CODEN [USA]: IAJPBB ISSN: 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES

http://doi.org/10.5281/zenodo.3365641

Available online at: http://www.iajps.com ***Research Article***

TO DETERMINE THE SIMVASTATIN EFFECTS ON SENSITIVITY OF INSULIN IN TYPE 2 DIABETIC PATIENTS

[1]Dr Aftab Rabbani, [2]Dr Komal Zia Rao, [3]Dr Mohammad Atiq Ur Rehman

[1]MBBS MRCP, Associate Professor, Sharif Medical and Dental College Lahore., [2]Allama Iqbal Medical College Lahore., [3]MBBS MRCP, Assistant Professor, Sharif Medical and Dental College Lahore.

Article Received: June 2019 **Accepted:** July 2019 **Published:** August 2019

Abstract:

Objective: *To investigate the simvastatin treatment effects on sensitivity of insulin in type II diabetic patients.*

Study Design: *A randomized case control study.*

Place and Duration: *In the Medicine Unit II of Jinnah Hospital, Lahore for Six months duration from January 2019 to June 2019.*

Methodology: *In total 100 cases of type 2 diabetes in both sexes were selected for study. Into 2 groups; Patients were divided randomly. 50 subjects were treated with simvastatin 40 mg / day for 3-months and 50 subjects as control. The anthropometric characteristics were same in both groups like (diabetes duration, age, blood pressure and BMI) and biochemical (fasting plasma glucose, serum creatinine, lipid profile and fasting insulin level). By homeostasis model for insulin resistance (HOMA-IR); Insulin resistance was determined earlier and later three months of management with simvastatin (40 mg / day).*

Results: *Simvastatin (40 mg / day) significantly reduced cholesterol, LDL and triglyceride levels, but have no affect significantly on sensitivity of insulin as determined by HOMA-IR. Though, sensitivity of insulin was increased in people with insulin resistance (decreased HOMA IR 1.92; p = 0.001).*

Conclusion: *Although treatment with simvastatin did not affect insulin sensitivity in the short term (3 months), all patients had a significant lipid lowering effect.*

Key words: *Diabetes, insulin sensitivity, lipid profile, simvastatin.*

Corresponding author:

Dr. Aftab Rabbani,

MBBS MRCP, Associate Professor,

Sharif Medical and Dental College Lahore.

QR code

Please cite this article in press Aftab Rabbani et al., ***To Determine the Simvastatin Effects on Sensitivity of Insulin in Type 2 Diabetic Patients.,*** *Indo Am. J. P. Sci, 2019; 06(08).*

INTRODUCTION:

According to the (IDF) International Diabetes Federation, diabetes is estimated to affect 194 million people worldwide in 2003 and 299-333 million people in 2025[1-3]. Globally Pakistan is on 6th rank. There were 6.2 million DM cases in 2003, and will rise to 11.6 million people with diabetes. The resistance of Insulin is believed to play an important part in the advancement of diabetes[4]. Although the level of diet, physical activity and genetics also supposed to play role, the precise cause of type 2 diabetes resistance to insulin is not clear[5-6]. Use of statins in sensitivity of insulin in patients with type II diabetes has a role. On atorvastatin and simvastatin, 2 various analysis conducted which stated that statins increased the effect of insulin in type II diabetic patients. The positive effects of statins on the insulin sensitivity on type II diabetes were not observed. For hypercholesterolemia treatment, statins are widely used in clinical practice. It is significant to distinguish the insulin effects on sensitivity in practice[7]. If other analysis authorises the opinion that statins increase sensitivity of insulin and decrease the type 2 diabetes onset, the apparent advantage of cardiovascular interferences in clinical judgements may be increased significantly and longstanding cost-benefit scrutiny. These interferences may be larger, it was more favourable than earlier analysis[8-9]. Therefore, our objective was to explore whether treatment with simvastatin (40 mg / day) for 3-months affected insulin sensitivity in Type II diabetic patients identified by Homeostasis Model Assessment (HOMA-IR).

MATERIALS AND METHODS:

This randomized case control study was held in the Medicine Unit II of Jinnah Hospital, Lahore for Six months duration from January 2019 to June 2019. 100 total people with type II diabetes were selected from OPD. The procedures and purpose of the analysis were clarified to all patients. Into 2 groups; Patients were divided randomly. 50 subjects were treated with simvastatin 40 mg / day for 3-months and 50 subjects as control. The subjects who were using antihypertensive drugs or metformin advised to continue their treatment, but the quantity was adjusted throughout the study period.

