American Journal of Internal Medicine
2024, Vol. 12, No. 3, pp. 33-39
https://doi.org/10.11648/j.ajim.20241203.12

Research Article

Effect of Dihydropyridine Calcium Channel Blockers (CCB) on the Progression of Diabetic Nephropathy in Aranyaprathet Hospital, Sakeaw Province, Thailand

Teerapon Pattanapisansak*

Medical Department, Aranyaprathet Hospital, Aranyaprathet, Thailand

Abstract

Importance From Thailand, has standardized therapeutic drugs of Calcium channel blockers (CCB) in reduce the progression of chronic renal failure in diabetic and hypertension that is advantages for use in patients. However, use of Amlodipine that is more accessible and also a drug used by all community hospitals to treat patients, inexpensive and highly effective. *Objective* To study effective of Dihydropyridine Calcium channel blockers (CCB) on kidney function (eGFR), urinary protein creatinine and sugar blood level. *Design, Setting, and Participants* This study is retrospective cohort study by study in patients with diabetic nephropathy. By study in patients with diabetes nephropathy with stage 3 or higher and receiving Dihydropyridine Calcium channel blockers (CCB). *Exposures* Dihydropyridine Calcium channel blockers (CCB) in reducing the complications of diabetic nephropathy which is consistent with Strategy No.2 Providing quality and excellent health services. And literature reviews in Thailand have not found empirical evidence that mean Calcium Channel can reduce the complications of diabetic nephropathy. *Main Outcomes and Measures* The effectiveness of Dihydropyridine Calcium channel blockers (CCB) increases the complications of diabetic nephropathy. *Results* In volunteer, female patient proportion was 69.0%. Average age was 69.3 (± 9.69), minimum age is 40 years, maximum age is 97 years. Most patients were between 60-79 years, follow by 40-59 years follow by16.8% and more than 80 years 16.1%. In congenital disease, kidney disease, kidney failure, diabetes and hypertension are 100%, follow by 24% obesity and 0.2% cancer. The effect of Dihydropyridine Calcium channel blockers (CCB) on kidney function (eGFR), urine microalbumin and creatinine when compare with use drug CCB 2 groups including Amlodipine and Amlodipine+enalapril/losartan/valsartan. Found that volunteer that received CCB drug compare with month 3 and 12, the level of eGFR decreases (t=1.085) and Urine Microalbumin increases (t=1.496) by statistically significance (P = 0.002) and Dihydropyridine Calcium channel blockers (CCB) on Fasting blood sugar compares with month 3 and 12, Fasting blood sugar (t = 0.566) and HbA1C (t=0.677) was typically decreased significantly (P < 0.005). *Conclusions and Relevance* Calcium channel blockers (CCBs) was decline kidney function (decrease eGFR) and CCB leads to the decrease of eGFR and provides monitoring of CCB use, as this may lead to the decrease of kidney function.

Keywords

Effect, Dihydropyridine Calcium Channel Blockers (CCB), Diabetic Nephropathy

*Corresponding author: link0037_99@yahoo.com (Teerapon Pattanapisansak)

Received: 20 July 2024; **Accepted:** 24 August 2024; **Published:** 11 September 2024

1. Introduction

Diabetes mellitus is a chronic disease that is a major public health problem in the world. According to the World Health Organization report, in 2017, approximately 2.8% of all age groups had diabetes and predicted that by 2030 it will increase to 4.4%. This means that the number of cases will increase from 171 million to 366 million by 2030 [1, 2] and if going back to 2010, World Health Organization reported that diabetes is the leading cause of chronic kidney disease in the global population and approximately 10-20% of diabetes patient die from chronic kidney disease [2]. In Thailand, from the research of the Institute of Medical Research and Technology Assessment, found that the incidence of diabetes retinopathy was 23.7% and chronic kidney disease was 38.3%. In chronic kidney disease, from the research Thai SEEK Study by The Nephrology Society of Thailand in 2009, found that the incidence of chronic kidney disease stage 1-5 was 17.5% of the population with the prevalence of chronic kidney disease increasing with increasing age. And found that kidney disease patients entering end-stage renal disease were most likely caused by diabetic kidney disease, followed by hypertension nephropathy, hypertensive nephropathy, obstructive nephropathy, chronic glomerulonephritis, chronic urate nephropathy and polycystic [3, 4].

