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Effect of nebivolol and metoprolol treatments on serum asymmetric dimethlyarginine levels in hypertensive patients with type 2 diabetes mellitus

Tip 2 diyabetes mellituslu hastalarda nebivolol ve metoprolol tedavilerinin serum asimetrik dimetilarjinin düzeyleri üzerine etkisi

Dear Editor,

My thoughts relate to the article entitled "Effect of nebivolol and metoprolol treatments on serum asymmetric dimethylarginine levels in hypertensive patients with type 2 diabetes mellitus" and belongs to Oguz et al. (1). There are some points that should be attentively dwelt upon an original article's purpose oriented groups.

The statistically undifferentiated groups of metoprolol and nebivolol-treated as the percentages of oral antidiabetic drug users, diet-limited oral antidiabetic drug users and only diet-limited patients, subsidized the exclusion of the probable effects of diet on ADMA levels. In this way, that study, emphasized the importance of groups' assembly and selectivity. According to Fard et al (2), diet has an important effect on ADMA levels. In consequences, it is pleasure to see added statistical data according to the criticism on the present study.

Furthermore, to contribute to the next studies, it may be important to determine the correlation between the biochemical parameters (especially glucose and triglyceride) and ADMA levels in both treated groups and this determination may provide assistance to interpret the effects of ADMA levels on these patients in details.

The authors emphasized the neutral effects of nebivolol on ADMA levels. The word of "Neutral" is a chemical term. It clearly means that neither acid nor alkaline. According to my thoughts, the word "neutral" is used in wrong meaning in this study so; it is not the declaration of the article's real thought. Seen from this aspect, nebivolol has no effect on ADMA levels. It may be meaningful to use "no effect" instead of "neutral". That is why; scientific terms should be used attentively as in their meanings.

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Authors Reply

Dear Editor,

Many thanks for the evaluation and suggestions concerning our clinical study entitled "Effect of nebivolol and metoprolol treatments on serum asymmetric dimethylarginine levels in hypertensive patients with type 2 diabetes mellitus" (1) published in Anadolu Kardiyoloji Dergisi in December 2007.

The term "neutral effect" is commonly used in literature while mentioning metabolic effects of drugs (2-3). For example, it is known that calcium channel blockers have neutral effect on serum lipid levels and insulin resistance (4). In our study the statement that the effect of nebivolol, a beta-blocker agent, on serum asymmetric dimethylarginine (ADMA) levels, which is a metabolic parameter, is neutral, has been used to stress that nebivolol treatment does not lead to any increase or decrease in serum ADMA levels.

It has been reported that there is an association between serum ADMA levels and biochemical parameters such as hyperglycemia and high triglyceride levels (5, 6). However we agree that there is need for more comprehensive researches evaluating the effects of these parameters on serum ADMA levels.

Kind regards,

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Preanalytical factors for non-HDL cholesterol measurements/ Serum lipid profiles including non-high density lipoprotein cholesterol levels in Turkish school-children

*Non-HDL kolesterol ölçümlerinde preanalitik faktörler/ Türk okul çocuklarında serum lipid profili ve non-HDL kolesterol düzey*leri

Dear Editor,

I have read the paper entitled "Serum Lipid Profiles Including non-High Density Lipoprotein Cholesterol Levels in Turkish

School-Children" by Uçar et al. (1) with great interest. I agree with the authors but two major points in the paper should be re-evaluated:

(1) The authors stressed that the measurement of non-HDL cholesterol does not require overnight fasting.

(2) The authors found a strong positive correlation between non-HDL cholesterol and LDL cholesterol in the study population

In clinical laboratories, preanalytical factors such as, hemolysis, icterus, drugs, and especially lipemia are important. To prevent lipemia, patients should be starved prior to drawing blood (2). The authors suggested that starving is not necessary for measuring non-high density lipoprotein (HDL) cholesterol, and based their claim on a previous study, which had obtained non-HDL cholesterol by calculation using total cholesterol and HDL (3). Their claim is definitely not valid for two important reasons: preanalytical conditions and the inappropriate comparison of reference intervals.

