Assessment of Effect of Intensive Blood Pressure Therapy in Patients with Type 2 Diabetes Mellitus: A Clinical Study

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ABSTRACT

Introduction: In diabetes mellitus patients, risk of cardiovascular disease is increased. Blood pressure in diabetic persons when assessed for risk of cardiovascular diseases, it was found that they exerted effect on major cardiovascular events among high-risk persons with type 2 diabetes. In support of this recommendation, there is lack of sufficient evidence in the literature. Therefore, we conducted this randomized clinical study to evaluate the effect of intensive blood pressure control in type 2 diabetes.

Material and methods: A total of 1025 patients with type 2 diabetes were included in the present study. A randomized intensive or standard glycemic control was assigned to all the participants. Patients with type 2 diabetes having glycated haemoglobin level of equal to more than 7.5% with history of cardiovascular disease were included in the present study. Patient with body mass index of more than 45, history of any other systemic illness or any known drug allergy were excluded from the present study. For participants in the intensive therapy group, visits to assess blood pressure were scheduled once a month for 4 months and every 2 months thereafter; for participants in the standard-therapy group, follow-up was done initially at 30 days time followed by quarterly per year check up. All the results were analyzed by SPSS software.

Results: Mean age of the patients undergoing intensive and standard therapy was 62.4 and 62.5 years respectively. Mean fasting glucose levels of the plasma in patients with intensive and standard therapy was found to be 177.1 and 172.8 mg/dl respectively. 195.2 And 190.5 mg/dl were the mean value of the serum total cholesterol levels in the patients undergoing intensive and standard therapy respectively. While comparing the mean cholesterol levels in two groups with patients undergoing intensive therapy having higher values in comparison to patients undergoing standard therapy, significant results were observed. No significant results were obtained while comparing the mean values for primary outcome in patients whereas while significant results were obtained while comparing the non-fatal stroke percentage per year in intensive therapy group and standard therapy group.

Conclusions: No strong evidence exists which could prove that of intensive blood-pressure controls can decrease the frequency of major cardiovascular events in diabetic patients.

Keywords: Blood pressure, Diabetes, Intensive

INTRODUCTION

The risk of cardiovascular disease increases in diabetes mellitus patients by a factor of two to three at every level of systolic blood pressure.[1] On measurement of blood pressure (BP) in diabetic persons at risk of cardiovascular diseases, it was found to be below 120 mm Hg of systolic blood pressure which exerted effect on major changes occurring in the cardiac system among type 2 diabetic patients which are at higher risk as compared to other people.[4] In diabetic patients, recommendation of the seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure involves starting of the medicinal therapy in such patients to achieve systolic blood pressure of less than 130 mm of mercury.[1-3] There is, however, a paucity of evidence from randomized clinical trials to support these recommendations. Therefore, we conducted this randomized clinical study to evaluate the effect of intensive blood pressure control in type 2 diabetes.

MATERIAL AND METHODS

A randomized clinical trial was conducted for the present study at 20 different tertiary health care centres. A total of 1025 patients with type 2 diabetes, based on inclusion exclusion criteria, were included in the present study. A randomized intensive or standard glycemic control was assigned to all the participants. Out of all the subjects included in the study, 550 were assigned to the placebo group along with simvastatin while remaining 475 were randomly assigned to intensive or standard blood control trials. Ethical approval was taken by the research committee of the committee of health care centre after giving in written the entire study protocol. All the patients were pre-informed about the research protocol and written consent was obtained from them. Criteria described previously in the literature were considered as standard in the present study for including patients in the present study.[5] Patients with type 2 diabetes having glycated haemoglobin level of equal to more than 7.5% with history of cardiovascular disease were included in the present study. Patient with body mass index of more than 45, history of any other systemic illness or any known drug allergy were excluded from the present study. All those subjects who had blood pressure of higher than 130 mm of mercury and lower than 180 mm of mercury and were on hypertensive drug therapy also came under inclusion criteria for present study.[6] Treatment strategies that are used to lower blood pressure were used in the current study. Approach described in the literature was used in the present study for the management of the blood pressure.[4] Assessment of the occurrence of self-reported symptoms of swelling or of dizziness on standing during the previous month was done at baseline and at 1, 3, and 4 years after randomization. For participants in the intensive therapy group, visits to assess blood pressure were scheduled once a month for 4 months and every 2 months thereafter; for participants in the standard-therapy group, follow-up was done

