Endokrynologia Polska/Polish Journal of Endocrinology
Tom/Volume 60; Numer/Number 5/2009
ISSN 0423–104X

Dyslipidaemia and its management in diabetic patients in an academic centre in Iran

Leczenie dyslipidemii u chorych na cukrzycę w ośrodku akademickim w Iranie

Elham Faghihimani, Peyman Adibi, Masoud Amini

Isfahan University of Medical Sciences, Isfahan, Iran

Abstract

Introduction: Dyslipidaemia is accompanied with increased cardiovascular events in diabetic patients. Today there have been some improvements in the management of dyslipidaemia using lifestyle modification and medications. In this study we evaluate the management of dyslipidaemia in an academic centre.

Material and methods: This is a descriptive study, from January 2003 until December 2007. All type 2 diabetic patients who were more than 30 years old and had at least 2 visits per year were eligible for including.

Results: Overall, 1179 patients (70.2% women) were assessed. Mean LDL-C in 2003 was 124.6 ± 34.6 mg/dL, and decreased to 109.7 ± 28.9 mg/dL in 2007 ($p < 0.05$). 21.0% of patients in 2003 and 40.5% of them in 2007 had LDL-C < 100 mg/dL. TG did not change during these years. There was an increase in the use of statins from 76.3% to 84.3% (p-value < 0.05) during the 5 years since 2003, but a decrease in the use of fibrates.

Conslusions: Although recently we have made improvements in the control of dyslipidaemia in diabetic patients, we have not reached our goals. Of late, physicians have emphasized the use of statins in diabetic patients, which has resulted in much better levels of LDL-C, but still less than half of the patients are at ideal levels. In conclusion, we should revise our point of view to begin and intensify treatment of dyslipidaemia in diabetic patients, to achieve the goal of treatment and prevent cardiovascular events optimally.

(Pol J Endocrinol 2009; 60 (5): 353–356)

Key words: *dyslipidaemia,type 2 diabetes, statins*

Streszczenie

Wstęp: Dyslipidemia u chorych na cukrzycę wiąże się ze zwiększoną częstością zdarzeń sercowo-naczyniowych. W leczeniu dyslipidemii obejmującym modyfikację stylu życia i farmakoterapię nastąpił znaczny postęp. Celem niniejszego badania była ocena leczenia dyslipidemii w ośrodku akademickim.

Materiał i metody: Badanie obejmowało okres od stycznia 2003 roku do grudnia 2007 roku. Do badania włączono wszystkich chorych na cukrzycę typu 2 w wieku powyżej 30 lat, którzy odbywali co najmniej 2 wizyty rocznie.

Wyniki: Oceniono łącznie 1179 chorych (70,2% stanowiły kobiety). Średnie stężenie cholesterolu frakcji LDL w 2003 roku wynosiło 124,6 ± 34,6 mg/dl. Uległo ono obniżeniu i wynosiło 109,7 ± 28,9 mg/dl w 2007 roku ($p < 0,05$). Odsetek chorych, u których stężenie cholesterolu frakcji LDL było niższe niż 100 mg/dl wynosił 21,0% w 2003 roku i 40,5% w 2007 roku. Stężenie triglicerydów nie zmieniło się w tym okresie. W okresie 5 lat od 2003 roku nastąpiło zwiększenie częstości stosowania statyn z 76,3% do 84,3% ($p < 0,05$), zmniejszyło się natomiast zużycie fibratów.

Wnioski: Mimo że w ostatnich latach nastąpiła poprawa w zakresie kontroli stężenia lipidów u chorych na cukrzycę, nadal rzadko udaje się osiągnąć cele terapii. W najnowszych doniesieniach podkreśla się, że stosowanie statyn u chorych na cukrzycę powoduje znaczne obniżenie stężenia cholesterolu frakcji LDL, jednak docelowe wartości uzyskuje nadal mniej niż połowa pacjentów. Podsumowując, należy zrewidować dotychczasowe poglądy na temat leków hipolipemizujacych i wcześniej rozpoczynać intensywną terapię dyslipidemii u chorych na cukrzycę, aby osiągnąć cele leczenia i zapewnić optymalną prewencję zdarzeń sercowo-naczyniowych.

