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Letter to Editor

All About Lercanidipine: Ten Questions and Answers

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INTRODUCTION

Dihydropyridine calcium channel blockers (DHP-CCBs) are first–line drugs in antihypertensive therapy, either as monotherapy, or in combination with other antihypertensive drugs, as recommended by ESC/ESH [1]. Lercanidipine, a third-generation calcium channel blocker, is characterized by high vascular selectivity, high lipophilic properties, slow onset and long duration of pharmacological effect. Therefore, lercanidipine is different from a number of other CCBs [2].

1. What are the most important pharmacological properties?

Dihydropyridine-CCBs reversibly inhibit voltage-activated L-type Ca++ channels, located in the smooth muscle cells of the arteries [3,4]. The reduction of intracellular calcium level leads to vasodilation and consequently to blood pressure (BP) reduction. Differently from other dihydropyridine CCBs, lercanidipine inhibits both L and T calcium channels [5]. There is evidence that T channels are particularly expressed in the renal efferent arterioles, while L channels are particularly located in the afferent arterioles [6,7].

Therefore, lercanidipine blocking both L and T channels, dilates afferent and efferent renal arterioles and thereby prevents the increase of glomerular pressure. The result is a decrease of filtration fraction and, therefore, a kidney function protective effect [8].

2. What is the evidence of antihypertensive efficacy?

Double-blind, randomized, comparative trials and large open, observational studies have shown that, lercanidipine (5-20mg once daily) significantly decreases systolic and diastolic blood pressure (SBP/DBP), assessed either as office and home measurement or as 24-hours monitoring (ABPM). Responder rate (SBP/DBP reduction greater than 20 and 10 mmHg respectively) is achieved by 62%-72% of patients [9,10,11]. The antihypertensive efficacy of lercanidipine has also been successfully reported in patients with isolated systolic hypertension, [12,13], with diabetes, [14] and with cardiovascular disease [15]. The therapeutic activity does not differ statistically from that of amlodipine, felodipine, nifedipine GITS, lacidipine, manidipine, [16], losartan [17] and candesartan [18].

3. What about the duration of the antihypertensive effect?

Blood pressure reduction during lercanidipine treatment is sustained throughout 24-hour, with a significant reduction of morning BP rise and BP variability [10,11,19,20].

4. Is the antihypertensive effect different according to the age and gender of patients?

The antihypertensive effect of lercanidipine is not different between young and elderly patients, as well between women and men [10, 21].

5. What is the relationship between lercanidipine and endothelial dysfunction?

Essential hypertension is associated with impaired endothelium-mediated nitric oxide (NO) release, induced by oxidative stress. Therefore, the vascular tone shifts to vasoconstriction, resulting in higher peripheral vascular resistance [22]. In patients with essential hypertension, lercanidipine significantly increases endothelium-mediated vasodilation, through the release of NO. Additionally the drug shows, antioxidant activity, lowering some markers of

oxidative stress, as lipoperoxides, isoprostanes and malondialdehyde and asymmetric dimethylarginine [20,23,24,25].

6. What is the effect on Augmentation Index/Central aortic SBP?

Lercanidipine significantly reduces the Augmentation index, as well the aortic SBP and pulse pressure [13,20].

The increase in central aortic pressure is a marker of arterial stiffness and is involved in the development of cardiovascular events [26,27,28]. Lercanidipine, improving arterial stiffness and decreasing aortic pressure, shows a cardiovascular protective effect in hypertensive patients.

7. What about the effect on sympathetic system?

Differently from felodipine and nifedipine, chronic administration of lercanidipine, does not induce sympathetic activation, and does not increase plasma norepinephrine level. This aspect has an important clinical relevance considering that, in hypertensive patients, sympathetic overdrive is associated with tachycardia and development of cardiovascular events [29,30].

8. What is the evidence of renal protection?

Hypertension remains a major risk factor for kidney disease [31]. Lercanidipine blocking both L and T channels, dilates afferent and efferent renal arteries, thus decreases intraglomerular pressure. The result shows that lercanidipine reduces chronic kidney disease progression [32]. This is evident considering that lercanidipine lowers microalbuminuria in patients with type 2 diabetes similarly to ramipril, as reported in the DIAL study [33]. The improvement of renal function with was also obtained in patients with chronic renal failure [34] and in subjects after renal artery intervention for atherosclerotic lesions [35] in whom lercanidipine significantly increased glomerular filtration rate, after 6 months of treatment and decreased proteinuria.

9. What are the pleiotropic effects?

Lercanidipine improving endothelial function and increasing NO bioavailability shows an atheroprotective effects. NO decreases oxidative stress, reduces vascular intimal and smooth muscle cell proliferation, decreases the plasma levels of E-selectin, P-selectin, adhesion molecules, inhibits cholesterol accumulation, LDL oxidation and platelet aggregation to the endothelium. Through these effects, lercanidipine decreases the risk of atherothrombotic events [11,36,37]. Moreover, in hypertensive patients lercanidipine treatment is associated with a regression of microvascular structural changes, evaluated as wall-to-lumen ratio [20].

10. What about the tolerability?

Lercanidipine is well tolerated, with a very low rate of adverse events, such as dizziness, headache, flushing, palpitations, and vertigo. [38, 39]. Particularly, compared with other CCBs (amlodipine, nifedipine, felodipine) lercanidipine, decreases ankle edema, by 56% [16 40]. Chronic treatment does not change laboratory parameters [4,41] and is associated with very low (2.1%–<1%) withdrawal rate [10,42].

Conflicts of interest

Gokhan Faikoglu and Kubra Saygisever-Faikoglu are employees of Recordati.

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