Inclusion criteria: Above age of 30 years, type II diabetes and blood pressure below 140/90 mmHg.

Exclusion criteria: severe heart, kidney or liver problems, a history of kidney transplantation, a current history of alcohol or drug dependence, planning to conceive during pregnancy or work, use of insulin, steroids or statins, higher LDL levels at 130 mg / dl and above 1.5 mg / dl serum creatinine.

Data collection: Weight, height, blood pressure and BMI were measured and on pre-designed questionnaire, other information was recorded. Biochemical parameters: BSF, BSR, fasting lipid profile (triglycerides, cholesterol, LDL, HDL) were measured using sandwich technique and ELISA 303 standard methods. ALT and Serum creatine kinase levels were also calculated before and after the analysis.

Insulin sensitivity assessment: By homeostasis model (HOMA-IR) evaluation Insulin sensitivity was determined as follows: glucose (mmol / l) Insulin (mu / ml) /22.6. On sensitivity of insulin; the simvastatin effect was classified as ineffective, increased and decreased in HOMA-IR values after treatment for 3-months.

Statistical analysis: For data analysis, SPSS version 19.0 was used and to compare the main characteristics between the control group and drug group; Chi square test (for categorical variables) were used. To determine statistical importance of variations before and after treatment of incessant variables; Paired sample T test was used.

RESULTS:

The biochemical and anthropometric properties of the patients in the control group and was managed with simvastatin at the beginning of the study given in Table I.

Table-I: Anthropometric characteristics of Type 2 Diabetes Subjects in Control and Simvastatin group

Variable	*Control group (n=39)*	*Simvastatin group (n=42)*
†Gender		
Male	26(66.7%)	23(54.8%)
Female	13(33.3%)	19(45.2%)
†Family History		
No	14(35.9%)	17(40.5%)
Yes	25(64.1%)	25(59.5%)
†Systolic Blood Pressure		
<130 mmHge	15(42.9%)	16(40.0%)
≥130 mmHg	20(57.1%)	24(60.0%)
†Diastolic Blood Pressure		
<85 mmHge	26(74.3%)	24(60.0%)
≥85 mmHg	9(25.7%)	16(40.0%)
*Age (in years)	49.72 ± 8.51	49.93 ± 10.69
*Duration of diabetes (in years)	7.66 ± 4.91	6.13 ± 5.29
*BMI (Kg/m^2)	27.97 ± 4.76	27.59 ± 4.33

† Numbers (percentages) reported for categorical variables.

The ratio of men and women in both groups was same. The proportion of patients with a positive blood pressure and diabetes family history was same equally in groups. Both groups diabetes duration, age, serum creatinine levels and BMI were assessed. The biochemical parameters mean values were given in Table II done at the start and end of the analysis (after 3-months) in the control group.

Table-II: FPG, Insulin and Lipid Profile of Control group

Variable	*Control group*	
	Baseline	*After 3 months*
Fasting Plasma Glucose (mg/dl)	156.32 ± 46.64	162.82 ± 70.39
Insulin (µU/mL)	10.03 ± 5.68	8.23 ± 3.97
Total Lipids (mg/dl)	716.43 ± 76.59	711.83 ± 123.04
Cholesterol (mg/dl)	167.85 ± 17.58	166.52 ± 18.97
Triglycerides (mg/dl)	135.13 ± 33.26	148.85 ± 80.75
HDL (mg/dl)	41.37 ± 2.06	40.52 ± 2.48
LDL (mg/dl)	100.23 ± 15.99	95.6 ± 19.47

Table III shows the biochemical parameters values performed at the beginning and finish of the study (after treatment for 3-months with simvastatin).

