Evaluation of periodontal status in type 2diabetic patients on statin therapy

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Abstract

Background: Dyslipidemia is prevalent in type 2 diabetes mellitus (DM). Statin drugs were first used to treat hypercholesterolemia and later to treat dyslipidemia particularly in DM. However, it was found that they also have an anti-inflammatory pleiotropic effect. Chronic periodontitis is a continuous inflammatory process whose progression is modulated by the presence of DM.

Aim of study: To assess the association between the use of statin drugs and any improvement in periodontal status.

Materials & methods: Eighty (40 males and 40 females) type 2 diabetic patients were enrolled in this study. Patients were selected consecutively but with consideration of sex and exclusion criteria to compose two groups:

- Forty (20 males and 20 females) patients who were on a statin drug for at least six months and were assigned as the (Statin group).
-Forty (20 males and 20 females) patients who received no statin drug at any time and were assigned as (Non statin group).

Periodontal status was evaluated by periodontal disease index (PDI) which includes plaque, calculus, and periodontal components of this index.Assessment of glycemic control included serum glucose assay and HbA_{1c} assay.Lipid profile assay included estimation of serum total cholesterol (TC), serum triglycerides (TG), high density lipoprotein cholesterol (HDL-C), and calculation of low density lipoprotein (LDL-C).

Results: The difference between the mean levels of HbA_{1c} in statin group and non statin group was statistically non significant (8.61±1.82% vs. 9.10±1.26% respectively). There were no significant differences between statin group and non statin group in regard to the mean levels of TC, HDL-C, and LDL-C. The mean level of TG was higher in statin group and the difference was statistically of high significance (151.10±55.02 vs. 122.43±34.39 mg/dl, $P<0.01$). The mean values of plaque, calculus, and periodontal disease index were lower in statin group than in non statin group. The difference in plaque index was statistically highly significant (1.31±.0.57 vs. 1.70±0.50, $P<0.01$), while the differences in calculus index and periodontal disease index were statistically significant (0.61±0.47 vs. 0.87±0.65, and 2.75±0.89 vs. 3.16±.0.78 respectively, $P< 0.05$).

Conclusion: Diabetic patients on statin therapy exhibited fewer clinical signs of periodontal disease than those without statin therapy.

Key words: Diabetes mellitus, Dyslipidemia, Statins, Periodontitis

Introduction

Diabetes mellitus (DM) is a metabolic disorder characterized by hyper-glycemia due to defective secretion or activity of insulin [1].

Type 2 diabetes is caused by resistance to insulin combined with a failure to produce enough additional insulin to compensate for the insulin resistance and commonly affects people who are obese and older in age [2]. Dyslipidemia is prevalent in type 2 diabetes and the most common pattern of dyslipidemia in such patients is an elevated triglycerides (TG) level and decreased high density lipoprotein- cholesterol (HDL-C) level [3]. The concentration of low density lipoprotein–cholesterol (LDL-C) in diabetic patients is usually not significantly different from non diabetic individuals but diabetic patients can have an elevated level of non HDL-cholesterol (LDL-C plus very low density lipoprotein cholesterol; VLDL-C). Type 2 diabetic patients typically have a preponderance of smaller, denser LDL particles, which possibly increases atherogenicity even if the absolute concentration of LDL-C is not significantly increased [3].

Statin drugs are inhibitors of hydroxymethylglutaryl coenzyme A (HMG-CoA) reductase, the key regulatory enzyme of cholesterol synthesis. They were developed for the reduction of serum cholesterol levels [4]. Then they were used successfully in the prevention and treatment of coronary heart disease [5, 6]. Recently, interest has been focused on the non-cholesterol-dependent, pleiotropic effects of statins [7, 8]. The anti-inflammatory pleiotropic effect of statins is supposed to result from an inhibition of the isoprene modification of signal transducers of inflammation [7].

Chronic periodontitis is a continuous inflammatory process that results in an irreversible destruction of soft tissue and bone [9] and is known to be associated with signs of systemic inflammation [10]. Progression of periodontal disease is modulated by host factors such as the presence of (DM), [11] smoking [12], and hypertension [13]. Severity of periodontitis has also been reported to have a relation to glycemic control in type 2 diabetic patients [12, 14]. Since statin drugs are commonly prescribed for the treatment of

dyslipidemia in DM [15], our aim is to assess the association between the use of statin drugs in type 2 diabetic patients and any improvement in periodontal status.

Materials & Methods

Settings:

This study was conducted in the National Diabetes Center, University of Al–Mustansiriya, Baghdad, Iraq in the period from January to March 2009.

