EDITORIAL

Combination of hypertension and hypercholesterolemia: do we have an adequate response?

Marijana Tadic[1], Cesare Cuspidi[2]

1 Department of Internal Medicine and Cardiology, Charité – Universitätsmedizin Berlin, Berlin, Germany
2 Clinical Research Unit, University of Milan-Bicocca and Istituto Auxologico Italiano, Meda, Italy

RELATED ARTICLE

by Niklas et al, see p. 864

Correspondence to:
Marijana Tadic, MD, PhD, Charité – Universitätsmedizin Berlin, Department of Internal Medicine and Cardiology, Augustenburgerplatz 1, 13353 Berlin, Germany, phone: +49176323760011, email: marijana_tadic@hotmail.com
Received: October 15, 2019.
Accepted: October 16, 2019.
Published online: December 23, 2019.
Pol Arch Intern Med. 2019; 129 (12): 852-854
doi:10.20452/pamw.15115

Arterial hypertension and hypercholesterolemia constitute a dangerous combination that is frequently seen in clinical practice despite a wide range of medications that are available for both conditions. Both represent important modifiable risk factors for cardiovascular disease and one could expect that their control should not constitute a significant clinical problem. However, quite the opposite is evident from everyday clinical practice. This raises the question why the management of these modifiable risk factors is that difficult in the modern era of very potent drugs for blood pressure control and lipid lowering. Does the main issue lie in their potency, cost-effectiveness ratio, compliance, or perhaps something else?

The current Polish multicenter national health survey by Niklas et al[1] published in this issue of *Polish Archives of Internal Medicine* (*Pol Arch Intern Med*), which included 6170 participants, showed that age-standardized prevalence of coexisting hypertension and hypercholesterolemia was 34.6%, and the prevalence of concomitant hypercholesterolemia in patients with hypertension was 69.7%.[1] Age-standardized control of hypertension, hypercholesterolemia, and both conditions in the entire study group was 24.3%, 11.2%, and 5.4%, respectively.[1] Interestingly, among patients with both conditions, the highest control rate of hypertension, hypercholesterolemia, and both hypertension and hypercholesterolemia was reported in the group with the oldest patients, namely, older than 80 years of age (37.7%, 29.2%, and 17%, respectively).[1] The National Health and Nutrition Examination Survey from 2001 to 2002 demonstrated that the overall prevalence of hypertension, hypercholesterolemia, and their combination was 30%, 47%, and 18%, respectively.[2] Control of hypertension and hypercholesterolemia was achieved in only 9% of patients and was low in all groups.[2] The National Health and Nutrition Examination Survey from 1988 to 2010 reported that 60.7% to 64.3% of patients with hypertension had also hypercholesterolemia.[3] The same study showed that the prevalence of patients with well-controlled hypertension and dyslipidemia increased from 3% to 35% in years from 1988 to 2010.[3]

These findings demonstrate that the prevalence of concomitant hypertension and hypercholesterolemia is very high in the global population, but also that large percentage of treated patients remain uncontrolled.[1-3] One should also keep in mind that these studies used the definition of dyslipidemias from older guidelines, which are currently different and very strict.[4] According to the authors of the guidelines, the goals of the risk factor management are no smoking, total cholesterol of 4 mmol/l or lower, and systolic blood pressure of 120 mm Hg or lower.[4] The target value for low-density lipoprotein (LDL) in primary prevention in individuals with low risk is less than 3 mmol/l, in those at moderate risk, less than 2.6 mmol/l, and at high risk, less than 1.8 mml/l.[4] Considering the average age, mean blood pressure, and total cholesterol level of the participants in the current Polish study,[1] it is clear that majority of study participants were at high or very high cardiovascular risk, which further implied that target LDL level should be less than 1.8 mmol/l.[4] This low LDL cutoff value used in the present study probably could explain a somewhat higher percentage of dyslipidemias, as well as uncontrolled dyslipidemias in the Polish study in comparison with studies performed in the United States years ago.[2,3]

Niklas et al[1] analyzed the potential reasons that could have been responsible for well-controlled arterial hypertension and hypercholesterolemia, separately and together. They showed that advanced age, female sex, obesity, diabetes, coexisting cardiovascular disease, and the Systematic Coronary Risk Estimation (SCORE) of less than 5% were related with well controlled hypertension and hypercholesterolemia, separately. Higher education and obesity (body mass index ≥30 kg/m^2) were associated only with controlled hypertension, but not controlled hypercholesterolemia, whereas smoking was related with with poor control of hypertension and dyslipidemia.[4] Interestingly, physical activity was not related with better control of hypertension and hypercholesterolemia. Very similar predictors were obtained for concomitant well-controlled hypertension and hypercholesterolemia.[4]

