Treatment in Hypertension: Non-Pharmacologic and Pharmacologic Approach

Amanda Tiksnadi, MD

Abstract

The goal of hypertension treatment is to lower high blood pressure and protects important organs, like the brain, heart, and kidneys from damage. Many researches revealed that treatment for hypertension has been associated with reductions in stroke (35-40%), heart attack (20-25%), and heart failure (> 50%).

In general, either non-pharmacological or pharmacological approach or both is used to treat hypertension, depends on the initial level of risk. Non-pharmacological approach is all about lifestyle changes, which includes maintain a healthy diet and weight, physical exercise, and reduce sodium and alcohol intake, smoking cessation, etc. It is recommended for all groups of CV risk stratification: low, moderate, high, and very high risk.

Pharmacological approach needs more special medical consideration, e.g. when to initiate drug treatment, blood pressure target treatment, which drug to start, use of combination treatment, etc.

The decision on when to start pharmacological treatment strategies all importantly depends on the initial level of risk. Blood pressure target treatment should consider co-existing diabetic and other associated clinical conditions such as stroke, myocardial infarction, renal dysfunction, and proteinuria. There are conditions favoring use of some antihypertensive drugs versus others. There are also some possible combinations between some classes of antihypertensive that proven to be beneficial in treating hypertension.

EXTENDED ABSTRACT

Blood Pressure Variability : The Importance in Hypertension and How to Control It.

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Recommendations of major guidelines in hypertension(HT) diagnosis and managementare still based on isolated clinical bloodpressure (BP) measurements. The evaluation of BP relatedcardiovascular (CV) risk is based to the assessment of mean BP values.(1)

Mean BP has indeed been proven to be a powerful risk factor for CV events, but data collected these years from many studies have shown that instability,fluctuation,variability in BP is of utmost important in the progression of organ damage and in triggering CV events.(1-8)

These findings were made possible thanks to the introduction of the Ambulatory BP Monitoring (ABPM).There are many advantages of this technique. More measurements than with the conventional BP measurement can be obtained,it provides a profile of BP over 24-h period, allowing identificationof BP fluctuations and informing the efficacy of anti-HT medications over 24-hperiod.(2,3.4)

BP variability is a multifaceted phenomenon.BP values may vary by more than 50-60 mmHg over 24-h.These variations originate from short-lasting pressor - and depressor episodes,from regular occurrence of higher day-time and lower night-time values, the day- night BP differences being usually around 15-20 mm Hg.(5)

BP variability (BPV) has been assessed by calculation of the standard deviation (s.d) of 24-h systolic,diastolic and mean arterial pressures. Other indices for BPV are BPV among half-hours,BPV within half-hours. BP vary also between months and seasons (*Pamela Study).*These studies also show that BPVincrease with increasing age of the subjects:studies in essential HT have shown that the s.d for 24-h rises progressively with increasing levels of BP.(5)

The mechanism of BPV is not fully known,several evidences have however showed that behavioral,neural,reflex,humoral factors,compliance to anti-HT treatment influence this phenomenon.BPV and sympathetic activity becomes progressively greater from normotensive to mild- and more severe essential HT.(5)

A recent large study have shown that BPV(the difference between BP measured at various visits) is a strong predictor of stroke and to a lesser extent to coronary events, heart failure. RothwellPM has done many studies .He concluded that BPV, whether measured on clinic visits or on ABPM, is a strong predictor of stroke and that Calcium Channel Blockers (CCB) and to a lesser extent Thiazide diuretics aresuperior to other drugs in reducing BPV, the older beta blockers (BB) increase BPV and should

only be used if there are compelling indications like Ischemic Heart Disease.(6-10)

The X-CELLENT study has shown that age,BP,heart rate variability were the major determinants of BPV. Amlodipine and IndapamideSR were the only effective anti-HT agents in reducing BPV.The mechanism underlying the reduced BPV is notyet clear. Results of the recent ASCOT-BPLA substudy (2010) showed that Amlodipine/Perindopril was more effective in reducing variability in SBP (both clinic and ABPM) than B-blocker/Thiazide in Hypertensive patients. In both treatment groups with well controlled mean BP,a five fold increased risk of vascular events was detected if their visit-to-visit variability in systolic BP was high. The better reduction in BPV explained the differences in stroke and cardiovascular events between Amlodipine/Perindopril and B-blocker/thiazide in this sub study (12)

Despite the many researches regarding BPV,there is still a need to study the mechanisms of BPV, its accurate detection and the means to reduce it. We need a readily applicable measure of variability which might be achieved by ABPM.Improved methods of collecting data to detect trends in BP in the office and home must be as well achieved, so that data could be obtained from prospective studies.