Patients:

Eighty (40 males and 40 females) diabetic patients, attending the outpatient clinics of the National Diabetes Center for routine follow up, were enrolled in this study. Patients whose ages were ≥ 40 years were included. Medical history was taken by interviewing of patients. Exclusion was made for those having concurrent acute illness or other major systemic disease such as hypertension. Smokers were also excluded. Patients were selected with consideration of sex and exclusion criteria to compose two groups:

- Forty (20 males and 20 females) patients who were on a statin drug for at least six months. They were using minimal prophylactic dose and according to the type used (simvastatin [Zocor®] 10 mg / day or fluvastatin [Lescol®] 40 mg / day). They were assigned as (Statin group).
- Forty (20 males and 20 females) patients who received no statin drug at any time. They were assigned as (Non statin group).

Dental examination:

Dental measurements were performed by a single experienced examiner. Periodontal status was assessed using periodontal disease index which includes plaque, calculus, and periodontal components of the index [16].

Teeth examined: maxillary right first molar, maxillary left central, maxillary left first bicuspid, mandibular left first molar, mandibular right central, mandibular right first bicuspid. If any of the teeth are missing or unerupted, then only the teeth present are examined. The patients who were enrolled in this study had to have up to eleven teeth.

Laboratory analyses:

Specimen:

Serum samples were used for fasting blood glucose and lipid profile. Whole blood specimens that were collected in EDTA tubes were used for HbA_{1c}. The biochemical analyses were performed on the same day of the visit of a patient.

Blood glucose assay:

Serum Glucose was measured by enzymatic method using kits supplied by Biocon company, Germany.

HbA_{1c} assay:

HbA_{1C} was measured by Bio-Rad VARIANT Hemoglobin Testing System (Bio–Rad Laboratories, Inc., Hercules, CA 94547, USA). The system program utilizes principles of ion-exchange high-performance liquid chromatography (HPLC) for the automatic separation of HbA_{1c}. The reportable range for HbA_{1c} on the VARIANT Hemoglobin A_{1c} Program is 3.6% – 17.0%.

In such system the Hemoglobin A_{1c} ranges are interpreted as follows:

Hemoglobin A_{1c} (%)	Degree of Glucose Control
> 8	A treatment is needed
< 7	Goal
< 6	Non-diabetic Level

Lipid profile assay:

Serum total cholesterol and serum triglycerides were determined by totally enzymatic methods [17, 18]. Estimation of serum HDL-C was done by precipitation with phosphotungstate-$MgCl_2$ solution followed by enzymatic determination of cholesterol in the supernatant [19]. Estimation of serum LDL-C was done by the calculation method of Friedwald formula [20].

Statistical analysis:

Data was presented in simple statistical measures of number, percentage, range, mean and standard deviation. Statistical analysis was done by using Student's t-test for the significance of differences of the quantitative data between two means. A probability value ($p<0.05$) was considered to be statistically significant.

Results

Patients who were recruited in this study had diabetes mellitus for a duration of (2-25) years in statin group and (2-22) years in non statin group with mean values of 6.35±5.61 and 7.65± 6.59 years respectively. Their age ranges were (40-66) years in statin group and (40-69) years in non statin group with mean values of 51.53± 8.52 and 54.55± 8.12 years respectively. The differences between the two groups were statistically non significant **(Table 1).**

The mean levels of fasting blood sugar and HbA_{1c} in statin group were 172.45±43.17 mg/dl and 8.61±1.82 % respectively while in non statin group were 178.10±71.31 mg/dl and 9.10±1.26 % respectively. The differences between the two groups were statistically non significant **(Table 2).**

Table 1: Clinical and dental characteristics of statin group and non statin group of type 2 diabetic patients

Characteristics	Groups	Range	Mean ± SD (N=40)	P- value
Age (year)	**Statin group**	40-66	51.53± 8.52	**NS**
	Non statin group	40-69	54.55± 8.12	
Duration of DM (year)	**Statin group**	2-25	6.35± 5.61	**NS**
	Non statin group	2-22	7.65± 6.59	
Number of teeth	**Statin group**	11-28	21.73± 5.59	**NS**
	Non statin group	11-28	19.33± 6.42	

N : number , SD: standard deviation NS: non significant

Table 2: Assessment of glycemic control in statin group and non statin group of type 2 diabetic patients

	Group	Mean ± SD (N=40)	P - value
Fasting serum sugar (mg / dl)	**Statin group**	172.45± 43.17	**NS**
	Non statin group	178.10± 71.31	
HbA_{1c} (%)	**Statin group**	8.61± 1.82	**NS**
	Non statin group	9.10± 1.26	

N : number SD : standard deviation NSnonsignificant

The mean serum levels of TC, TG, HDL-C, and LDL-C were compared between statin group and non statin group **(Table 3).** There were no significant differences between the two groups in regard to the mean levels of TC, HDL-C, and LDL-C. The mean level of TG was higher in statin group compared to non statin group and the difference was statistically of high significance (151.10±55.02 vs. 122.43±34.39 mg/dl, P<0.01).

