Statin untuk Pencegahan Primer Komplikasi Kardiovaskular pada Pasien DM tipe 2 dengan Profil Lipid yang baik: Laporan Berbasis Bukti

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Kata Kunci: Diabetes mellitus tipe 2, dislipidemia, statin, profil lipid normal, kardiovaskular
Statin Administration for Primary Prevention of Cardiovascular Complication Among Type 2 Diabetic Patients with Good Lipid Profile: Evidence Based Report

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Abstract: One of the most fatal complications in diabetic patients is diabetic heart disease. Dyslipidemia becomes one of many risk factors that contribute to the occurrence of cardiovascular complication among diabetic patients. Some studies showed the effectiveness of statin in improving lipid profile among type 2 diabetic patients with dyslipidemia, which finally reduce the occurrence of cardiovascular complication. This report aims to identify whether statin is effective in preventing cardiovascular complication among diabetic patients with normal lipid profile. A search was conducted on PubMed and Google. After the selection of title and abstract was done using inclusion and exclusion criteria. Eleven original articles were found, but only three studies were used. All selected studies were critically appraised for its validity, importance and applicability. All three studies showed the reduction in cardiovascular complication and mortality related to cardiovascular. The relative risk reduction ranged from 18-37.5%. The absolute risk reduction ranged from 1.9%-3% and number needed to treat ranged from 33-53. Beside the reduction in cardiovascular complication, statin therapy was also proven to decrease the occurrence of cerebrovascular complication among type 2 diabetic patients. The administration of statin is effective in reducing the risk of cardiovascular complication among type 2 diabetic patients with normal lipid profile. J Indon Med Assoc. 2011;61:363-7.

Keywords: Type 2 Diabetes mellitus, dyslipidemia, statin, normal lipid profile, cardiovascular disease.

Introduction

Diabetes mellitus (DM) is a metabolic disorder characterized by hyperglycemia. Diabetes mellitus causes a wide variety of chronic complications on so many organs such as: eyes, kidney and blood vessels in long term. DM is commonly accompanied by others metabolic disorders. ¹ ²

The prevalence of DM increased in the last two decades. The number of DM cases increased from 30 millions cases in 1985 to 177 millions cases in 2000.² According to International Diabetes Federation, there will be 380 millions patients with DM in 2025. The prevalence of Type 2 DM in Indonesia is 5.7%.³ As the number of DM patients increased worldwide, the number of DM patients with complication would increase eventually.

Diabetic heart disease is the number one cause of mortality among DM patients. It is due to the premature atherosclerosis process.⁴ Diabetic heart disease refers to heart disease that happens among diabetic patients due to metabolic factors interaction. Compared with people who do not have diabetes, diabetic patients have twice to four times the risk of developing coronary heart disease. Diabetic patients develop coronary heart disease at younger age compared to those who do not have diabetes.¹ ⁵

Many studies show the effectiveness of statin in improving lipid profile among type 2 diabetic patients with dyslipidemia.¹ ⁶ A normal lipid profile will reduce the occurrence of cardiovascular complication eventually. This report is made to identify whether statin administration is effective as primary prevention of cardiovascular complication among type 2 diabetic patients with normal lipid profile.

Clinical Question

Is statin administration effective as primary prevention for cardiovascular complication among type 2 diabetic patients with normal lipid profile?

Method

The search was conducted on PubMed,⁸ and Google, on April 2⁴th and 4⁴th 2011, using the keywords “adult,” “statin,” “diabetes” and “cardiovascular” along with its synonyms and related terms (Table 1).
Search strategy, results and the inclusion and exclusion criteria are shown in a flowchart (Figure 1).

![Flow Chart of Search Strategy](image_url)

Figure 1. Flow Chart of Search Strategy

After the selection, critical appraisal was done using several aspects based on Center of Evidence-based Medicine, University of Oxford for therapy study (Table 2).10

Result

From the selection and filtration, eleven articles were obtained, out of which only three full-text articles were available. These three articles were appraised and considered to have a good validity and relevance. Three articles, obtained after searching, selection and filtration method, reported the use of statin for good to borderline lipid profile.