However, after adjustment for covariates, only female sex, concomitant cardiovascular disease, and frequent medical visits were independent predictors of well-controlled hypertension and hypercholesterolemia.[4] The strongest association was observed for concomitant cardiovascular disease. Hypercholesterolemia control was positively associated with comorbid diabetes, cardiovascular disease, and with controlled hypertension.[4] Hypercholesterolemia control was inversely related with smoking. The control of both hypertension and hypercholesterolemia was more frequent in patients with cardiovascular disease, frequent medical visits, and higher education. Smoking doubled the risk of uncontrolled hypertension and hypercholesterolemia.[4]

These controversial results deserve particular attention. Namely, the results show that concomitant diabetes and cardiovascular disease were predictors of better control of both hypertension and hyperlipidemia.[4] The reason is that these patients are under more strict medical control, which is confirmed by the fact that they had also more frequent medical visits. However, the question arises why the prevalence of well-controlled hypertension and hypercholesterolemia was that low—only 5.4%—if these patients regularly took their medications and therefore had satisfactory compliance.[4] The authors speculated that the reason for this low percentage of controlled hypertension and hypercholesterolemia might be poor compliance and adherence to proscribed medications and they suggested that the usage of polypill would significantly improve control of blood pressure and hyperlipidemias. This is not completely supported by their results, which clearly showed that patients with other cardiovascular diseases, diabetes, and more frequent medical check-ups had better control of both blood pressure and lipid levels. One could conclude that these patients actually had higher compliance and adherence than those with isolated hypertension or dyslipidemias.

The other important point that should be considered is synergistic effect of antihypertensive, antidiabetic, and antihyperlipidemic drugs.[5] The benefit of adding a statin to antihypertensive treatment was well established in several studies. The findings from the HOPE-3 (Heart Outcomes Prevention Evaluation-3) study demonstrated that cholesterol-lowering agents combined with antihypertensive therapy could prevent cardiovascular events and decrease the combined endpoint by almost 30%.[6] The lipid-lowering arm of the ASCOT-LLA (Anglo-Scandinavian Cardiac Outcomes Trial) revealed that adding a statin to the antihypertensive treatment was related with a 36% reduction in nonfatal myocardial infarction and fatal coronary heart disease and a 27% reduction in the incidence of fatal and nonfatal stroke in patients with hypertension who were at high risk.[7] However, not all studies demonstrate a synergistic effect. Namely, in the ALLHAT (Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial) it was reported that the addition of pravastatin did not lead to a significant reduction in all-cause mortality and coronary artery disease when compared with standard care.[8]

Not only do statins added to antihypertensive therapy reduce cardiovascular morbidity and mortality, they also have antihypertensive effects. Atorvastatin increases sodium efflux across the membrane of renal cells, reduces activity of L-type channels, and decreases influx of calcium into smooth muscle cells.[5] On the other hand, amlodipine inhibits smooth muscle cell proliferation, platelets and leukocytes adhesion to endothelial surface, and lipid peroxidation, as well as increase of nitric oxide production.[5] The combination of amlodipine and atorvastatin results in improved nitric oxide release, reduced inflammation markers, reduced atherosclerotic plaque size and calcification, improved vascular compliance, reduced left ventricular mass index, and improved insulin sensitivity.[5]

Similar benefit is obtained after combining antidiabetic and antihypertensive medications. The body of data showing antihypertensive effects of antidiabetic drugs is continuously growing.[9,10] Recent investigations showed that benefits from sodium-glucose cotransporter 2 inhibitors might result from their effects on osmotic diuresis and mild natriuresis, which result in a reduction of preload.[11,12] Use of sodium-glucose cotransporter 2 inhibitors did not change plasma renin activity or urinary aldosterone in diabetic patients with hypertension.[12]

All these mechanisms could potentially explain why diabetes and cardiovascular disease are "protective" factors that contribute to well-controlled hypertension and hypercholesterolemia in the present Polish study.[1] Protective effect of female sex on blood pressure control was confirmed in this study and is a new finding. However, after adjustment for other confounding factors, female sex was not independently associated with better control of hypercholesterolemia or concomitant hypertension and hypercholesterolemia. This could be explained by age-related hormonal changes in women that are responsible for increased levels of lipids and 3-hydroxy 3-methylglutaryl coenzyme A reductase dysregulation, which contribute to less efficient statin action in postmenopausal women.[13]

There are several important limitations that deserve to be properly addressed. There is an important selection bias due to a very low reporting rate (45.5%), which implies that less than half of the available participants actually accepted to take part in the study. The information regarding groups of medications (antihypertensive, antidiabetic, antihyperlipidemic, etc) that participants were taking was not available, which could have also potentially biased the results. It is also not clear which cardiovascular diseases were present in the population. It would be helpful to know how many patients had myocardial infarction, stroke, atrial fibrillation, or peripheral vascular disease. Medications that are used in these conditions could also interfere with the results regarding control of blood pressure and cholesterol levels.

