic effect or serious adverse events and only gastrointestinal symptoms could be related. Compared with placebo, it was more frequently associated with flatulence (73.2%), diarrhea (43.6%) and abdominal cramps and discomfort was found to be 25%.[10].

In our study it have been found that BMI did not showed a significant difference in obese and non obese patients before and after Acarbose treatment. It is usually calculated by dividing weight (in kilograms) by square height (in meters)[3]. The total review patients including both obese and non obese showed significant difference. Chien- Wen Chou et al in their study showed the same results. Here obese patients change in BMI were considered as not significant and non obese patients change in BMI showed a p value of (p= 0.0579).But the total patients had a significant decrease in body weight after treatment which showed a significant p value. (p <0.05)[11].

In our study it has been shown that obese patients showed significant reduction FBS, PPBS and HbA1C. (P value of 0.0005, 0.0006 and <0.0001). In case of non obese patients FBS and PPBS didn't showed a significant result but HbA_{1C} showed significant difference. Chein –Wen Chou et al in their study suggested that both obese and non obese patients showed significant differences in FBS, PPBS and HbA_{1C}. All the parameters in obese patients and non obese patients showed a significant p value[11].

From the study which we have done it showed significant reduction in FBS, PPBS and HbA1C when Acarbose was combined with other antidiabetics. The study population was divided into three groups where patients on oral hypoglycemic agents alone was considered as group I and patients taking combination of Acarbose with oral hypoglycemics was group II and the group III consist of both oral hypoglycemics and Insulin. Monotherapy using Acarbose was not seen in any of the patients. The p value for FBS in the first two groups were found to be not significant but in the third group it was found to be significant. The values of PPBS in the second and third group was significant (p=0.018) and (p=002). The p value of HbA_{1C} in the last two groups were highly significant. (p= 0.0007) and (p=0.043)

L.Saniorgio et al in their study revealed the significant reduction produced in blood glucose values when Acarbose was added to the current medications. Here the study population was divided into two groups. Group I consist of patients taking combination of Acarbose with oral hypoglycemics. Group II consist of patients undergoing treatment with Insulin alone or in combination with oral hypoglycemics. The P value of the three parameters in Group I were found to be <0.004, <0.0005 and <0.05.Similarly the P values in Group II was found to be <0.004, <0.0006 and <0.02. When Acarbose was stopped the blood glucose values increased[7].

Our study is a short term study involving only a small number of study population. Hence in the future controlled long term studies involving large number of patients are still needed to be carried out to evaluate if the advantages of addition of Acarbose are persistent and whether it is possible to obtain a reduction in vascular complications and mortality.

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Table 1: Shows 't' test for the PPBS reduction in obese and non obese patients (n=35)

S.No	Category	Baseline PPBS value (mean±SE)	PPBS at review (mean±SE)	PPBS Reduction (mean± SE)	p value
1	Obese	271.26± 15.67	225.74± 14.04	45.52 ± 11.58	0.0006**
2	Non Obese	284.88 ± 26.41	259.38 ± 17.50	25.5 ± 10.98	0.0532

Table 2: Shows 't' test for HbA_{1C} Reduction in obese and non obese patients (n=35)

S.No	Category	Baseline HbA1C value (mean± SE)	HbA1C at review (mean ± SE)	HbA1C reduction (mean± SE)	p value
1	Obese	8.96 ± 0.38	7.71 ± 0.39	1.25 ± 0.25	<o.ooo1**
2	Non Obese	8.07 ± 0.85	7.41 ± 0.65	0.66 ± 0.30	0.03*

Table 3: Shows 't' test for the mean difference between baseline and review values of PPBS in each group of review patients (n=61)

Drugs	Baseline PPBS value (mean± SE) mg/dl	PPBS at review (mean± SE) mg/dl	PPBS Reduction (mean± SE) mg/dl	p value
Oral hypoglycemic drugs (n=26)	264.73± 10.29	262.08± 9.18	2.65 ± 3.73	0.484
Acarbose + Oral hypoglycemics (n=16)	263.87 ± 22.16	223.75 ± 16.86	40.12 ± 15.25	0.018*
Acarbose + Oral Hypoglycemics + Insulin (n=19)	283.42± 16.34	241.58± 16.37	41.84±11.81	0.002**

Table 4: Shows t test for the mean difference between baseline and review values of HbA_{1C} in each group of review patients (n=61)

Drugs	Baseline HbA1C value (mean± SE) mg/dl	HbA1C value at review (mean± SE) mg/dl	HbA1C Reduction (mean± SE) mg/dl	p value
Oral hypoglycemics (n=26)	9.17 ± 0.24	9.12 ± 0.19	0.05 ± 0.11	0.692
Acarbose + Oral hypoglycemic (n=16)	8.9 ± 0.80	7.76 ± 0.53	1.14 ± 0.37	0.0007*
Acarbose + Oral Hypoglycemics + Insulin (n=19)	8.31 ± 0.49	7.07 ± 0.77	1.24 ± 0.48	0.043**