(Endokrynol Pol 2009; 60 (5): 353–356)

Słowa kluczowe: *dyslipidemia, cukrzyca typu 2, statyny*

Peyman Adibi, M.D., Isfahan University of Medical Sciences, Isfahan, Iran, tel.: 00983117923060, faks: 00986687898,
e-mail: adibi@med.mui.ac.ir

Introduction

The prevalence of diabetes mellitus (DM) is increasing around the world [1]. Today we know that diabetes mellitus is a metabolic disorder that is associated with hyperglycaemia, hypertension, dyslipidaemia, and insulin resistance. Dyslipidaemia in DM is defined by elevated triglycerides (TG), low high-density lipoprotein cholesterol (HDL-C), and small dense low-density lipoprotein cholesterol (LDL-C) particles. Total cholesterol and LDL-C concentration is usually similar to that found in the general population [2–4].

This lipid deregulation is accompanied by elevated cardiovascular disease risk [5]. In the UK prospective diabetes study, 49% of deaths in diabetics within 10 years were due to cardiovascular events [6]. Data such as these show the significance of controlling dyslipidaemia as a cardiovascular risk factor in diabetic patients. Results from recent trials show a reduction of cardiovascular disease in patients who receive lipid-lowering therapy in the context of both primary and secondary prevention [7–9].

It has been shown that, although increasing numbers of diabetic patients are tested for dyslipidaemia, fewer patients reach target goals [10–12]. Data from Eastern countries also show poor control of dyslipidaemia in diabetes mellitus [13–15]. The aim of the present study was to evaluate dyslipidaemia and its management among type 2 diabetics in a Middle Eastern population in an academic centre in Iran, and to compare this with other countries.

Material and methods

In this descriptive study we evaluated diabetic patients in an ambulatory setting in the Endocrinology and Metabolism Research Centre (EMRC) of Isfahan University of Medical Science from January 2003 to December 2007.

Patients were eligible for inclusion if they were more than 30 years of age, had type 2 diabetes mellitus, and had at least two visits per year. This clinic included both primary and specialty practices. Patients were referred to the centre by physicians from around the town; all the patients had files in the centre, including all of the follow up data obtained during regular visits. The physicians were trained general practitioners and internists. The follow up of patients in this centre was in accordance with the American Diabetes Association (ADA) guidelines. Overall, 1179 patients were evaluated for blood pressure, lipid profiles, HbA_{1c}, and course of treatment.

Data were collected from computerized forms in the centre. For each patient, all the venous blood samples were collected after 8 hours of fasting, and were analyzed using an enzymatic method. The results were saved in a central computer.

Statistical methods

Data are presented as mean (±SD) values for continuous variables. Lipid profiles were classified as controlled and uncontrolled, according to ADA guidelines, i.e. LDL-C < 100 mg/dL, Total cholesterol < 200 mg/dL, HDL > 40 mg/dL, and TG < 150 mg/dL. HBA_{1c} was considered acceptable when it was less than 7 percent.

Coronary artery disease was selected as a major macrovascular outcome of diabetes and hyperlipidaemia and their treatment aim. It was defined as positive if the patient developed some kind of acute coronary syndrome, including myocardial infarction, unstable angina pectoris, investigated, cardiologist-approved or coronary angiogram-proven stable angina and its equivalents, and sudden cardiac death.

Comparisons between means of variables between different measurement times were performed using paired student t-test. Correlation of continuous quantitative variables, including lipid levels, HBA1c, and BMI, was calculated using linear regression after establishing essential data characteristics. Classified lipid levels and HBA1c as well as CAD were cross tabulated, and Chi-square tests were utilized to establish possible effects.

All comparisons were considered as significant at $p < 0.05$. Analysis was done using SPSS statistical package version 13.

