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Short Perspective

Call to Action! Hypertension and Dyslipidemia in Mexico: Underestimated Deadly Duo

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Summary

Background: High blood pressure and dyslipidemia are risk factors that begin silently and share many pathophysiological mechanisms of tissue damage.

Aim: Draw attention to this binomial (Hypertension and dyslipidemia) that is highly prevalent in Mexico and is mainly responsible for the leading atherothrombotic process as a cause of death in Mexico and the world.

Methods: Reflective analysis of the evidence accumulated in the last 20 years. We launch key messages and support why every hypertensive patient should be treated with a statin.

Results: We call for awareness to measure lipid levels and blood pressure twice a year from the age of 20 and to detect these devastating nosological entities as soon as possible. We remove the myth that PCSK9 inhibitors as well as the small interfering RNA of its synthesis are only for familial dyslipidemia. Measurement of serum Lp(a) should be routine, especially if you have a history of your own and family cardiovascular events.

Conclusion: We should be aware of the little impact that health strategies have had to stop the main cause of death in Mexico. Every hypertensive patient should receive a statin, even if their serum LDLc levels are apparently normal. The great challenge of optimal control of the population with hypertension and/or dyslipidemia continues. The small interfering RNA synthesis PCSK9 should also be considered when conventional therapies are not sufficient and this situation is not infrequent.

More Information

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Introduction and key messages

High blood pressure and dyslipidemia are two of the most common cardiovascular risk factors and frequently coincide. The main causes of death in Mexico and the world are cardiovascular diseases led by ischemic heart disease. The pathophysiological mechanisms of damage progression in hypertension and dyslipidemia begin with endothelial dysfunction, initiating intra- and extracellular signaling cascades that culminate with progressive structural changes, among which progressive atherothrombosis stands out.

Key messages

- The majority of patients who live with hypertension frequently have other risk factors, among which dyslipidemia stands out.
- It is urgent that the general population knows the high frequency of these entities and goes after the age of 20 at least twice a year to have their blood pressure and lipid levels measured.
- The high rate of hypertension and dyslipidemia explain a large part of the main cause of death in Mexico and the world, cardiovascular diseases.
- Unfortunately, the majority of hypertensive patients at the time of their diagnosis in Mexico have at least two associated cardiovascular risk factors and around 50% also have dyslipidemia.
- Systemic Atherothrombotic Hemodynamic Syndrome (SHATS) favors higher LDLc encrustation even with apparently not elevated levels in the blood; therefore:
- The use of a statin in non-dyslipidemic hypertensive patients is fully justified in our setting. The non-

intensive dose is recommended or, at doses and combinations according to the risk level and LDLc levels.

- The lipid profile and Lp[a] levels should be routinely measured, especially if there is a family history of cardiovascular events.
- About 20% of dyslipidemic patients will not reach goals in LDLc levels according to their risk, so other therapies such as PSCK9 inhibitors and the new small interfering RNA of PSCK9 synthesis should always be kept in mind and not only in familial dyslipidemia.
- We call on the health authorities and society to disseminate and take concrete actions in order to know, treat, and control these pathological entities responsible for the high mortality rate in our country.

According to INEGI, during 2023, 841,318 registered deaths were recorded in Mexico. Of these, 43.9% corresponded to women and 56.1% to men. Of the total deaths, 90.0% were due to diseases and health-related problems and 10.0% were due to external causes (accidents, homicides, and suicides, mainly). The five main causes of death nationwide were firstly heart diseases, followed by diabetes mellitus, malignant tumors, liver diseases, and accidents [1]. Non-communicable diseases have established themselves as a clear threat not only to human health but also to development and economic growth. These claim ~ 160 deaths/100.000 habs, and are currently the main killer of a large part of the world's population [2].