In Summary :The value of office and out-of-office BP have been demonstrated and established.Lowering mean BP, as is common in our daily practice is still of importance and should continue.Evidences have shown that long-term average of BP as well as long-term variability of BP, both provide complimentary prognostic implications.

References.

1. Rothwell PM. Limitations of the usual blood-pressure hypothesis and importance of variability, instability, and episodic hypertension. Lancet2010 ;375(9718):938-48.

2. BiloG,Parati G. Rate *of* blood pressure changes assessedby24 h ambulatory blood pressure monitoring*:* another meaningful indexof blood pressure variability? J Hypertens 2011 Jun;29(6):1054-8.

3. Logan AG. Ambulatory Blood Pressure Monitoring : It is time to move on! Journal of Hypertension 2010: 28 ;2000-2002.

4. O'Brien E. Ambulatory blood pressure monitoring*:* 24 hour blood pressure controlas atherapeutic goalforimproving cardiovascular prognosis.Medicographia2010 :32 ; 241-249.

5. Mancia G, Grassi G. Mechanisms and clinical implications of Blood Pressure Variability. Cardiovasc.Pharmacol2000 :35;515-619.

6. RothwellPM,HowardSC,Dolan E et al. Prognostic significanceof visit-to-visit variability, maximum systolic blood pressure, and episodic hypertension. Lancet 2010: 375; 895-905.

7. Hansen TW,Li Yan, Staessen JA. Blood Pressure Variability remains an elusive predictor of Cardiovascular outcome. Am J of Hypertension2009 :22:1;3-4.

8. Wang TD, Sheu WHH. Fromcasual blood pressure measurementtolong-term blood pressure burden*:* better elucidationof theassociation between versatile blood pressuresandcardiovascular events*.* Hypertension Research 2011:34 ;49-51.

9. Clement DL.Blood Pressure Variability : A New Life ?.http://www.escardio.org/communities/councils/ccp/e-journal/vol 9no 38 :2011.

10. Webb AJS et al. Effectsofantihypertensive-drug classoninterindividual variation inblood pressureandriskof stroke*:* asystematic reviewand meta-analysis*.* Lancet 2010 :375; 906-15.

11. Zhang Yi et al. Effect of anti-hypertensive agents on Blood Pressure Variability :The Natrilix SR versus Candesartan and Amlodipine in the reduction of Systolic Blood Pressure in Hypertensive patients.(X-CELLENT) Study. Hypertension 2011: 58; 155-160.

12. Vandzhura V. medicographia 2010: 32 (3); 281-289.

Abstract

HYPERTENSION SYNDROME :

Challenge for Better Outcomes

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The guidelines in hypertension (HT) define hypertension as an elevation of arm cuff blood pressures (BP) exceeding 140/90 mmHg. Consequently to reduce Cardiovascular (CV) morbidity mortality related to HT, BP must be reduced to less than 140/90 mmHg.

Data from Framingham Study however, have shown that BP is directly related to CV events, even at levels below the definition of Hypertension by JNC-7. (1) High normal BP was associated with 7 fold increased of CV diseases. Lowering BP in the normotensive population reduces morbidity and mortality.

A meta analysis of large scale interventional studies found that a reduction in BP, decreases the risk of both fatal and non fatal stroke, but less than expected reduction was found in fatal and non fatal CV disease events. High BP is not the only cause of high CV morbidity mortality rates associated with HT. Indeed BP reduction is of utmost importance in reducing CV morbidity mortality but there are other factors contributing to the risk of CV events and death.(2)

HT is a heterogeneous complex syndrome, comprising many abnormalities. The other factors than BP is also of importance regarding the adverse outcomes of HT. These factors are : intermittent HT, BP variability, pathophysiologic heterogeneity of sustained HT, relationship between ages, systolic BP and pulse pressure, differences between cuff BP and Central Systolic Pressure in the prediction of CV events, the need to consider global CV risk in the BP management. (3)

Literatures from the past few decades show that the definition of HT has changed. The American Society of Hypertension in a paper *"Expanding the definition and classification of HT"*, stated that there is more to HT than just BP.