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How to cite this article: Gopal Batni. Assessment of effect of intensive blood pressure therapy in patients with type 2 diabetes mellitus: a clinical study. International Journal of Contemporary Medical Research 2016;3(8):2463-2466.

initially at 30 days time followed by quarterly per year check up. Those factors were considered as potential adverse effects in which examination was done such as clinical and laboratory variables, including serum potassium and creatinine levels and estimated glomerular filtration rate.[7]

STATISTICAL ANALYSIS

All the results were analyzed by SPSS software. Chi-square test and student t-test were used for assessing the level of significance. P-value of less than 0.05 was taken as significant values.

RESULTS

Figure-1 highlights the mean values for various details of demographic data and habit history of the patients. Mean age of the patients undergoing intensive and standard therapy were 62.4 and 62.5 years respectively. Majority of the patients in both the treatment therapy group were males. A significant major proportion of the patients in both intensive therapy group and standard therapy group had education of minimum of graduation. Mean weight of the patients was 90 kg in intensive therapy group and 88 kg in standard therapy group. Mean values for cardiovascular details of the patients with and without medication in the two study groups is shown in Figure-2. Mean systolic and diastolic pressure of patients without medication in intensive therapy group was 140.2 and 76.1 mm of Hg respectively. Mean systolic and diastolic pressure of patients without medication in standard therapy group was 140 and 75.8 mm of Hg respectively. Figure-3 shows the mean values for biochemical parameters of the patients on standard and intensive therapy. Mean percentage of glycated haemoglobin values in patients on standard therapy and intensive therapy were found to be 8.4 and 8.5 percent respectively. Mean fasting glucose levels of the plasma in patients with intensive and standard therapy was found to be 177.1 and 172.8 mg/dl respectively. 195.2 And 190.5 mg/dl were the mean value of the serum total cholesterol levels in the patients undergoing intensive and standard therapy respectively. Table-1 shows the p-value for the baseline characteristics of the patients. Significant results were obtained while comparing the mean cholesterol levels in two groups with patients undergoing intensive therapy having higher values in comparison to patients undergoing standard therapy (p-value < 0.05). Table-2 highlights the outcome of the patients at primary and secondary level. No significant results were obtained while comparing the mean values for primary outcome in patients whereas while significant results were obtained while comparing the non-fatal stroke percentage per year in intensive therapy group and standard therapy group.

DISCUSSION

One of the most common metabolic diseases requiring measurement of sustained hyperglycaemia for its diagnosis if type 2 Diabetes mellitus. People with type 2 diabetes are at elevated risk for a number of serious health problems, including cardiovascular disease, premature death, blindness, kidney failure, amputations, fractures, frailty, depression, and cognitive decline.[8] After adjustment for other risk factors, an increase of 1% in the glycated hemoglobin level is associated with an increase of 18% in the risk of cardiovascular events, a rise in more than 10% of the death risk, and an increase of 37% in the risk of retinopathy or renal failure.[9-11] A reduction in the outcome of therapeutic strategies further lowering the glycated hemoglobin levels is suggested by the graded relationship between the glycated hemoglobin level and cardiovascular events and death. Some of the previous clinical trials support this hypothesis.[8] However; adequate testing of this hypothesis is still required in large scale. Hence, we conducted this randomized clinical study to evaluate the effect of intensive blood pressure control in type 2 diabetes.