Calcium channel blockers (CCBs) are one kind of drugs that use to treat diseases of the heart and blood vessels by use as a drug to widen the coronary arteries control high blood pressure and treat cardiac arrhythmias. These drugs are widely used but it can cause severe toxicity if eating a lot. CCBs are divide according to the structure into 3 groups including phenylalkylamines group includes verapamil, dihydropyridines group includes nifedipine, amlodipine, nimodipine and benzothiazines group includes diltiazem. The mechanism of action is to block or inhibit the occurrence of Ca^{2+} and has more effect on the heart and blood vessels and has less effect on the skeletal muscle because contraction of skeletal muscles must use Ca^{2+} in cells [5-9]. In addition, Amlodipine and Manidipine is an effective, safe, and reducing ankle edema when comparing the effect of lowering blood pressure between amlodipine (5 – 10 mg) and manidipine (10 – 20 mg) in mild – moderate hypertension patients. After 24 weeks of treatment, 2 of drugs have no difference in lowering blood pressure. However, in Thailand, Manidipine use has a high cost [9] which in Thailand is commonly used. But in abroad, Calcium channel blockers widely use in the treatment of diabetic patients because Dihydropyridine Calcium channel blockers (CCB) can help slow the progression of diabetic patients with kidney disease. This will be effective in excreting protein in the urine and reduce the rate of kidney function and progression of chronic renal failure. According to many researches in America, Dihydropyridine Calcium channel blockers (CCB) is list on the national list of essential medicines and found that the use of Calcium channel blockers (CCB) classified as Phenalkylamines is verapamil can reduce the progression of chronic renal failure in diabetic patients and high blood pressure. And able to reduce high blood pressure in diabetic patients whose blood pressure averages between 95 and 106 mmHg [10-13]. In addition, previous study has compared the effectiveness of using lower blood sugar and high blood pressure in America population. By more effective than other drugs use in the experiment which found that has properties and mechanisms of action that help slow down the progression of kidney failure in diabetic and high blood pressure patients [14-17]. In addition, in abroad said to be effective in using Calcium channel blockers (CCB) in diabetic patients without hypertension and kidney disease. The use of Calcium channel blockers (CCB) with diabetic patients without any diseases that can reduce protein in urine. It was also noted that basal protein levels were associated with levels of blood pressure reduction in slowing the progression of CKD. The research of chronic kidney disease in diabetes population that association with level of blood pressure reduction in slowing the progression of CKD in African and America [10, 13, 18].

This study is to study the effectiveness of Dihydropyridine Calcium channel blockers (CCB) in reducing the complications of diabetic nephropathy which is consistent with Strategy No.2 Providing quality and excellent health services. And literature reviews in Thailand have not found empirical evidence that mean Calcium Channel can reduce the complications of diabetic nephropathy. Therefore, this study is the source of new knowledge in the treatment of diabetic nephropathy patients and the usefulness of this study for planning and treating patients to appropriately reduce the complications of diabetic nephropathy of Sa Kaew province in the future' may need to be separated into two sentences to be more understandable.

2. Methods

This study is retrospective cohort study by study in patients with diabetic nephropathy. By study in patients with diabetes nephropathy with stage 3 or higher and receiving Dihydropyridine Calcium channel blockers (CCB).

After the research framework has been reviewed and certified by the Human Research Ethics Committee of King Prajadhipok's Hospital. The study authors proceeded by

1) Collect the information in the research record form
2) Use data for statistical analysis

2.1. Research Tools

Research record form consist of general information including sex, age, congenital disease, duration of kidney and diabetes disease, waist circumference, (Body Mass Index) BMI, family history of kidney and diabetes disease, smoking history, drinking history, laboratory results namely Fasting Blood Sugar (FBS), Hemoglobin A1C (HbA1c), kidney function (eGFR), Serum Creatinine and Urine Microalbumin.