The JNC-6 agree that the degree of BP elevation has to be coupled to the presence or absence of other risk factors as a guide to treatment, but the JNC-7 decided to use BP cut points (>140/90mmHg) combined with a set of compelling indications. The proposed new definition of HT from the HT Writing Group is : *HT is a progressive CV syndrome arising from complex and interrelated etiologies. Early markers of the syndrome are often present before BP elevation is observed, therefore, HT can not*

be classified solely by BP thresholds. Progression is associated with functional and structural cardiac - and vascular abnormalities that damage the heart, kidneys, brain, vasculature, and other organs, and leads to premature morbidity and death.(4)

Studies have shown that vascular remodeling and left ventricular hypertrophy are independent with the degree of elevated BP and may even precede increased BP, suggesting they are not in response to that elevation. They appear to result from genetic – and environmental factors that also contribute to high BP. (5-6) The combination of elements of the HT syndrome can determine the impact of elevated BP for an individual patient.

Regarding HT as a syndrome, the American Heart Association and The American College of Cardiology have stated four categories of variables to classify patients : BP, CV risk factors, early diseases markers, and target organ damage. The 2007 European Society Hypertension (ESH) Guideline for the management of arterial HT and the 2009 Updated ESH guidelines recognize the importance of the assessment of total CV risk in the management of HT to make the decision for treatment initiation.(7)

It seems that in the evaluation and treatment of hypertensive patients, we have to go beyond BP, besides still regarding the primacy of BP.

References :

1. Messerli FH. Clinician's Manual : Treatment of Hypertension. 3rd edition 2011, Springer Healthcare.
2. Glasser SP. Hypertension Syndrome and Cardiovascular Events. Postgraduate Medicine vol 110(5).
3. Izzo JL, Giles TD, Materson BJ. Defining the Syndrome of Hypertension. Hypertension Primer 4th Edition 2008, American Heart Association, Dalls, Texas, Lippincott Wiliams and Wilkins USA.
4. Pickering TG. Do We Really Need A New Definition of Hypertension?. The Journal of Clinical Hypertension Vol 7(12) Dec 2005.
5. Mulvany MJ. Are Vascular Abnormalities A Primary Cause or Secondary Consequence of Hypertension? Hypertension 1991; 18(Suppl.3) : 53-57.
6. Radice M. et.al. Left Ventricular Structure and Function in Normotensive Adolescents with a genetic predisposition to Hypertension. Am Heart J 1986;111(1):115-120.
7. Mancia G, Stephane L. Reappraisal of European Guidelines on Hypertension Management 2011 Springer Healthcare.

Which group of Patients will Benefit Most in Hypertension Management with Beta Blockers

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ABSTRACT.

After 2006, the use of β-blockers as first-line therapy in hypertensive patients has been somewhat controversial. Anyway, a recent review of the European Society of Hypertension guidelines shows that these agents show off similar BP lowering efficacy to other classes of agents, prompting a crosscheck of the utility of these agents in various patient populations. Moreover to their use as a potential first-line therapy in uncomplicated hypertension, β-blockers have a particular role in patients with hypertension and comorbidities such as heart failure or coronary artery disease, hypertensive patients with increased sympathetic activity, diabetic patients with hypertension, hypertensive patients with atrial fibrillation with a rapid ventricular rate, hypertension in pregnancy. One advantage which β-blockers give is the additional protective effects in patients with prior cardiovascular events. Some of the disadvantages associated with β-blockers appear more related to the older drugs in this class and further appraisal of the efficacy and safety profile of newer β-blockers will give support to the current guideline recommendations in in selected patient populations.

Keywords: selected patient populations – hypertension - first-line therapy - β-blockers

METODE PENGUKURAN TEKANAN DARAH YANG BAIK????

Ekawati Dani yulianti

ABSTRAK

Latar Belakang : Hipertensi berdasarkan *Joint National Committee* (JNC) VII merupakan tekanan darah sistol yang sama atau melebihi 140 mmHg (≥ 140) dan atau sama atau diastol melebihi 90 mmHg (≥ 90). Berbagai faktor dapat mempengaruhi hasil pengukuran seperti faktor pasien, alat dan tempat pengukuran. Sering terjadi kesalahan pengukuran tekanan darah yang diakibatkan oleh metode yang tidak akurat, variabilitas tekanan darah yang *inherent* dan pengaruh kondisi pemeriksa.
Tujuan : Untuk memperoleh kontrol tekanan darah yang baik diperlukan pengukuran yang akurat dengan berbagai macam metode yang telah direkomendasi, lokasi dan persiapan pengukuran.
Metode : Pengukuran darah dapat menggunakan metode The Auscultatory – Mercury, Aneroid, sfigmomanometer hibrid, pemeriksaan dengan ambulatory. Lokasi pengukuran yang sering dilakukan adalah di daerah: lengan atas, pergelangan tangan yang dipengaruhi oleh tekanan hidrostatik dan jari tangan yang tidak direkomendasikan. Persiapan pengukuran dipengaruhi oleh faktor pasien, posisi tubuh, ukuran *cuff*.
Kesimpulan : Untuk memperoleh kontrol tekanan darah yang baik harus diperhatikan metode yang direkomendasi, lokasi dan persiapan pengukuran.