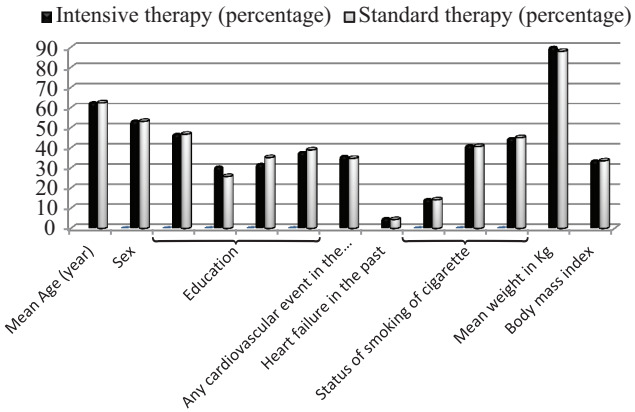

Figure-1: Mean values for details of data of different demographic and habit history of the patients.

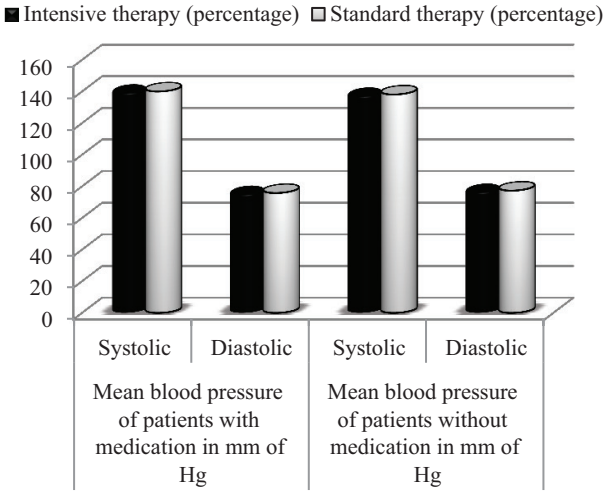

Figure-2: Mean values for cardiovascular details of the patients with and without medication

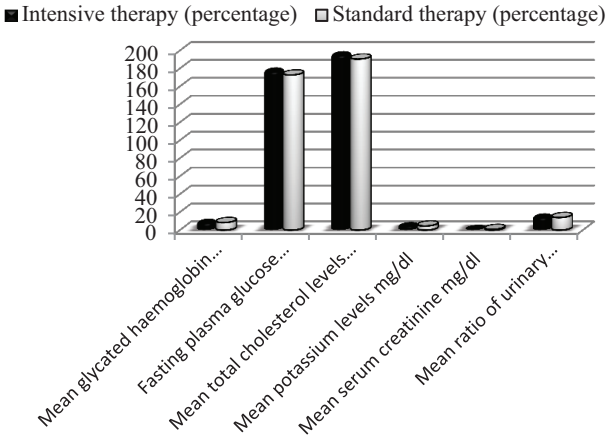

Figure-3: Mean values for biochemical parameters of the patients on standard and intensive therapy.

Parameters		Intensive therapy (percentage)	Standard therapy (percentage)	p-value
Mean Age (year)		62.4	62.5	0.51
Sex	Male	53.3	53.2	0.45
	Female	46.7	46.8	0.62
Education	Less than high school	30.5	25.8	
	High school	31.8	35.2	
	Graduate	37.7	39.0	
Any cardiovascular event in the past		35.8	34.8	0.85
Heart failure in the past		4.9	4.4	0.15
Status of smoking of cigarette	Current	14.3	14.2	0.54
	Former	41.1	40.7	
	Never	44.6	45.1	
Mean weight in Kg		90	88	0.71
Body mass index		33.5	33.6	0.81
Mean blood pressure of patients with medication in mm of Hg	Systolic	140.2	140.0	0.41
	Diastolic	76.1	75.8	0.51
Mean blood pressure of patients without medication in mm of Hg	Systolic	138.2	138.1	0.45
	Diastolic	77.4	77.3	0.81
Mean duration of diabetes in years		9	10	0.81
Mean glycated haemoglobin level in %		8.5	8.4	0.09
Fasting plasma glucose levels mg/dl		177.1	172.8	0.09
Mean total cholesterol levels mg/dl		195.2	190.5	0.03*
Mean potassium levels mg/dl		4.6	4.6	0.81
Mean serum creatinine mg/dl		0.8	0.8	0.81
Mean ratio of urinary albumin to creatinine		14.5	14.0	0.41
*: Significant				

Table-1: Baseline characteristics of the patients.