Results

Body mass index increased minimally by about 0.36 kg/m^2 during the period from 2003 to 2007 ($p < 0.01$). Systolic and diastolic blood pressure were decreased respectively (mean Systolic blood pressure: 137.9 ± 17 mm Hg to 131.7 ± 19 mm Hg; Mean diastolic blood pressure: 88.4 ± 9 mm Hg to 82.0 ± 10 mm Hg).

Overall, 70% of patients were dyslipidemic, (total cholesterol ≥ 200 mg/dl or LDL-C ≥ 100 mg/dL or triglycerides ≥ 150 mg/dL) a result which was similar to other reports.

Mean of LDL-C in 2003 was 124.6 ± 34.6 mg/dL and decreased to 109.7 ± 28.9 mg/dL in 2007 (p-value < 0.05). Of course, this decrease of LDL-C was associated with increase of TG from 181.7 ± 120.5 mg/dL in 2003 to 191.0 ± ± 89.2 mg/dL in 2005 (p-value < 0.05), but again decreased to 174.7 ± 76.1 mg/dL in 2007.

HDL-C did not change significantly (mean = 44.5 ± ± 10.6 mg/dL) but total cholesterol also decreased from 199.07 ± 66.5 mg/dL to 184.8 ± 60.0 mg/dL (p-value < 0.05) during these years, so HDL/cholesterol ratio increased from 22.25% to 24.47% ($p < 0.01$). These chan-

Table I. *Drug treatment in 2003 and 2007*

Tabela I. *Stosowanie leków w latach 2003 i 2007*

% of patients who receive	2003	2007	p-value
Statin	76.3%	84.3%	0.02
Fibrate	20.5%	6.5%	0.00
Both	3.2%	9.2%	0.00

Table II. *Patients at goal of treatment in 2003 and 2007*

Tabela II. *Odsetek chorych, u których osiągnięto cele leczenia w latach 2003 i 2007*

% at goal	2003	2007	p-value
HbA_{1c}	32.8%	36.4%	0.08
Blood pressure	29.6%	50.6%	0.00
LDL-C	21.0%	40.5%	0.00
TG	43.2%	42.7%	0.8

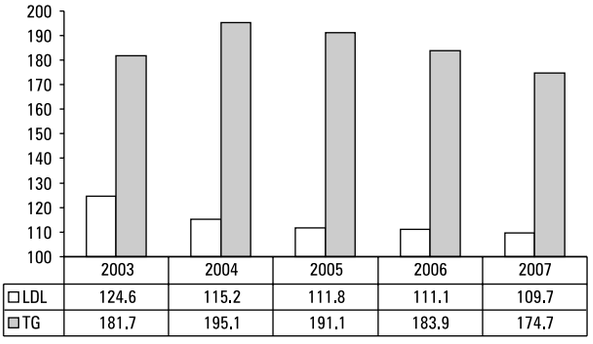

Figure 1. *Trends in LDL-C and TG levels during 5 years*

Rycina 1. *Zmiany stężeń cholesterolu frakcji LDL i triglicerydów w ciagu 5 lat*

ges were seen in all age groups and there were no differences between men and women.

In the year 2003, the mean of HbA_{1c} was 7.9 ± 1.7% and was not significantly altered in year 2007 (7.6% ±1.5%). During the follow-up period, HBA_{1c} was negatively but weakly correlated with LDL, total Cholesterol, and TG levels (r was 0.139, 0.178, and 0.174, respectively; $p < 0.05$). When HBA1c level less than 7 percent was set as the optimal goal, patients with acceptable HBA1c had significantly more chance to have controlled TG level in 2003, i.e. 56 percent of those with good HBA_{1c} had TG under 150 mg/dL whereas 38 percent of uncontrolled HBA_{1c} cases had acceptable TG ($p < 0.01$). Similar findings, but to a lesser extent, were seen for total cholesterol (61 and 52%, respectively) but not for LDL ($p = 0.113$). This relation changed in 2007 for cholesterol, and absolute reduction in risk of effect of HBA_{1c} on total cholesterol deceased to 5 percent due to HBA_{1c}.