Kata Kunci : Hipertensi – Metode pengukuran– Kontrol tekanan darah yang akurat.

Abstract

The Pathophysiology of Hypertension

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High blood pressure remains one of the most prevalent health problems facing humans. Among the causes of hypertension, more than 90% are essential which implies no clear identifiable etiology. Althogh several genehas been identified as a hypertensinogenic, there is still no single gene or group of genes responsible for hypertension. Essential hypertension has been extensively researched but there are no single cause and no single mechanism underlying the increased blood pressure. Therefore it is multifactorial and multimechanism. Blood pressure may increase as a result of an increase in cardiac output and or elevation in systemic vascular resistance. These two component of blood pressure have their own causes and factors that contribute to increase in blood pressure. Interaction between cardiac output and systemic vascular resistance to increase in blood pressure is exceedingly complex. The interplay involves many systems including local (vascular) and systemic factors. Renal sodium handling, sympathetic nervous system, renin angiotensin pathway are among the major player in high blood pressure. To make the matter more complex, environmental factors such as dietary habit, psychological stress, drug interactions may influence the rise in blood pressure. Pharmacological agents had been developed to block the suspected pathways of hypertension. Current pharmacological treatment for hypertension should be tailored according to known pathophysiological nature of high blood pressure.

Keywords: essential hypertension - pathophysiology

Neurologic Aspects in the Treatment of Hypertensive Crisis

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Abstract.

The appropriate and timely evaluation and treatment of patients with severely elevated blood pressure is essential to avoid serious adverse outcomes. Most importantly, the distinction between a hypertensive emergency (crisis) and urgency needs to be made. A sudden elevation in systolic (SBP) and/or diastolic blood pressure (DBP) that is associated with acute end organ damage (cardiovascular, cerebrovascular, or renal) is defined as a hypertensive crisis or emergency. In contrast, acute elevation in SBP and/or DBP not associated with evidence of end organ damage is defined as hypertensive urgency. In patients with a hypertensive emergency, blood pressure control should be attained as expeditiously as possible with parenteral medications to prevent ongoing and potentially permanent end organ damage. In contrast, with hypertensive urgency, blood pressure control can be achieved with the use of oral medications within 24–48 hours.

Common neurologic emergencies in the setting of hypertensive crisis include hypertensive encephalopathy, intracerebral hemorrhage, and acute ischemic stroke. Severe hypertension is very common in the setting of acute stroke, and there is controversy surrounding the goal blood pressure.

In intracerebral hemorrhage, there is typically disruption of the cerebral autoregulation of blood flow in the area of the bleed, and blood flow and oxygen delivery are dependent on systemic perfusion pressure. The American Heart Association recommends treating hypertension in the setting of an intracerebral bleed only when blood pressure is more than 180/ 105 mm Hg. Mean arterial pressure should be maintained below 130 mm Hg.

In patients with ischemic stroke, perfusion pressure distal to the obstructed vessel is low, and compensatory vasodilatation of these blood vessels occurs to maintain adequate blood flow. A higher systemic pressure is required to maintain perfusion in these dilated blood vessels. Most patients, irrespective of pre-ischemic blood pressure control, experience a sustained rise in blood pressure during cerebral ischemia, including transient ischemic attack. Therefore, in patients with ischemic stroke, blood pressure should be carefully observed for the first 1 to 2 hours to determine if it will spontaneously decrease. Only a persistently mean arterial pressure over 130 mm Hg or a systolic blood pressure over 220 mm Hg should be carefully treated. In this setting, mean arterial pressure should be lowered by 15% to 20%.

Hypertensive encephalopathy is a severe end-organ manifestation of the hypertensive process. Gradual lowering of the blood pressure frequently leads to rapid improvement of neurologic symptoms. If patients

do not improve within 6 to 12 hours, evaluation for other causes of the encephalopathic process should be undertaken.