Lipemia is an important interferent for common tests, including total cholesterol and HDL-cholesterol measurements, and cannot be ignored. Furthermore, even if we could measure total cholesterol and HDL-cholesterol or any other biochemical parameters correctly with sophisticated methods, and solve all analytical problems, we cannot omit starvation prior to analysis. We compare patients' test results with reference values and make our decisions on the basis of this comparison.

For a realistic and objective comparison in clinical practice, the preanalytical condition of patients should be the same as that of the reference population. To determine the reference interval in the reference population, we generally take samples at the same time of day (usually in the morning and preferably between 07:00 and 09:00 AM) under standard preanalytical conditions. All subjects should abstain from food after 2200 hr the evening before specimen collection (4). If we measure non-HDL cholesterol in non-starved patients, we should compare patient results with a reference interval that was obtained from a non-starved reference population. Therefore, overnight fasting is necessary for measuring non-HDL cholesterol as well as for other biochemical tests for a realistic comparison with reference values, even if no analytical problems exist.

The second important point is that the authors found a strong positive correlation between non-HDL cholesterol and low-density lipoprotein (LDL) cholesterol in their study population. In my opinion, this is not a special condition for Turkish school-children and these results could be seen in any population. If we examine the relationship between lipid parameters, we can see the situation clearly.

If we neglect serum intermediate density lipoprotein (IDL) and lipoprotein(a) [Lp(a)] concentrations, we can write

non-HDL cholesterol=LDL cholesterol + VLDL cholesterol [1].

We can see from equation 1 that the concentration of non-HDL cholesterol is dependent on the concentration of LDL cholesterol, i.e., LDL cholesterol is not an independent variable. Both very low-density lipoprotein (VLDL) and LDL contain apolipoprotein B100; consequently, we may assume that the strong positive correlation between LDL and non-HDL cholesterol levels is to be expected and is not informative. I think the correlation between non-HDL cholesterol and clinical parameters would be more informative than the correlation with LDL-cholesterol.

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Authors Reply

Dear Editor,

We appreciate the author for his/her interest in reference to our article entitled "Serum lipid profiles including non-High Density Lipoprotein Cholesterol Levels in Turkish School-Children" that was recently published in Anadolu Kardiyoloji Dergisi (1). The author drew attention to the potential effect of pre-analytical, analytical, and biological factors on serum lipid and lipoprotein parameters.

While the measurement of low-density lipoprotein cholesterol (LDL-C) is widely considered as the gold standard as part of lipid profile for screening of coronary artery disease, also has some limitations. The LDL-C is typically calculated with the Friedwald formula, which requires the measurement of total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C) and triglycerides (TG) (2). Because triglyceride levels can fluctuate significantly in relation to the patient's fasting status, estimation of LDL-C levels requires overnight fasting. Furthermore, these calculated LDL-C values include also intermediate-density lipoprotein cholesterol (IDL-C) levels and lipoprotein (a) to varying degrees. For these limitations, the measurement of non-high-density lipoprotein cholesterol (non-HDL-C) levels (with total cholesterol minus HDL-C formula) has been proposed as a better screening tool for coronary artery disease risk assessment and the measurement does not require overnight fasting (3-4). Although we have written that the measurement of non-HDL cholesterol do not require overnight fasting, we had obtained venous blood samples from children after at least 12 hours fasting in the morning hours as we have noted in the methods section of our article. So, there is not any limitation for making comparison between our results and those of any other studies including starved subjects. We did not compare lipid levels of our study population with those of other populations and we estimated our own mean and percentile values. On the other hand, we think that the percentile values for all lipid parameters which were reported in our study may be used as reliable reference values especially for Turkish children, because our study includes quite a large population including 2896 children (1467 girls and 1429 boys) that can be representative for Turkish school-children.