All of the dyslipidemic patients in this centre were treated with lifestyle modification and medications such as statins, fibrates, or both (Table I). As shown in table 1, use of statins (as opposed to fibrates) has increased during recent years, and the number of patients who reach the goal of treatment according to ADA guidelines (LDL-C < 100 mg/dL, Total cholesterol<200 mg/dL, HDL > 40 mg/dL) has increased (Table II). This statement was not shown to be correct for TG (Fig. 1). It was shown that being in a controlled TG state in 2003 was a predictor of TG control status in 2008; 72% of those with under 150 mg/dL TG remained controlled in 2007.

The rate of development of CAD at the end of the follow-up period was lower in those with optimal LDL than uncontrolled LDL levels (32% *v.* 60%); optimal cholesterol also negatively affected CAD incidence (39% *v.* 60%).

Discussion

In this observational study, we showed an increased use of statins as lipid lowering agents, and consequently better control of lipids between 2003 and 2007 in the general diabetic population. This improvement due to use of statins, not fibrates, resulted in a decrease of LDL-C but not of TG, a finding that may have been assumed previously due to the pharmacological characteristics of statins. It was also reconfirmed in our findings when we found a strong correlation of start time and end time TG control status.

Other factors like HbA_1C, systolic, and diastolic blood pressure also improved during these years, but still are not ideal to any significant degree. Less than half of the patients had $HbA_{1c} < 7\%$, which was similar to other studies, and for blood pressure, the results were much better; about 57% of patients had BP less than 130/80 mm Hg, although it was better than in some other studies [11–15].

LDL-C was less than 100 mg/dL in about 40% of our patients in 2007. One study in Kuwait has shown that LDL-C less than 100 mg/dL was seen in 14% of diabetic patients in an outpatient clinic [16]. Another study in the US has shown that 46.1% of diabetic patients of academic centres had LDL-C less than 100 mg/dL [11]. This means that we have improved the control of dyslipidaemia much better than our neighbouring countries.

Despite these generally favourable improvements in the management of dyslipidaemia in diabetic patients and the use of lipid lowering agents in about 84% of patients, only 40.6% have ideal LDL-C. This might po-

ssibly show that although our physicians start the lipid-lowering agents they do not intensify the agent according to the patients lipid levels, or perhaps the maximal drug effect does not match acceptable lipid levels in some. This may be investigated in future studies regarding the dose-effect relation for statin-lipid model and drug efficacy in our setting.

One interesting result of the present study was the discovery of a weak correlation between HBA_{1c} and lipid profiles. This finding was also previously reported by Khan [17] and Grant [18]. Surely, when the data of HBA1c become left skewed (i.e. the major proportion of patients are distributed within the lower levels of HBA_{1c}), then the expected correlation would not be large. In the other words, when you achieve relatively optimal goals in glycaemic control, other means must be used to improve patient outcome.

Several causes have been proposed regarding why physicians do not prescribe enough drugs [19–22]. One problem is that they might be afraid of side effects of the combination of statin and fibrates. The use of statins in diabetic patients has been emphasized recently resulting in a decrease in use of fibrates (20.5% to 6.5% between 2003 and 2007); only 9.2% of patients received both drugs that resulted in no improvement of TG level between 2003 and 2007.

In our next study we would like to evaluate the effect of dosage and intensification of medications in dyslipidaemic patients. A limitation of this study is that we assessed the management of dyslipidaemia within a group of diabetic patients in an academic centre, and also that we chose patients with regular visits. So, it does not show the situation in the whole diabetic population.

Another limitation is that we do not have enough data from non-diabetic patients to compare the results. A strength of this study is that the data were collected over a 5-year period, enabling the assessment of trends in lipid levels.