Currently, a high percentage of these deaths occur in low- and middle-income countries (such as Mexico). Half of those who die from chronic non-communicable diseases are in the prime of their productive years and, therefore, disability and lives lost each year are determining factors in endangering competitiveness across their borders. The national program derived from the 2019-2024 national development plan contemplates the priority concern of addressing head-on the main challenges that slow down the economic and social development of the country, demands the active participation of everyone, and requests that knowledge be taken as a framework of reference. Avant-garde international organization with economic conscience, to generate its own [3].

The silent risk factors causing the development of atherosclerosis and its systemic complications (heart attack, stroke, renal failure, heart failure, peripheral arterial disease, blindness) are hypertension and dyslipidemia. Its catastrophic consequences represent a true brake on the economic and social development of a country and Mexico does not escape this rule. Dyslipidemia facilitates the development of hypertension, while the collaboration of these two silent killers enhances cardiovascular-renal-metabolic-neurological (CARMEN) risk [4].

Dyslipidemia & hypertension

The prevalence of dyslipidemia is higher in the adult hypertensive population, although the prevalence in the non-hypertensive population is very worrying. The prevalence of dyslipidemia goes hand in hand with other factors as well, such as age, body mass index, and gender. The prevalence of dyslipidemia in the hypertensive population in the age group 35 to 54 years is ~50%, however, in overweight women after 55 years of age it rises to 64.6%, and in obese women up to 77% [5].

Unfortunately, as was demonstrated in the arterial hypertension registry (RIHTA), the request for a lipid profile in the adult population with hypertension is very low. The percentage of patients treated with diabetes and hypertension with a statin is < 30% when the recommendation is 100%. Furthermore, it has been proven that treatment with statins produces an increase in the function of PCSK9, which causes an escape phenomenon that attenuates their lipid-lowering effect [6].

Effective treatment with a statin or its combination with ezetimibe can achieve the desired goals by up to 70%. However, in practice, its use is ignored and the percentage of high-risk patients with optimal LDLc levels does not reach 40% and their LDLc levels are generally > 70 mg/dl [7].

Additionally, if statin or statin/ezetimibe use is far from optimal; the detection of patients who require other therapies such as the use of PSCK9 inhibitors is even more suboptimal. This aspect is very relevant since the use of this strategy has been shown to significantly reduce LDLc levels and achieve goals [8-10].

The erroneous idea that PSCK9 inhibitors are used only in cases of familial dyslipidemia has distorted their real scope. It is known that in general statin therapy can reduce LDLc levels by up to 50% in non-familial dyslipidemias and up to 18% more is added with the combined use of ezetimibe. Therefore, individuals with LDLc > 160 mg/dl will hardly achieve effective LDLc goals with these therapies and therefore, the use of other alternatives such as PSCK9 inhibitors should always be considered [11,12].

Lipoprotein (a) and cardiovascular risk

What is Lp(a)? Should you get your blood levels tested? Lp(a) is a type of lipid or fat in the body that has a structure similar to Low-Density Lipoprotein (LDL), often called "bad cholesterol." Like LDL cholesterol, Lp(a) deposits cholesterol in the arteries and can appear in plaque. It is also found in the cells that line small blood vessels and in tissues where endothelial regeneration and repair occur.

The composition of the lipoprotein, which is included in other lipoproteins, has also made it a major target of research [12-14].

Lp(a) is more complex than LDL, it acts as a molecule that promotes coagulation and this, among other characteristics, seems to make it even worse than LDL as a risk marker for cardiovascular disease [15]. Elevated levels of Lp(a) are a risk factor for cardiovascular disease. For decades, elevated Lp(a) levels have been linked to an increased risk of cardiovascular disease [16]. This includes heart attacks, strokes, and a variety of conditions such as irregular heart rhythms, heart valve diseases, and limited circulation in the lower part of the body.

Between 20% and 25% of the world's population are believed to have elevated levels of Lp(a) [17]. Current lipid-lowering medications have not provided a sufficient reduction in Lp(a) level, except for pro-protein convertase subtilisin/kexin inhibitors [14-16].