Outcome		Intensive therapy (percentage / year)	Standard therapy (percentage / year)	p-value
Primary outcome		1.82	2.10	0.30
Secondary outcomes	Myocardial infarction (non-fatal)	1.15	1.30	0.35
	Stroke(non-fatal)	0.32	0.49	0.02*
	Death (cardiovascular cause)	0.55	0.47	0.84
*: Significant				

Table-2: Outcome of the patients at primary and secondary level

Inspite of the significant difference of mean systolic blood pressure between intensive-therapy group and the standard-therapy group, no significant reduction in the death rate or outcome of primary cardiovascular diseases is seen in intensive antihypertensive therapy was observed. Also, as far as secondary outcome is concerned, no significant benefit was observed. Intensive blood-pressure management did reduce the rate of total stroke and nonfatal stroke when compared statistically (p-value <0.05). Similar results were obtained by previous studies in the literature where results of two meta-analyses correlated with our results.[12,13] Arguedas et al conducted a clinical research to determine the association of decrease in blood pressure with reduction in mortality in diabetic patients. They searched the Databases of Abstracts of Reviews of Effectiveness (DARE) and the Cochrane Database of Systematic Reviews for related reviews. From the results, they concluded that no strong evidence exists in the patients of their study which could show a significant correlation of lowering of blood pressure with rate of mortality in diabetic patients.[14] Gerstein et al analyzed the long term effects of intensive lowering of blood glucose levels on the cardiovascular outcomes. They analyzed patients with type 2 diabetes and cardiovascular diseases and randomly assigned them with intensive therapy or the standard therapy to assess the cardiovascular risk factors. From the results, they concluded that in comparison to standard therapy, intensive therapy for more than three and half years showed a reduction of five year nonfatal myocardial infarction. At the same time, it also increased the 5 year mortality rate.[15] Gerstein et al conducted an investigation to assess that whether cardiovascular events are reduced in diabetic patients with intensive therapy to target normal glycated haemoglobin levels. They analyzed 10,251 patients of mean age of 62.2 years with a median glycated haemoglobin level of 8.1%. From the results, they concluded that in comparison with the standard therapy, the use of intensive therapy did not significantly reduction in major cardiovascular events when targeted normal glycated haemoglobin levels for 3.5 years.[16] Duckworth et al assessed the effect of intensive glucose control on cardiovascular events in patients with type 2 diabetes. They randomly assigned 1791 military veterans of mean age of 60.4 years who had a suboptimal response to therapy for type 2 diabetes to receive either intensive or standard glucose control. From the results, they concluded that

no significant effect of intensive glucose control in patients with poorly controlled type 2 diabetes is seen on the rates of major cardiovascular events.[17] Xie et al evaluated the effect of intensive blood pressure lowering on cardiovascular and renal outcomes. They searched the data bases for trials published between Jan 1, 1950, and Nov 3, 2015. From the results, they concluded that lowering of intensive blood pressure provided greater vascular protection than standard regimens.[18]

CONCLUSION

From the observation found in the present study, it can be concluded that no strong evidence exist which could prove that of intensive blood-pressure controls can reduce the frequency of major cardiovascular events in diabetic patients. Further studies in future are recommended for better exploration of this area of medical field.

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Source of Support: Nil; **Conflict of Interest:** None

Submitted: 02-07-2016; **Published online**: 13-08-2016