References

1. Beckman JA, Greager MA, Libby P. Diabetes and atherosclerosis: epidemiology, pathophysiology, and management. JAMA 2002; 287: 2570–2581.
2. Schernthaner G, Kostner G, Dieplinger H et al. Apolipoproteins (A-I, A-II, B), LP (a) Lipoprotein and lecithin: cholesterol acyltransferase activity in diabetes mellitus. Atherosclerosis 1983; 49: 277–293.
3. Gary A, Grundy S. Management of dyslipidemia in NIDDM. Diabetes Care 1990; 13: 153–169.
4. Austin MA, Edwards KL. Small, dense low density lipoproteins, the insulin resistance, syndrome and non-insulin-dependent diabetes. Curr Opin Lipidol 1996; 7: 167–171.
5. Charles A. Reasner. What is the most effective strategy for managing diabetic dysliplidemia? Atherosclerosis supplements 2005; 6: 21–27.
6. UK Prospective Diabetes Study Group. Effect of intensive blood-glucose control with metformin on complications in overweight patients with type 2 diabetes (UKPDS 34). Lancet 1998; 352: 854–865.
7. Cannon CP, Braunwald E, Mccabe CH et al. Intensive versus moderate lipid lowering with statins after acute coronary syndromes. N Eng J Med 2004; 350: 1495–1504.
8. Colhoun HM, Betteridge J, Durrington PN et al. Primary prevention of cardiovascular disease with atorvastatin in type 2 diabetes in the collaborative atorvastatin diabetes study (CARDS): multicentre randomized placebo-controlled trial. Lancet 2004; 364: 685–696.
9. Heart Protection study collaborative group. MRC/BHF heart protection study of cholesterol lowering with simvastatin in 20536 high risk individuals a randomized placebo controlled trial. Lancet 2002; 360: 7–22.
10. Beaton SJ, Nag SS, Gunter MJ et al. Adequacy of glycemic, Lipid and blood pressure management for patients with diabetes in a managed care setting. Diabetes Care 2004; 27: 694–698.
11. Grant RW, Buse JB, Meigs JB. Quality of diabetes care in U.S. academic medical centers: Low rates of medical regimen change. Diabetes Care 2005; 28: 337–442.
12. Saaddine JB, Cadwell B, Gregg EW et al. Improvements in diabetes processes of care and intermediate out comes: United States, 1988–2000. Ann Intern Med 2006; 144: 465–479.
13. Akanji AQ. Diabetic dyslipidemia in Kuwait. Med Princ Pract 2002; 11 (Suppl. 2): 47–55.
14. Ismail IS, Nazaimoon W, Mohamad W et al. Ethnicity and glycemic control are major determinants of diabetic dyslipidemia in Malaysia. Diabet Med 2001; 18: 501–508.
15. Hammoudeh AI, Haddat J, Al-Mousa E et al. Is dyslipidemia in middle eastern patients with type 2 diabetes mellitus different from that in the west? The Jordan Hyperlipidemia and Related Targets Study (JOHARTS-3). Clinical Diabetes (Middle East edition) 2006; 3: 128–131.
16. Al-Adsani A, Memon A, Sureshnity A. Pattern and determinants in type 2 diabetes mellitus patients in Kuwait. Acta Diabetol 2004; 41: 129–135.
17. Khan Ha, Sobki SH, Khan SA. Association between glycemic control and serum lipid profile in type 2 diabetic patients: HbA1c predicts dylipidemia. Clin Exp Med 2007; 7: 24–29.
18. Grant T, Soriano Y, Marantz PR et al. Community-based screening for cardiovascular disease and diabetes using HbA1c. Am J Prev Med 2004; 26: 271–275.
19. Phillips LS, Branch WT, Cook CB et al. Clinical inertia. Ann Intern Med 2001; 135: 825–834.
20. Kedward J, Dakin L. A qualitative study of barriers to the use of statins and the implementation of coronary heart disease prevention in primary care. Br J Gen Pract 2003; 53: 684–689.
21. Parnes BL, Main DS, Dickinson LM et al. Clinical decisions regarding HbA_1c results in primary care: a report from CaReNet and HPRN. Diabetes Care 2004; 27: 13–16.
22. Hicks PC, Westfall JM, Van Vorst RF et al. Action or inaction? Decision making in patients with diabetes and elevated Blood pressure in primary care. Diabetes Care 2006; 29: 2580–2585.