2.2. Statistical Analysis

General information of volunteer including sex, age, congenital disease, duration of kidney and diabetes disease, waist circumference, BMI, family history of kidney and diabetes disease, smoking history and drinking history. Analyzed by descriptive statistic including Frequency and Percentage Inferential T-Test statistic, ANOVAincluding P-Value < 0.05 at a statistically significant level.

3. Results

In volunteer, female more than male was 69.0%. Average age is 69.3 (±9.69), minimum age is 40 years, maximum age is 97 years. Most of age are between 60-79 years, follow by 40-59 years 16.8% and more than 80 years 16.1%. In congenital disease, kidney disease, kidney failure, diabetes and hypertension are 100%, follow by obesity 24% and cancer 0.2%.

3.1. Rick Factors of Volunteer

In drinking history, used to drink was 4.0% and still drinking 0.7%. In smoking history, used to smoke was 6.1% and still smoking 0.2%. In food consumption behavior, mostly eaten salty 59.1%, follow by sweet 36.6%. In addition, sample group are eaten salty and sweet 95.3% and mostly are not exercise 51.3%.

3.2. The Effective of Use of Dihydropyridine Calcium Channel Blockers (CCB) on Kidney Function (eGFR), Protein in Urine and Creatinine

The effective of use of Dihydropyridine Calcium channel blockers (CCB) on kidney function (eGFR), protein in urine and creatinine when compare with use drug CCB 2 groups including Amlodipine and Amlodipine+enalapril/losartan/valsartan. Found that volunteer that received CCB drug compare with month 3 and 6, the level of eGFR decreased (t=1.018) by statistically significant (P 0.001) and level of Urine Microalbumin compare with month 3 and 6, that affects the level of protein in the urine increases (t=1.638) by statistically significant (P 0.002). In a while, receiving CCB is not affect to level of creatinine.

The effect of Dihydropyridine Calcium channel blockers (CCB) on kidney function (eGFR), urine microalbumin and creatinine when compare with use drug CCB 2 groups including Amlodipine and Amlodipine+enalapril/losartan/valsartan. Found that volunteer that received CCB drug compare with month 3 and 12, the level of eGFR decreases (t=1.085) and Urine Microalbumin increases (t=1.496) by statistically significant (P 0.002).

The effectiveness of Dihydropyridine Calcium channel blockers (CCB) on Fasting blood sugar compares with month 3 and 12, Fasting blood sugar (t = 0.566) and HbA1C (t=0.677) was typically decreased significantly (P < 0.005).

3.3. The Effective of Dihydropyridine Calcium Channel Blockers (CCB) on Kidney Function (Mean eGFR)

Table 1. *Mean eGFR (ml/min/1.73m²) before and after administration (Dihydropyridine Calcium channel blockers (CCB)) classified by disease and follow-up by Repeated measure ANOVA.*

Disease	Mean ± SD (mmHg)			
	Baseline	Follow up (6 months)	Follow up (9 months)	End Point (1 year)
DM+HT	82.77 ± 470.78	52.60 ± 18.45	66.30 ± 8.742	47.04 ± 13.76
Renal Failure	79.57 ± 341.72	46.93 ± 20.76	43.27 ± 18.18	39.26 ± 12.60

Source	Type III Sum Of Squares	df	Mean of Squares	F	P-Value
Time	186.33	2	62.111	0.858	0.021
Patients	212.323	2	72.428		
Disease	62.896	1	62.896	0.109	0.017
Error	435.523	103	577.31.4		

*df: degrees of Freedom, F: F-test

Table 1. The data were analyzed using split plot ANOVA. Patients were divided into two groups: Diabetes Mellitus (DM) and Hypertension (HT) or DM alone or HT alone and renal failure group. The eGFR values for DM and HT or DM alone or HT alone was statistically different (P=0.017), and the mean eGFR at all three visits at 1 year of follow-up was statistically different (P=0.021). It was concluded that Dihydropyridine Calcium channel blockers. (CCB) can increase the glomerular filtration rate of patients with DM and HT or DM alone or HT alone and renal failure group. And at 1 year follow-up, it can slow down the incidence of nephrotic syndrome in patients with DM and HT or DM alone or HT alone and in the kidney failure group.