Discussion

Colhoun HM et al7 conducted a study to evaluate whether the administration of 10 mg of atorvastatin is significantly useful in reducing the occurrence of primary cardiovascular complication among diabetic patients with good lipid profile. The result of this study is that the administration of 10 mg of atorvastatin everyday reduce the risk of cardiovascular complication as much as 37% with the Control Event Rate (CER) was 5.5%, Experimental Event Rate (EER) was 3.6%, Relative Risk Reduction (RRR) was 34.5%, Absolute Risk Reduction (ARR) was 1.9% and Number Needed to Treat (NNT) was 53 (p=0.001).

Collins R. et al8 also found a significant reduction in the occurrence of cardiovascular complication. This study involved 20 536 patients, aged between 40-80 years old with good to borderline lipid profile. In the simvastatin group there were 357 patients (3.5%) who finally got cardiovascular complication compared with 574 patients (5.6%) in the placebo group. RRR was 37.5%, ARR was 2.1% and NNT was 47.

Goldberg et al8 conducted a study about the administration of pravastatin in 586 diabetic patients. The patients involved in this study have good-borderline lipid profile. The result of this study was the administration of pravastatin reduced mortality rate due to coronary heart disease. The RRR was 18%, ARR was 3%, and NNT was 33.

Colhoun et al7, Collins et al9 and Goldberg B et al9 showed similar result that the administration of statin in diabetic patients with good clinical profile will eventually lead to reduction of cardiovascular complication.

Colhoun et al7, Collins et al9 and Goldberg B et al9 showed that statin administration significantly reduce the occurrence of cardiovascular risk as much as 37%, 37.5% and 46% respectively. Beside the reduction of cardiovascular complication, Colhoun et al7 also showed a 48% reduction in the occurrence of stroke. According to this study, statin administration is proven to be effective and safe.

The ARRs in these three studies ranged from 1.9 -3% and the NNT ranged from 33-55. The NNT from these three journals can still be considered beneficial since preventive measure that produced small effects in large numbers of patients will have high NNT.

Statin administration is considered safe due to the minimal side effect occurred during this study. Out of 2838 patients participated in this study only a small proportion of patients were diagnosed to have rhabdomyolisis (61 patients in statin group and 72 patients in placebo group).

Beside cardiovascular complication, Collins et al9 and Goldberg B et al9 also provided the comparison of mortality rate among the two groups. The mortality rate reduction in
the statin group is mainly due to the reduction of cardiovascular complication. As stated above, cardiovascular complication is the leading cause of mortality among diabetic patients.

Statin is a widely known drug and well distributed acrossed Indonesia. Some statins are affordable and can be purchased with prescription in any pharmacy. According to statin characteristics and its efficacy, statin can be used as a preventive measure of cardiovascular complication among diabetic patients.

Conclusion

All three studies gave the same recommendation that the administration of statin is a safe and effective way to reduce cardiovascular complication among type 2 diabetic patients with good lipid profile. Besides the reduction of cardiovascular complication, these studies also concluded that statin therapy reduce the mortality rate and the occurrence of cerebrovascular complication. Unfortunately, there was no definite lipid profile range as to begin statin therapy, so risk factors stratification could be put into consideration when presented with a diabetic patient with good lipid profile. It is also crucial to encourage a healthy lifestyle modification to all diabetic patients before implementing any medication. Although the side effects observed in these study is minimal, follow-up is recommended for all patients receiving statin therapy. Rhabdomyolysis, the most common side effect of statin therapy, can be identified by creatine-kinase examination.

Recommendation for Clinical Use

These report can be translated into clinical practise with the following example. A 46 years old man was diagnosed with type 2 diabetes mellitus. This patient had been smoking for more than 20 years and rarely had exercise. According to physical examination, the patient was in a good condition and there was no diabetic complication observed. The laboratory findings were all within normal range, including lipid profile (total cholesterol, tryglyceride, LDL and HDL). There were no abnormality found on the X-ray and electrocardiography examination. Beside the regular prescriptions of oral diabetic medication, the doctor also prescribed atorvastatin 10 mg to be consumed once daily. The statin prescription for this patient is an effective preventive measure for cardiovascular complications.

References

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