A comparison was made between mean values of plaque, calculus, and periodontal disease index in statin group and non statin group (**Table 4).** All mean values were lower in statin group. The difference in plaque index was statistically of high significance (1.31±.0.57 vs. 1.70±0.50, P<0.01), while the differences in calculus index and periodontal disease index were significant (0.61±0.47 vs. 0.87±0.65, and 2.75±0.89 vs. 3.16±.0.78 respectively, P< 0.05) **(Table 4).**

Table 3: lipid profile of statin group and non statin group of type 2 diabetic patients

Lipid analyte	Groups	Mean ± SD (N=40)	P- value
TC (mg/dl)	**Statin group**	218.80± 55.03	**NS**
	Non statin group	222.50± 49.30	
TG (mg/dl)	**Statin group**	151.10± 55.02	**P<0.01**
	Non statin group	122.43± 34.39	
HDL-C (mg/dl)	**Statin group**	44.50± 6.82	**NS**
	Non statin group	44.48± 3.49	
LDL-C (mg/dl)	**Statin group**	144.08± 51.32	**NS**
	Non statin group	153.54± 47.15	

SD : standard deviation NS : non significant

Table 4: Periodontal evaluation of statin group and non statin group of type 2 diabetic patients

Periodontal disease Index components	Group	Mean ± SD (N=40)	P- value
Plaque index (PI)	**Statin group**	1.31± 0.57	**P<0.01**
	Non statin group	1.70± 0.50	
Calculus index (CI)	**Statin group**	0.61± 0.47	**P<0.05**
	Non statin group	0.87± 0.65	
Periodontal disease index (PDI)	**Statin group**	2.75± 0.89	**P<0.05**
	Non statin group	3.16± 0.78	

SD : standard deviation

Discussion

Statins are in the first order of priorities for treatment of dyslipidemia in type 2 DM [3,15]. Their important role in such treatment was reinforced by the finding that they significantly reduced coronary heart disease (CHD) events and total mortality in diabetic subjects with high LDL cholesterol [21] as well as in patients with average LDL cholesterol levels who already have clinical CHD [22].

The results of lipid profile assay in our patients revealed that mean levels of TC and LDL-C in statin group were comparable or somewhat lower than in non statin group while the mean level of HDL-C was comparable between the two groups. This is consistent with the studies which reported that statins do good lowering of LDL-C and modest raising of HDL-C [23], and it is a good achievement for statin therapy.

The finding of a TG mean level in statin group that was significantly higher than in non statin group is related to the fact that the stain group patients are diabetics who already have hypertriglyceridemia.. Although specific targets for treatment of hypertriglyceridemia are not provided in the current clinical practice guidelines[24], a desirable TG level has been suggested to be < 1.7 mmol/L (<150 mg /dl) [23] since below this level of TG there are fewer associated metabolic abnormalities such as low HDL-C, small dense LDL particles and postprandial lipemia [25].It is important to mention that statins are acting as moderate reducers of TG level only in high doses while in our patients minimal prophylactic doses of statins were used [23]. High doses of statins are not recommended in DM and their prescription carries the risk of more side effects [26].

Periodontal disease index decreased significantly in study patients on statin therapy. It is not probable that a difference in glycemic control between the study groups has a role in such difference in periodontal status because measures of glycemic state (fasting serum sugar and HbA_{1c}) were comparable between the two study groups. The improvement in the periodontal status is more probably related to statin therapy since statins are known to have pleiotropic anti-inflammatory effects [7,8]. If this important finding is confirmed by prospective studies, it may lead to a better approaches in the management of periodontitis.

Our study revealed also a decrease in dental plaque index in statin group that was statistically of high significance in statin group. This is consistent with the finding in some studies [27] although they were unable to explain the causative mechanism. Calculus formation also decreased significantly. This may be due to a decrease in plaque formation in statin group as calculus is the last stage in the maturation of dental plaque [28].However, a relation to the lipid lowering effect of statins is still possible. For example, some researchers have reported that statins could decrease gallstone formation [29].

In conclusion, diabetic patients on statin therapy exhibit fewer clinical signs of periodontal disease than diabetic patients without statin therapy.

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