Table 2. *Mean Creatinine (mg/dl) Before and After (Dihydropyridine Calcium channel blockers (CCB)) classified by disease and follow-up by Repeated measure ANOVA.*

Disease	Mean ± SD (mmHg)			
	Baseline	Follow up (6 months)	Follow up (9 months)	End Point (1 year)
DM+HT	82.77 ± 470.78	52.60 ± 18.45	66.30 ± 338.742	47.04 ± 13.76
Renal Failure	79.57 ± 341.72	46.93 ± 20.76	43.27 ± 18.18	39.26 ± 12.60

Source	Type III Sum Of Squares	df	Mean of Squares	F	P-Value
Time	131.061	2	50.402	0.399	<0.001*
Time*Disease	34.675	2	13.335	0.106	0.120
Patients	435.120	2	126.280		
Disease	391.813	1	391.813	0.735	0.019
Error	5491.243	103	533.119		

Table 2. The split-plot ANOVA data was analyzed by dividing patients into two groups: DM and HT or DM alone or HT alone and renal failure group. Dihydropyridine Calcium or HT alone were statistically different (P=0.019), and the mean creatinine at all three doses at 1 year (End Point) of follow-up was statistically different (P=0.019). It was concluded that Dihydropyridine Calcium channel blockers (CCB)) increased creatinine-lowering capacity, with mean nephrotic syndrome at 1-year follow-up, was 39.26 ±12.60 and patients in the DM group and HT or DM alone or HT alone 47.04 ±13.76 subjects. statistically significant and can slow down the progression of kidney disease *(Figure 1)*.

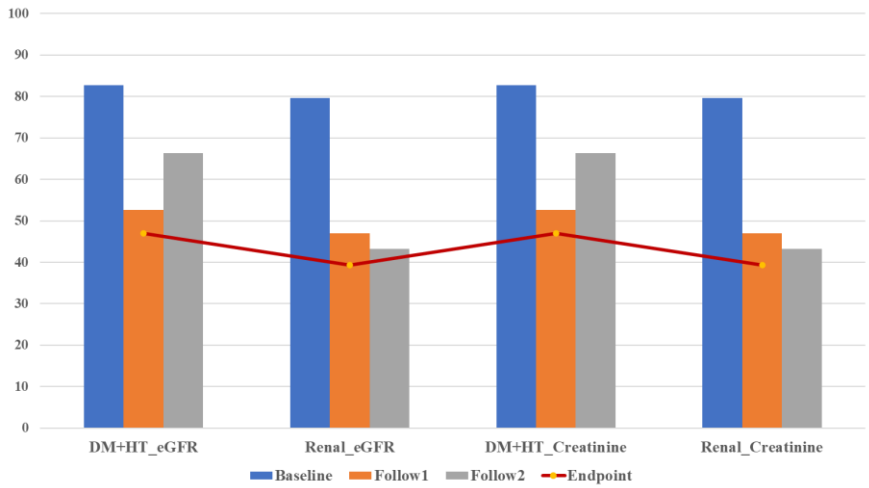

Figure 1. *Comparison of baseline and endpoint between the mean values of eGFR and Creatinine.*

Table 3. *Number of patients with chronic kidney disease that can control the level of FBS before and after receiving (Dihydropyridine Calcium channel blockers (CCB)).*

Clinical Outcomes	N (%)			
	Baseline	Follow up (6 months)	Follow up (9 months)	End Point (1 year)
FBS > 130 mg/dl	77 (67.0)	78 (67.8)	71 (61.7)	68 (59.1)
FBS <= 130 mg/dl	38 (33.0)	37 (32.2)	44 (38.3)	47 (40.9)

** df=3, p=0.035*

Table 3, the number of patients with chronic kidney disease that can control the level of FBS before and after receiving. The three doses of Dihydropyridine Calcium channel blockers (CCB) were statistically different. In conclusion, after 1 year of follow-up (Dihydropyridine Calcium channel blockers (CCB)) increased the ability to control FBS levels decreased.