Systemic Atherothrombotic Hemodynamic Syndrome (SHATS) in arterial hypertension

The association between Blood Pressure (BP) and Cardiovascular Events (CVD) has generally been based solely on mean BP. BP variability (VBP) is associated with increased organ damage and CVD independently of or beyond average home BP. To explain this association, Systemic Hemodynamic Atherothrombotic Syndrome (SHATS) has been proposed. The SHATS hypothesis indicates that hemodynamic stress increases vascular disease and vice versa, leading to a vicious cycle of association between hemodynamic stress and vascular disease; This association provides not only the risk but also the trigger for CVD events. Evidence of SHATS gradually accumulated. We demonstrated that arterial stiffness synergistically amplified the association between hemodynamic stress and cardiac overload/CVD events in patients with at least one CVD risk factor. Thus, friction phenomena + endothelial dysfunction make the endothelial barrier more vulnerable, allowing greater ease of LDLc embedding even when serum levels are apparently normal. The above justifies the routine use of statins in all patients living with high blood pressure [18].

Novel and very promising lipid therapies

Small interfering ARN (Inclisiran): The Orion 10 and Orion 11 studies demonstrated that the application of a biannual injection of small interfering ARN can reduce the hepatic synthesis of PCSK9. This therapy is the most innovative and with the most promising results. It should always be kept in mind when Statin, Statin+ezetimibe are not enough to achieve goals [19].

Pooled analysis of three recent ORION trials has shown that twice-yearly administration of inclisiran reduces LDL cholesterol by 50% in a variety of patient groups, with only mild adverse effects. The ORION-4 trial is testing a new LDL cholesterol-lowering drug called inclisiran in men at least 40 years old and women at least 55 years old who have previously had a heart attack or stroke or had surgery to unblock or bypass an artery in the legs. These people have a higher risk of having heart and circulatory complications in the future, so they could benefit significantly from cholesterol-lowering treatments.

Unlike many drugs designed to lower cholesterol levels, such as statins, which are taken as daily tablets, inclisiran is given to patients as a subcutaneous injection only twice a year. Inclisiran has been approved for use in the UK as a treatment with a well-tolerated safety profile and is now available to lower cholesterol in some people who have had a heart attack or stroke in certain circumstances. Final results are awaited from the ORION-4 study where each participant has been randomly assigned by a computer to receive inclisiran or a placebo injection. (The placebo injection is the same as the inclisiran injection but does not contain any active medication). To make the results as reliable as possible, neither the doctor nor the participants know whether they are receiving inclisiran or a placebo. Participants have been asked to stay in the trial for about five years and attend clinical appointments near their homes about every six months. Inclisiran undoubtedly has a place in the therapy of cases with dyslipidemia, it is possible that the number of patients who require it is greater than what is said since as more scrutiny of dyslipidemia is carried out, the number of cases will be greater.

Conclusion

This call to action is forceful and forceful; all primary care physicians and specialists should routinely request lipid profiles. High-risk patients such as diabetics or high-risk hypertensive patients should be treated with statins, even regardless of serum cholesterol level. LDLc goals should be optimized to < 100 mg/dl in low-risk cases; to less than 70 mg/dl in cases of intermediate risk (the vast majority of hypertensive and diabetic patients) and to less than 54 mg/dl in those at high and very high risk.

Lipoprotein (a) measurement should become popular and be measured in all medium-high and very high-risk patients, even in patients with a family history of ischemic heart disease and early family death.

The use of antilipemic therapy with Statin, Ezetimibe, and, where appropriate, PSCK9 inhibitors and Incliseran to achieve optimal goals is still far from being adequate in our country. The new therapy with small interfering RNA to reduce hepatic PCSK9 synthesis has already given effective and very promising results.

Since atherosclerosis and its complications are responsible for the main causes of death in Mexico and the world, the detection and treatment of the main risk factors such as dyslipidemia, hypertension, obesity, and diabetes, this call must be disseminated and, above all, become action!!

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