Generally, the therapeutic approach is dictated by the particular presentation and end-organ complications. The ideal pharmacologic agent for the management of hypertensive emergency would be fast-acting, rapidly reversible, and titratable without significant effect. The appropriate therapeutic approach in each patient will depend on the clinical presentation of the acute end-organ damage. The preferred agents include nitroprusside, nicardipine, esmolol, labetalol, fenoldopam, and nitroglycerine. Parenteral therapy is generally preferred, and strategies include use of sodium nitroprusside, beta-blockers, labetalol, or calcium-channel antagonists.

In acute neurological cases, labetalol and calcium-channel antagonist is also recommended, because of both experimental and human data have indicated that may increase CBF, however it has a little effect on ICP while lowering blood pressure.

Beta Blockers in the Management of Hypertension: An Asian Perspective

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Abstract

The Asia Pacific region accounts for approximately half of the worldwide burden of cardiovascular disease. High blood pressure is an important contributor to this burden, with a population-attributable fraction of hypertension for cardiovascuar disease reported to be as 66% in Asia countries. It is anticipated that by 2025, the number of hypertensive individuals in China and India alone will increase to >500 million.

Rates of hypertension control remain low in most Asian countries. In China, for example, 18.8 percent of the population had hypertension. However, only 30.2 percent oh the hypertensive patients were aware of their condition, 24.7 percent were treted, and 6.1 percent achieved blood pressure control. It is clear that an increased awareness and effective treatment of hypertension will be crucial to reducing the burden of cardiovascular disease within the region.

Following publication of the National Institute of Clinical Excellence (NICE) Guidelines in 2006, the use of β-blockers as first-line therapy in hypertension has been somewhat controversial. However, a recent reappraisal of the European Society of Hypertension guidelines highlights that these agents exhibit similar BP lowering efficacy to other classes of agents, prompting a re-examination of the utility of these agents in various patient populations.

That is important to address this controversy and provide an Asian perspective on the place of β-blockers in current clinical practice and the benefits of β-blockade in selected patient populations. In addition to their use as a potential first-line therapy in uncomplicated hypertension, β-blockers have a particular role in patients with hypertension and comorbidities such as heart failure or coronary artery disease, including those who had a myocardial infarction. One advantage which β-blockers offer is the additional protective effects in patients with prior cardiovascular events. Some of the disadvantages attributed to β-blockers appear more related to the older drugs in this class and further appraisal of the efficacy and safety profile of newer β-blockers will lend support to the current guideline recommendations in Asian countries and encourage increased appropriate use of β-blockade in current clinical practice within Asia.

Abstrak

PERAN ANTIHIPERTENSI KOMBINASI DALAM MENINGKATKAN EFEKTIFITAS TERAPI
Fokus pada kombinasi Olmesartan dan Amlodipin

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Joint Committee National (JNC) 7 2003 dan *European Society of Hypertension (ESH)/ European Society of Cardiology (ESC) 2007,* keduanya merekomendasikan pemakaian obat antihipertensi kombinasi dalam terapi hipertensi dengan kondisi-kondisi tertentu. JNC 7 2003 mengatakan bahwa, 1) kebanyakan pasien hipertensi membutuhkan dua atau lebih obat antihipertensi untuk mencapai sasaran tekanan darah <140/90 mmHg atau <130/80 mmHg bagi yang diabetes atau mengalami penyakit ginjal kronik; 2) bila tekanan darah >20/10 mmHg di atas sasaran, dianjurkan untuk memulai terapi dengan obat antihipertensi kombinasi, salah satu di antaranya adalah diuretik. *ESH/ESC* 2007 dalam statemennya mengatakan, 1) kebanyakan pasien hipertensi membutuhkan dua atau lebih obat antihipertensi untuk mencapai tekanan darah sasaran, 2) kombinasi obat antihipertesi dosis rendah seharusnya dipilih sebagai langkah pertama pada terapi hipertensi grade 2 atau 3, atau pasien dengan risiko kardiovaskuler tinggi atau sangat tinggi. Rekomendasi-rekomendasi di atas didasarkan atas berbagai studi yang sudah membuktikan bahwa, 1) terapi hipertensi dengan obat antihipertensi kombinasi lebih efektif dibandingkan dengan monoterapi, 2) kepatuhan pasien menjadi lebih tingi, 3) frekuensi efek samping obat menjadi lebih rendah. Beberapa studi juga sudah merekomendasikan jenis-jenis obat antihipertensi apa saja yang dapat dikombinasikan di antaranya, 1) diuretik dengan *Angiotensin Converting Enzyme(ACE) inhibitor, Calcium Channel Blocker (CCB) dan Angiotensin Receptor Blocker (ARB,* 2) *ACE inhibitor* dengan *CCB,* 3) *ARB* dengan *CCB.* Sedangkan kombinasi antara ACE inhibitor dan ARB hanya dipergunakan pada kondisi tertentu yaitu hipertensi dengan proteinuria yang berat (ONTARGET *study* 2009*).* Studi-studi di atas juga membuktikan bahwa kombinasi dalam tablet tunggal (*fixed dose*) lebih menguntungkan dibandingkan tablet terpisah.