Table-III: Changes in Biochemical parameters in Drug Group

Variable	*Drug Group*	
	Baseline	*After treatment*
Fasting Plasma Glucose (mg/dl)	153.55 ± 56.70	147.95 ± 34.49
Insulin (µU/mL)	9.59 ± 6.12	8.87 ± 4.64
Total Lipids (mg/dl)*	750.13 ± 148.54	682.42 ± 106.50
Cholesterol (mg/dl)*	171.9 ± 22.49	156.93 ± 14.03
Triglycerides (mg/dl)*	169.85 ± 103.21	134.59 ± 44.10
HDL (mg/dl)	40.39 ± 3.45	41.18 ± 2.47
LDL (mg/dl)*	100.55 ± 18.79	89.20 ±13.33
CPK (mg/dl)	113.53 ± 34.53	118.92 ± 17.89
ALT (mg/dl)	29.65 ± 31.19	22.0 ± 4.47

* p value < 0.05

Simvastatin [40 mg / day] (p value <0.001, p value = 0.003, p value = 0.003 and p value = 0.013) showed a significant reduction in total lipid, triglyceride, cholesterol and LDL levels earlier and later to management. As any change in CPK, it has no negative effect on muscle or liver. Simvastatin effects on sensitivity of insulin: There was no statistically important variation between the HOMA-IR values in the simvastatin-managed group. We also evaluated the simvastatin effects on sensitivity of insulin in subjects with type II diabetes by choosing the patients only having type 2 diabetes resistant to insulin. Therefore, all patients with higher HOMA-IR values were selected from 2.9 subjects at the beginning of the analysis. In this group; 20 total patients' subjects were recognised. At the beginning of the analysis, the HOMA - IR mean was 5.74 and after 3 months treatment with simvastatin, the mean HOMA - IR was 3.82. A statistically significant decrease in HOMA-IR value of 1.92 [p value = 0.001] was observed.

DISCUSSION:

Clinical analysis has reported optimistic statins effect on sensitivity of insulin in individuals with type 2 diabetes. Stewart et al. The euglycemic hyperinsulinemic shock method is a "gold standard" procedure for determining peripheral sensitivity of insulin and has been used in several studies. Current analysis has used HOMA-IR, a better technique of measuring sensitivity of insulin and equivalent to the euglycemic glucose fixation method[10-11]. Some studies on epidemiology have shown association between dyslipidemia and insulin resistance. The CARDIA study analyzed lipid levels and insulin in young white and black adults; He stated optimistic association between triglyceride concentration and plasma insulin between both racial groups[12]. Similarly, the French Telecom Study in 1992 compared the insulin resistance syndrome characteristics in the Caucasus and Caribbean and later establish that greater concentrations of insulin in the Caribbean group were then linked with increased triglyceride levels. Paolisso G et al indicated that statin management was related with advancement in decrease of insulin resistance and a decreased concentration of plasma triglyceride[13-14]. Therefore, the hypolipidemic statins effect on plasma triglycerides in our analysis may increase sensitivity of insulin as indicated by a decrease in fasting insulin levels, but this was not significant statistically[15]. This can be made more pronounced if the effect is observed after a long time.

CONCLUSION:

This study concluded that treatment with simvastatin in a short period of time (3 months) did not affect sensitivity of insulin, but in all subjects, it had significant lipid-lowering effect. Long-term analysis in large populations are needed to evaluate the statins effects on insulin sensitivity.

REFERENCES:

1. Ahmadizar, Fariba, Carolina Ochoa-Rosales, Marija Glisic, Oscar H. Franco, Taulant Muka, and Bruno H. Stricker. "Associations of statin use

with glycaemic traits and incident type 2 diabetes." *British journal of clinical pharmacology* 85, no. 5 (2019): 993-1002.