The aim of our study was to measure plasma lipids and lipoprotein levels, to evaluate the prevalence of dyslipidemia according to non-HDL-C levels besides the other conventional lipid parameters and also to evaluate serum lipid and lipoprotein levels according to age, gender difference and living areas in school-children. The author suggests that the strong correlation between LDL-C and non-HDL-C levels is to be expected because the concentration of non-HDL-C is dependent on the concentration of LDL-C. In our study serum non-HDL-C levels correlated with serum TC, TG, HDL-C, LDL-C and VLDL-C levels in both sexes. However, we highlighted the strong correlation between serum non-HDL-C and LDL-C levels, because of serum LDL-C level was classical indicator for cardiovascular diseases in children as well as in adults.

The author suggests that the correlation between non-HDL-C levels and clinical parameters would be more informative. In our study, we also evaluated and reported correlations of non-HDL-C levels with age, weight, height, total body fat percentage, body mass index and physical activity status for both sexes. We found positive correlations with age in both sexes, and with height, weight and total body fat percentage in boys but not in girls. Our findings indicate that the unfavorable situations affecting both anthropometric values (especially related with fatness) and lipid parameters, which lead to the male predominance in cardiovascular diseases in adults begin in childhood.

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Functional status of the quadricuspid aortic valve/An uncommon coincidence of congenital quadricuspid aortic valve accompanied by hypertrophic obstructive cardiomyopathy

Kuadriküspid aort kapağın fonksiyonel durumu/Konjenital kuadriküspid aort kapak ile hipertrofik kardiyomiyopatinin nadir birlikteliği

Dear Editor,

We read with interest the recent case report by Bilge and colleagues (1) about a patient with quadricuspid aortic valve (QAV). The authors state that "the anomaly of the quadricuspid aortic valve can also cause aortic stenosis" (1). We would like to make a comment regarding this matter to avoid any misunderstanding, which could be caused by this statement. While it is true, that quadricuspid aortic valve stenosis has been described (2), it is extremely rare. In the most comprehensive review of the QAV currently available 186 cases of this anomaly were identified from the literature (3). The functional status was known in 154 cases. Of these 115 (74.7%) were regurgitant, while combined aortic valve stenosis and regurgitation was found in 13 cases (8.4%). In only one case (0.7%) the aortic valve was stenotic. A normal functioning valve was detected in 25 cases (16.2%). Dysfunction of the QAV made surgery necessary in 45.2% of the cases (3).

Further, while the association of a QAV with hypertrophic obstructive cardiomyopathy may be rare (1) it is nonetheless often associated with other congenital heart defects. In 18.3% of the cases the QAV was associated with other congenital cardiac malformations, most common being anomalies of the coronary arteries (3, 4).

Therefore, anyone who is not so familiar with this rare congenital heart defect should keep in mind that the most prevalent hemodynamic abnormality associated with a QAV is aortic regurgitation, often leading to aortic valve repair or replacement (3). Further, a QAV is often associated with other congenital heart defects.

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Author Reply

Dear Editor,

Firstly, I would like to thank my colleagues for the valuable comments they have offered. Quadricuspid aortic valve (QAV) was first defined by Balington in 1862 (1).

The mechanism of this congenital malformation is not fully enlightened. One of the leading hypotheses is an abnormal septation of embryological truncus arteriosus. Normally, after the septation of the arterial trunk, three mesenchymal swellings develop in to semilunar leaflets of the aortic and pulmonary trunk. In the setting of quadricuspid aortic valve, the fourth cusp arises during the early stage of truncal septation, resulting from either different number of primordial aortic leaflets or abnormal cusp proliferation (2).

Hurwitz and Roberts (3) described seven different types of QAV depending on the size of the cusps. In literature, the most frequent types were type B (three equal cusps and one smaller cusp) and type A (four cusps of equal size). Although the echocardiographic findings might suggest the size of the leaflets, they do not always correlate with the surgical findings. Aortic insufficiency is the predominant valvular abnormality seen in QAV as you have already described in your letter (4). It has been hypothesized that a small accessory cusp may cause an abnormal distribution of the transvalvular forces and consequently lead to aortic regurgitation. The identification of a QAV with aortic regurgitation is important because the high risk of endocarditis. Thus, endocarditis prophylaxis and echocardiographic follow-up is appropriate in managing high-risk patients. Although the QAV frequently functions abnormally, stenosis is unusual. In most of the series, aortic stenosis was demonstrated between 7-12% (5).