4. Discussion

In volunteer, female volunteers than males that is different from the National Diabetes Statistics Report of Centers for Disease Control. In 2015, the prevalence of diabetes among men was 36.9%, higher than women 31.15%. In age, most group is age 60-79 years are associate with prevalence of diabetes in population age more than 18 years (approximately 84.1 million) was 33.9%, population age group of elderly (age more than 65 years) has high level of blood sugar 48.3% and close to the survey of Korea. For incidence of diabetes, report from American are between 40-74 years [7].

Risk factors of volunteer including drinking history and used of drink are 4.0% and still drinking is 0.7%. In smoking history, used to smoke is 6.1% and still smoking is 0.2%. In food consumption behaviors, mostly eaten salty is 59.1%, follow by 36.6%. In addition, sample group are eaten salty and sweet 95.3% and volunteer mostly is not exercise 51.3%. The study which is close to the study [20] that found type-2 diabetes 258 persons, smoking 86 persons (17.3%) and drinking 68 persons (13.7%). However, the study in abroad found that the risk factors for smoking and drinking more than Thailand. In food consumption behavior and exercise are not risk factors in the study and no clearly study in Thailand. The factor of food consumption and exercise is one of factors to have diabetes.

The volunteer receiving ASA drug for treatment is 100%, follow by Glipizide 81.6%, Metformin 71.3%, Simvastatin 67.7%, Amlodipine 5 mg 55.53%, Amlodipine 10 mg 44.47% by respectively. The study in abroad, the study of Menon Rena and team in 2012 found that Diabetic Nephropathy group that developed to CKD by most found in stage 4 (48.0%). The use of ASA drug that help eGFR and patient can control level of blood sugar are better. However, drug group of Calcium channel blockers (CCB) with diabetes without complications can reduce protein in urine. This study of chronic kidney disease in diabetes patients has notice about protein have correlation with lowering blood pressure in progression of chronic kidney disease in African and America [10, 13, 18]. From Thailand, has standardized therapeutic drugs but use of Calcium channel blockers (CCB) in Phenyalkylamines group has a mechanism that can reduce the progression of chronic renal failure in diabetic and hypertension that is advantages for use in patients. However, use of Amlodipine that is more accessible and also a drug used by all community hospitals to treat patients, inexpensive and highly effective. [10, 13].

When compare the result of weight, height, waist circumference and BMI between before and after receiving Dihydropyridine Calcium channel blockers (CCB), found that average weight after receiving CCB (62.35± 11.67), average waist circumference after receiving CCB (89.81± 14.54) and BMI (25.13± 3.95) less than before receiving CCB. However, height before and after receiving CCB are no difference.

The effective of Dihydropyridine Calcium channel blockers (CCB) on kidney function (eGFR), Urine Microalbumin and Creatinine compared to the two CCB groups, Amlodipine and Amlodipine+enalapril/losartan/valsartan, were compared in the CCB group. At Month 3 and Month 12, eGFR levels decreased and Urine Microalbumin increased statistically. However, as recommended by the KDIGO guidelines 2021 Clinical Practice Guideline for the Management of Blood Pressure in Chronic Kidney Disease and high blood pressure treatment guidelines. in general medicine, B. E. 2019 still recommends the use of drugs in the group renin-angiotensin system blockers ACEIs (angiotensin-converting enzyme inhibitors) or ARBs (angiotensin-receptor blockers) in hypertensive patients with proteinuria.