2. Reynoso-Villalpando, Gabriela Lizet, Cristina Sevillano-Collantes, Yeminia Valle, Inmaculada Moreno-Ruiz, Jorge Ramón Padilla-Gutiérrez, and Francisco Javier del Cañizo-Gómez. "ApoB/ApoA1 ratio and non-HDL-cholesterol/HDL-cholesterol ratio are associated to metabolic syndrome in patients with type 2 diabetes mellitus subjects and to ischemic cardiomyopathy in diabetic women." *Endocrinologia, diabetes y nutricion* (2019).
3. Mäkelä, Kari Antero, Juhani Leppäluoto, Jari Jokelainen, Timo Jämsä, Sirkka Keinänen-Kiukaanniemi, and Karl-Heinz Herzig. "Effect of physical activity on plasma PCSK9 in subjects with high risk for type 2 diabetes." *Frontiers in physiology* 10 (2019).
4. Lallukka-Brück, S., Isokuortti, E., Luukkonen, P.K., Hakkarainen, A., Lundbom, N., Sutinen, J. and Yki-Järvinen, H., 2019. Natural course of NAFLD and type 2 diabetes in HIV-positive subjects with and without combination antiretroviral therapy (cART)-associated lipodystrophy: a 16-year follow-up study. *Clinical Infectious Diseases*.
5. Young, Benjamin E., Seth W. Holwerda, Jennifer R. Vranish, David M. Keller, and Paul J. Fadel. "Sympathetic Transduction in Type 2 Diabetes Mellitus: Impact of Statin Therapy." *Hypertension* 74, no. 1 (2019): 201-207.
6. Son, Jang Won, Chul-Hee Kim, Mun Suk Nam, Ie Byung Park, and Soon Jib Yoo. "Efficacy and safety of prescription omega-3 fatty acids added to stable statin therapy in patients with type 2 diabetes and hypertriglyceridemia." *Journal of Lipid and Atherosclerosis* 8 (2019).
7. Bengaluru Jayanna, Manju, and Jennifer G. Robinson. "The extent to which statins have improved cardiovascular outcomes: Lessons from randomized trials and observational studies of "real world" practice in people with diabetes." *Diabetes, Obesity and Metabolism* 21 (2019): 17-27.
8. Hwang, J.H., Kim, A.R., Kim, K.M., Park, J.I., Oh, H.T., Moon, S.A., Byun, M.R., Jeong, H., Kim, H.K., Yaffe, M.B. and Hwang, E.S., 2019. TAZ couples Hippo/Wnt signalling and insulin sensitivity through Irs1 expression. *Nature communications*, *10*(1), p.421.
9. Kemps H, Kränkel N, Dörr M, Moholdt T, Wilhelm M, Paneni F, Serratosa L, Ekker Solberg E, Hansen D, Halle M, Guazzi M. Exercise training for patients with type 2 diabetes and cardiovascular disease: what to pursue and how to do it. A position paper of the European Association of Preventive Cardiology (EAPC). European journal of preventive cardiology. 2019 May;26(7):709-27.
10. D'Elia, L., P. Strazzullo, R. Iacone, O. Russo, and F. Galletti. "Leptin levels predict the development of insulin resistance in a sample of adult men–The Olivetti Heart Study." *Nutrition, Metabolism and Cardiovascular Diseases* 29, no. 1 (2019): 39-44.
11. Duflot, T., Moreau-Grangé, L., Roche, C., Iacob, M., Wils, J., Rémy-Jouet, I., Cailleux, A.F., Leuillier, M., Renet, S., Li, D. and Morisseau, C., 2019. Altered bioavailability of epoxyeicosatrienoic acids is associated with conduit artery endothelial dysfunction in type 2 diabetic patients. *Cardiovascular diabetology*, *18*(1), p.35.
12. Hwang, You-Cheol, Ji Eun Jun, In-Kyung Jeong, Kyu Jeung Ahn, and Ho Yeon Chung. "Comparison of the Efficacy of Rosuvastatin Monotherapy 20 mg with Rosuvastatin 5 mg and Ezetimibe 10 mg Combination Therapy on Lipid Parameters in Patients with Type 2 Diabetes Mellitus." *Diabetes & metabolism journal* 43 (2019).
13. Wrzosek, Małgorzata, Ada Sawicka, Michał Wrzosek, Paweł Piątkiewicz, Marek Tałałaj, and Grażyna Nowicka. "Age at onset of obesity, transcription factor 7-like 2 (TCF7L2) rs7903146 polymorphism, adiponectin levels and the risk of type 2 diabetes in obese patients." *Archives of medical science: AMS* 15, no. 2 (2019): 321.
14. Matikainen, Niina, Sanni Söderlund, Elias Björnson, Kirsi Pietiläinen, Antti Hakkarainen, Nina Lundbom, Marja-Riitta Taskinen, and Jan Borén. "Liraglutide treatment improves postprandial lipid metabolism and cardiometabolic risk factors in humans with adequately controlled type 2 diabetes: A single-centre randomized controlled study." *Diabetes, Obesity and Metabolism* 21, no. 1 (2019): 84-94.
15. Plat, Jogchum, Nadine Severins, and Ronald P. Mensink. "Improvement of pulse wave velocity and metabolic cardiovascular risk parameters through egg protein hydrolysate intake: A randomized trial in overweight or obese subjects with impaired glucose tolerance or type 2 diabetes." *Journal of functional foods* 52 (2019): 418-423.