

Alternate-day dosing of statins for secondary prevention of coronary artery disease/The comparison of the effects of standard 20 mg atorvastatin daily and 20 mg atorvastatin every other day on serum LDL-cholesterol and high sensitive C-reactive protein levels

Koroner arter hastalığının ikincil korunması için gün aşırı statin dozu/Günaşırı 20 mg atorvastatin tedavisinin serum LDL-kolesterolü ve yüksek duyarlı C-reaktif protein düzeyleri üzerine etkisinin günlük 20 mg atorvastatin tedavisi ile karşılaştırılması

Dear Editor,

We have read with great interest the article by Keleş T and coworkers (1). In that well-designed study, they indicated that alternate-day dosing of atorvastatin causes a significant lipid-lowering and antiinflammatory effects similar to that of daily administration and it may provide some cost savings (1).

Although, it has been known that statins reduce the risk of adverse cardiovascular events in patients with coronary heart disease (CHD), the optimal level of low-density lipoprotein cholesterol (LDL-C) is still unclear. Intensive statin treatment produces greater reductions in LDL-C and high sensitive C-reactive protein levels (hs-CRP) more than standard dose treatment. There are three major studies comparing high-dose versus standard-dose strategies are Aggrastat to Zocor (A to Z), The Reversal of Atherosclerosis with Aggressive Lipid Lowering (REVERSAL) and Pravastatin or Atorvastatin Evaluation and Infection Therapy-Thrombolysis In Myocardial Infarction 22 (PROVE-IT-TIMI 22). All of three studies demonstrated significant clinical benefit by intensive lipid-lowering therapy.

The use of statin therapy is known to reduce CRP level independent from cardiovascular risk factors. However, many patients have a high CRP level despite statin therapy. PROVE IT and MIRACL (Myocardial Ischemia Reduction with Aggressive Cholesterol Lowering C-reactive protein) studies showed that high-dose atorvastatin resulted in a significant reduction in inflammation markers (2). The efficacy of statin treatment was also supported by reduction in atherosclerotic burden measured by intravascular ultrasound (IVUS). The REVERSAL study was showed that intensive statin treatment halted the progression of coronary atherosclerosis, whereas standard therapy did not (3).

Alternate-day statin therapy seems to be efficacious in primary prevention and but there is no published data showing the efficiency in patients with acute coronary syndromes (ACS). Patients with ACS benefit from lowering of LDL-C to levels below current guideline recommendations and the greater benefit was found in the group with greater reduction. Nevertheless, Ray et al. (4) in PROVE IT-TIMI study indicated the requirement and beneficial effects of in-hospital and long-term use of intensive statin therapy in patients with ACS. These beneficial effects were apparent as early as 30 days and sustained over 2 years (4). The early benefits were seen likely to result from pleiotropic effects, whereas long-term events were resulted by the lowering of LDL-C. In addition, intensive statin therapy reduces the risk of hospitalization for heart failure after ACS.

Although many coronary risk factors were included in this study, body mass index (BMI) was not evaluated. Nicholls et al. (5) analyzed the results of REVERSAL study and they indicated that intensive statin treatment halted plaque progression (determined by IVUS) and vascular inflammation in obese patients whereas moderate therapy did not. Also, intensive therapy appears to decrease the adverse cardiovascular events in patients with previous coronary artery bypass surgery compared with moderate statin therapy.

Despite the beneficial effects of intensive statin therapy, alternate-day dosing might be efficacious and safe alternative to daily dosing for primary

prevention especially in patients who have discontinued the therapy secondary to side effects, most commonly myalgias. However, this treatment strategy is still controversial in patients with ACS.

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Author reply

Dear Editor,

We thank to authors for their comments on our previous article "The comparison of the effects of standard 20 mg atorvastatin daily and 20 mg atorvastatin every other day on serum low-density lipoprotein (LDL) cholesterol and high sensitive C-reactive protein levels (hs-CRP)"(1). We agree with their comments. Lipid lowering with statins is beneficial in patients with dyslipidemias for both primary and secondary prevention of coronary heart disease. The mechanisms of benefit are incompletely understood. Some part of the benefits of statin therapy is believed to be due to "pleiotropic" effects separate from the effect on LDL-C. Intensive statin therapy appears to be superior to standard dose in patients being treated for an acute coronary syndrome (2). In patients with stable coronary artery disease less intensive statin therapy compared with, more intensive statin therapy results in small reductions in cardiovascular events, but appears to have no effect on all-cause mortality (3). In addition, higher doses of statins are generally less well tolerated than lower doses, with higher rates of side effects including muscle and liver toxicity. For many patients, these side effects are minor (muscle pain or asymptomatic elevations of aminotransferases), however these may lead to patients discontinuing statin therapy and thus losing the clear mortality benefits of taking a statin rather than no therapy. A further issue to keep in mind is cost. The cost to society may also be excessive under some circumstances.

More than six million elderly adults in USA, are newly eligible for statin therapy based on a strict interpretation of the Justification for the Use of Statins in Primary Prevention: An Intervention Trial Evaluating Rosuvastatin (JUPITER) trial (4). The number of individuals eligible for statin therapy increases to more than 10 million adults when extrapolated to individuals with normal LDL-cholesterol levels, as determined by the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP) cutoff points, and elevated hs-CRP levels. In conclusion, alternate-day dosing may be efficacious and safe alternative to daily dosing for primary prevention in some individuals.

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Dilemma in the strategy of treatment: revascularization or medical treatment?

Tedavi stratejisinde ikilem: Revaskülarizasyon mu, tıbbi tedavi mi?

Dear Editor,

We have read, with a great interest, the paper titled "Dilemma in the strategy of treatment: revascularization or medical treatment" by Tatlı et al. (1) which gives rise to thought about patients without angina with coronary artery diseases. In their summary of the case, they reported literature search and their own opinions on the case having significant narrowing at the left anterior descending (LAD) and right coroner artery (RCA). Principally, we would like to mention that the one of the most striking point of the case was a 43-year-old female suffering from coronary artery disease. We advocate that the success for all treatment attempts (such as medical, percutaneous coronary intervention (PCI), coronary artery bypass surgery (CABG)) will be low without determination of the etiology of early atherosclerosis.

Besides the study of Hochman et al. (2) cited by the authors in their paper for the proof of revascularization of infarct related artery in the

treatment of late stage myocardial infarcts (MI) as being not entirely successful, more well-rounded study of Abbate et al. (3) reported a positive opinion on possibility of the revascularization in late stage cases.

Search of recently published literature revealed that there has been a debate in priority whether to use PCI or CABG in two vascular disease patients (4-6). Kimura et al. (4) compared the PCI and CABG and reported that there was no significant difference between two groups especially in asymptomatic patients with LAD and RCA clogging. However, Daemen et al. (5) also found no differences between groups, the repeated revascularization and major cerebrovascular attacks rates were higher in PCI groups. However this case, as pointed out by Eagle et al. (6) can be considered within the indication of class IIA of asymptomatic coronary artery two-vessel disease.

Our contribution to the authors own views politely stated and open for other ideas is that priority should be directed toward stress tests (myocardial perfusion scintigraphy, stress electrocardiography) before ventricular functions of patients deteriorate and evaluation of live tissue then if feasible PCI and CABG may practiced.

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Author reply

Dear Editor,

We appreciate the comments of the authors concerning our manuscript "Dilemma in the strategy of treatment: revascularization or medical treatment?"(1).