This study emphasized very unsatisfactory control of arterial hypertension and dyslipidemia in real-life circumstances. Age-standardized control of hypertension, hypercholesterolemia, and both conditions was only 24.3%, 11.2%, and 5.4%, respectively.[4] These results are devastating and show the scale of challenges that we are facing in these common conditions. Considering the fact that the study was performed in an urban area of a Central European country, we can anticipate how defeating the situation is in rural areas of undeveloped countries or even in developing ones. Call for action is finished and we definitely lost that game. Now is the time for the real battle with cardiovascular risk factors, and loosing is not an option anymore.

ARTICLE INFORMATION

DISCLAIMER The opinions expressed by the author are not necessarily those of the journal editors, Polish Society of Internal Medicine, or publisher.

CONFLICT OF INTEREST None declared.

HOW TO CITE Tadic M, Cuspidi C. Combination of hypertension and hypercholesterolemia: do we have an adequate response? Pol Arch Inter Med. 2019; 129: 852-854. doi:10.20452/pamw.15115

REFERENCES

1 Niklas A, Marcinkowska J, Kozela M, et al. Blood pressure and cholesterol control in patients with hypertension and hypercholesterolemia: the results from the Polish multicenter national health survey WOBASZ II. Pol Arch Intern Med. 2019; 129: 864-873.

2 Wong ND, Lopez V, Tang S, Williams GR. Prevalence, treatment, and control of combined hypertension and hypercholesterolemia in in the United States. Am J Cardiol. 2006; 98: 204-208.

3 Egan BM, Li J, Qanungo S, Wolfman TE. Blood pressure and cholesterol control in in hypertensive hypercholesterolemic patients: national health and nutrition examination surveys 1988-2010. Circulation. 2013; 128: 29-41.

4 Mach F, Baigent C, Catapano AL, et al; ESC Scientific Document Group. 2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk. Eur Heart J. 2019. pii:ehz455. [Epub ahead of print].

5 Ivanovic B, Tadic M. Fixed combination of amlodipine/atorvastatin: from mechanisms to trials. J Cardiovasc Pharmacol Ther. 2013; 18: 544-549.

6 Yusuf S, Lonn E, Pais P, et al; HOPE-3 Investigators. Blood-pressure and cholesterol lowering in persons without cardiovascular disease. N Engl J Med. 2016; 374: 2032-2043.

7 Sever PS, Dahlöf B, Poulter NR, et al. Prevention of coronary and stroke events with atorvastatin in hypertensive patients who have average or lower-than-average cholesterol concentrations, in the Anglo-Scandinavian Cardiac Outcomes Trial-Lipid Lowering Arm (ASCOT-LLA): a multicentre randomised controlled trieal. Lancet 2003; 361: 1149-1158.

8 Margolis KL, Davis BR, Baimbridge C, et al. Long-term follow-up of moderately hypercholesterolemic hypertensive patients following randomization to pravastatin vs usual care: the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT-LLT). J Clin Hypertens 2013; 15: 542-554.

9 Mamakou V, Eleftheriadou I, Katsiki N, et al. Antidiabetic drugs as antihypertensives: new data on the horizon. Curr Vasc Pharmacol. 2017; 16: 70-78.

10 Chrysant SG. Promising cardiovascular and blood pressure effects of the SGLT2 inhibitors: a new class of antidiabetic drugs. Drugs Today (Barc). 2017; 53: 191-202.

11 Kario K, Okada K, Kato M, et al. 24-hour blood pressure-lowering effect of an SGLT-2 inhibitor in patients with diabetes and uncontrolled nocturnal hypertension: results from the randomized, placebo-controlled SACRA Study. Circulation. 2018. [Epub ahead of print].

12 Amin NB, Wang X, Mitchell JR, Lee DS, Nucci G, Rusnak JM. Blood pressure-lowering effect of the sodium glucose co-transporter-2 inhibitor ertugliflozin, assessed via ambulatory blood pressure monitoring in patients with type 2 diabetes and hypertension. Diabetes Obes Metab. 2015; 17: 805-808.

13 Trapani L, Pallottini V. Age-Related Hypercholesterolemia and HMG-CoA reductase dysregulation: sex does matter (a gender perspective). Curr Gerontol Geriatr Res. 2010: 420139.