Kombinasi Olmesartan (mewakili ARB) dan Amlodipin (mewakili CCB), dalam berbagai studi juga meperlihatkan efektifitas yang baik. Hal ini disebabkan karena 1) kedua klas obat tersebut bekerja pada titik tangkap yang berbeda yaitu, ARB pada resistensi perifer sedangkan CCB pada otot polos arteriol, 2) pada ginjal, ARB mendilatasi vas eferen sedangkan CCB mendilatasi vas aferen. Kombinasi kedua klas obat tersebut juga mengurangi efek samping oedem yang sering ditimbulkan oleh CCB yang diberikan tersendiri.

Kata kunci : antihipertensi kombinasi, olmesartan dan amlodipin.

Are All Calcium Channel Blockers (CCBs) the same ?

Lercanidipine and Renoprotection

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ABSTRAK

Kalsium antagonis (CCB) dihidropiridin sering dilaporkan menimbulkan efek samping sehingga kita harus menghentikan penggunaannya atau mengganti dengan obat lain yang berbeda kelas. Lercanidipine (suatu CCB dihidropiridin) merupakan kalsium antagonis baru dengan sifat lipofilik dan selektifitas pembuluh darah yang tinggi, akibatnya dapat memberi efek anti hipertensi yang bertahap dan berlangsung lama, karena juga memiliki tolerabilitas yang baik dibandingkan dengan CCB dihidropiridin yang lain. Walaupun, masih banyak bahasan kontroversi tentang efek renoproteksi kalsium antagonis, namun juga terbukti semakin banyak manfaat yang diperoleh. Akhirnya disarankan untuk menambah kalsium antagonis untuk dapat memperbaiki fungsi ginjal pada penderita yang sebelumnya sudah diobati dengan *ACE inhibitor* maupun *Angiotensine Receptor Blocker* (ARB).

Pada **Zafra Study** (the Zanidip en Funcion Renal Alterada) suatu studi untuk menguji efek lercanidipine (suatu CCB dihidropiridin baru yang unik) dalam kemampuannya memperbaiki fungsi ginjal penderita CKD dengan proteinuria. Ternyata terbukti lercanidipine dapat memperbaiki klirens kreatinin dan menurunkan proteinuria secara bermakna. Jadi lercanidpine adalah CCB dihidropiridin yang renoprotektif.

Maka lercanidipine menjadi satu-satunya CCB dihidropiridin yang mempunyai sifat anti proteinuria, karena CCB dihidropiridin yang lain justru meningkatkan proteinuria. Hal ini berbeda dengan CCB non dihidropiridin yang memang sudah terbukti mempunyai sifat anti proteinuria misalnya diltiazem dan verapamil.

Lercanidipine, the unique dyhidropiridine CCB, adalah generasi baru lipofilik CCB, rumus molekulnya yang khusus membuat lercanidipine ini berebda dengan CCB dihidropiridin yang lain. Gugus *"protonated amin group"* membuat lercanidipine cepat hilang dari plasma sehingga membuat lercanidipine ini bersifat *short plasma half life*.

Gugus *"lipophilic anchor group"* membuat lercanidipine tersebut melekat kuat di membran sel dan bertahan lama di sini sehingga lercanidipine bersifat *long duration of action*.

CCBs & Renal Effects

	Lercanidipine	Amlodipine	Felodipine
Renal arterial Tree			
larger and medium	Dilatation	Dilatation	Dilatation
small arterioles	Dilatation	no effect	no effect
Glomeruli			
Mesangial cell	⇓	⇓	n.a
Afferent arterioles	**Dilatation**	**Dilatation**	**Dilatation**
Efferent arterioles	**Dilatation**	**Less effect**	**Less effect**
Glomerular pressure	**Normalized**	Increased	Increased
Renal regulation	n.a	completely	completely
Block			
Time-dependent	**Less**	More	More
Renal Injury			