The effectiveness of use Dihydropyridine Calcium channel blockers (CCB) on blood glucose levels were found when comparing the levels of Fasting blood sugar (FBS) and HbA1C at Month 3 and Month 9. At month 6 and month 12, Fasting blood sugar (FBS) and HbA1C were significantly reduced, show that Dihydropyridine Calcium channel blockers (CCB) [14-17, 25] have properties and mechanisms of action to reduce blood sugar levels in diabetic patients. which

corresponds to Previous studies have compared the effectiveness of using lower blood sugar and high blood pressure in the American population It is more effective than other drugs. used in the experiment show that It has properties and mechanisms of action that help slow down the progression of kidney failure in diabetic and high blood pressure patients. However, in foreign countries, the effectiveness of Calcium channel blockers (CCB) has been discussed. The CKD study in the diabetic population also noted that baseline protein levels were associated with lower levels of blood pressure in slowing progression of CKD in AFL. Rikan and American [10, 13, 18] For Thailand, there is already a standard treatment regimen. However, due to the use of Calcium channel blockers (CCB) in the Phenyalkylamines group There is a mechanism that can reduce the progression of chronic renal failure in diabetic patients. and high blood pressure Therefore, it is an advantage to be used to treat patients in the future. Amlodipine is a more accessible drug. It is also a drug used by all community hospitals to treat patients, is inexpensive and highly effective. [10, 13]

In addition, Calcium channel blockers (CCBs) in patients with diabetic nephropathy have mechanism to maintain fluid balance in the body, regulate water and minerals in the blood, removal of waste from the blood, secretion of hormones into the bloodstream that help slowing the deterioration of the kidneys including edema, high potassium [21-25], renal osteodystrophy, paleness and decreased protein in the urine. [26-31] The other study found that, Calcium channel blockers (CCBs) can reduce the mechanism of disease caused by high pressure within the renal blood vessels or intra-glomerular hypertension as a result of an increase in hormones prostanoids, nitric oxide, vascular endothelial growth factor (VEGF) with stimulation of renin-angiotensin-aldosterone systems (RAS) and endothelin systems that causing abnormalities in the autonomic control system of the blood vessels within the kidneys. Intra-glomerular hypertension cause of microalbuminuria, macroalbuminuria, mesangial matrix, thickening of GBM and pathology of glomerular epithelial cells or podocytes. [25, 26]

5. Limitations

Calcium channel blockers (CCBs) can reduce the mechanism of disease caused by high pressure within the renal blood, Calcium channel blockers (CCBs) was decline kidney function (decrease eGFR) and CCB leads to the decrease of eGFR and provides monitoring of CCB use, as this may lead to the decrease of kidney function.

6. Conclusions

This study was to collect retrospective data, if the research were to be use must concern with patients with impaired kidney function should be considered, patients with severe renal failure in stage 5 and drug use group of Calcium channel blockers (CCBs). This drug was decline kidney function (decrease eGFR).

Abbreviations

CCB Dihydropyridine Calcium Channel Blockers

Author Contributions

Teerapon Pattanapisansak is the sole author. The author read and approved the final manuscript.

Conflicts of Interest

The author declares no conflicts of interest.

References

[1] Wild S, Roglic G, Green A, Sicree R, King H. Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. Diabetes Care. 2004; 27(5): 1047-1053. https://doi.org/10.2337/diacare.27.5.1047

[2] World Health Organization: Media centre. Fact sheets. Diabetes. http://www.who.int/mediacentre/factsheets/fs312/en/ Accessed sep 30, 2019.

[3] Ingsathit A, Thakkinstian A, Chaiprasert A, et al. Prevalence and risk factors of chronic kidney disease in the Thai adult population: Thai SEEK study. Nephrol Dial Transplant. 2010; 25(5): 1567-1575. https://doi.org/10.1093/ndt/gfp669

[4] National Health Security office (NHSO), Thailand. National Health Security Fund Management Manual Year 2560; 4: 7–13.

[5] Centers for Disease Control. Morbidity and Mortality Weekly Report (MMWR). Morb Mortal Wkly Rep, 2013; 62(11), 209-212.