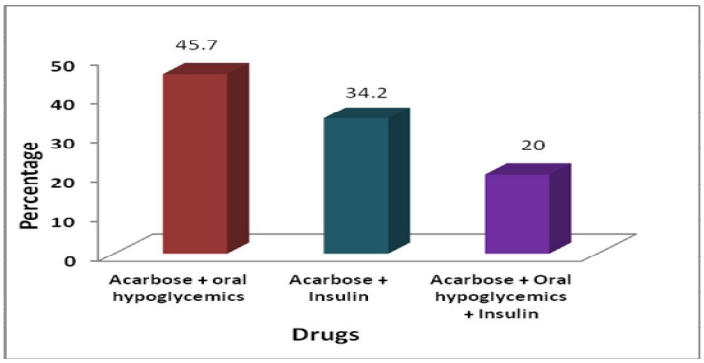

Fig. 1: Combination of Acarbose with other antidiabetic drugs

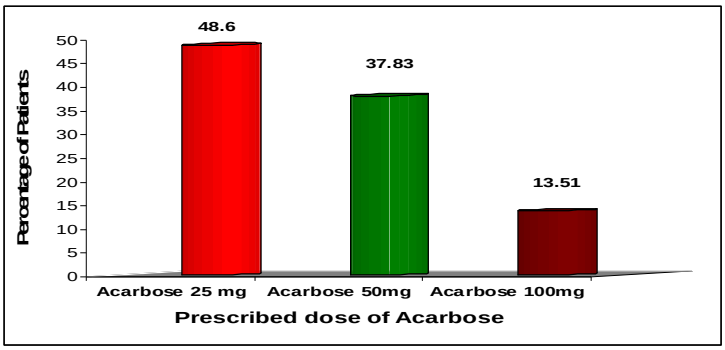

Fig. 2: Dose wise distribution of Acarbose among study population

REFERENCES

1. Li C, Hung YJ, Qamruddin K, Aziz MF, Stein H and Schmidt B. International Noninterventional Study of Acarbose Treatment In Patients With Type 2 Diabetes Mellitus. Diabetes Research and Clinical Practice. 2011;92:57-64.
2. Zeymer U. Cardiovascular Benefits of Acarbose In Impaired Glucose Tolerance And Type 2 Diabetes. International Journal of Cardiology. 2006;107:11-20.
3. Aronne LJ. Classification Of Obesity And Assessment Of Obesity -Related Health Risks. Obes Res. 2002;10:105S-115S.
4. Chou CW, Ou HY, Hsiao SH and Wu TJ. Differential Responses to Acarbose Between Obese And Non – Obese Patients With Type 2 Diabetes Mellitus. Int J Endocrinol Metab. 2006;4:63-69.
5. Lin BJ, Wu HP, Huang HS, Huarng J, Sison A, Kadir DKBA, Cho CG and Sridama W. Efficacy And Tolerability Of Acarbose In Asian Patients With Type2 Diabetes Inadequately Controlled With Diet And Sulfonylureas. Journal Of Diabetes and its complications. 2002;17:179-185.
6. Daousi C, Casson IF, Gill GV, Macfarlane IA, Wilding JPH and Pinkney JH. Prevalence of obesity in type 2 diabetes in secondary care: association with cardiovascular risk factors. Postgrad Med J. 2006;82(966):280-284
7. Sangiorgio L, Attardo T, Condorelli L and Lunetta M . Effect OF Treatment With AcarboseIn Elferly Overweight Type 2 Diabetic Patients In Poor Glycemic Control With Oral Hypoglycemic Agents Or Insulin. Archives Of Gerontology And Geriatrics 2000;31:27-34
8. Adeghate E, Schattner P and Dunn E. An update on the etiology and epidemiology of diabetes mellitus. Ann N Y Acad Sci. 2006 ;1084:1-29.
9. Wagner H, Degerblad M, Thorell A, Nygren J, Stahle A, Kuhl J, Brimsar TB, Ohrvik J, Efendic S and Bavenholm PN. Combined Treatment With Exercise Training And Acarbose Improves Metabolic Control and Cardiovascular Risk Factor Profile in Subjects With Mild Type 2 Diabetes. Diabetes Care. 2006;29(7):1471-1477.
10. Chiasson JL, Josse RG, Hunt JA, Palmason C, Rodger NW , Ross SA, Ryan EA, Tan MH and Wolever TMS. The Efficacy of Acarbose In The Treatment Of Patients With Non-Insulin-Dependent Diabetes Mellitus. Ann Intern Med. 1994;121:928-935.
11. Chou CW, Ou HY, Hsiao SH and Wu TJ. Differential Responses To Acarbose Between Obese And Non – Obese Patients With Type 2 Diabetes Mellitus. Int J Endocrinol Metab. 2006;4:63-69.