[6] Ryu S, Song J, Choi BY, et al. Incidence and risk factors for metabolic syndrome in Korean male workers, ages 30 to 39. Ann Epidemiol. 2007; 17(4): 245-252. https://doi.org/10.1016/j.annepidem.2006.10.001

[7] Sakeaw Province Public Health Office, Thailand. annual report. 2020.

[8] A rise in cytosolic Ca^{2+} is the key event in contraction Explanation: But note that some vasoactive substances may also increase the sensitivity of the contractile machinery to Ca^{2+}.

[9] Contraction may be caused by agents depolarizing the cell and thus opening voltagedependent Ca^{2+} channels. Explanation: Ca^{2+} entry through Ca^{2+} channels is a target for Ca^{2+} channel blockers such as nifedipine. (Fig4.10 on p67).

[10] Bakris GL. Microalbuminuria: prognostic implications. Curr Opin Nephrol Hypertens. 1996; 5(3): 219-223. https://doi.org/10.1097/00041552-199605000-00006

[11] Parving HH. The impact of hypertension and antihypertensive treatment on the course and prognosis of diabetic nephropathy. J Hypertens. 1990; 8: S187-S191.

[12] Peterson JC, Adler S, Burkart JM, et al. Blood pressure control, proteinuria, and the progression of renal disease. The Modification of Diet in Renal Disease Study. Ann Intern Med. 1995; 123(10): 754-762. https://doi.org/10.7326/0003-4819-123-10-199511150-00003

[13] Toto RD, Mitchell HC, Smith RD, Lee HC, McIntire D, Pettinger WA. "Strict" blood pressure control and progression of renal disease in hypertensive nephrosclerosis. Kidney Int. 1995; 48(3): 851-859. https://doi.org/10.1038/ki.1995.361

[14] Zing W, Ferguson RK, Vlasses PH. Calcium antagonists in elderly and black hypertensive patients. Therapeutic controversies. Arch Intern Med. 1991; 151(11): 2154-2162.

[15] Walker WG, Hermann JA, Anderson JE. Randomized doubly blinded trial of enalaprilvs hydrochlorothiazide on glomerular filtration rate in diabetic nephropathy. Hypertension. 1993; 22: 410.

[16] Saunders E, Weir MR, Kong BW, et al. A comparison of the efficacy and safety of a beta-blocker, a calcium channel blocker, and a converting enzyme inhibitor in hypertensive blacks. Arch Intern Med. 1990; 150(8): 1707-1713.

[17] Brazy PC, Stead WW, Fitzwilliam JF. Progression of renal insufficiency: role of blood pressure. Kidney Int. 1989; 35(2): 670-674. https://doi.org/10.1038/ki.1989.37

[18] Lash JP, Bakris GL. Effects of ACE inhibitors and calcium antagonists alone or combined on progression of diabetic nephropathy. Nephrol Dial Transplant. 1995; 10 Suppl 9: 56-62.

[19] American Diabetes Association. 2. Classification and Diagnosis of Diabetes. Diabetes Care. 2017; 40(Suppl 1): S11-S24. https://doi.org/10.2337/dc17-S005

[20] Theerapon Pattanapisansak. Progression of Kidney Disease n Type 2 Diabetic Patients: a Case Study of Aranyaprathet Hospital. Journal of Health Science 2019; 28: 639-49.

[21] Pornpen Srisawat. Glycated Hemoglobin Stardardization. Journal of the Medical Technologist Association of Thailand, 2007; 35(1), 1763-66.

[22] Salako BL, Finomo FO, Kadiri S, Arije A, Olatosin AO. Comparative effect of lisinopril and lacidipine on urinary albumin excretion in patients with type 11 diabetic nephropathy. Afr J Med Med Sci. 2002; 31(1): 53-57.

[23] Fogari R, Mugellini A, Zoppi A, et al. Effect of successful hypertension control by manidipine or lisinopril on albuminuria and left ventricular mass in diabetic hypertensive patients with microalbuminuria. Eur J Clin Pharmacol. 2005; 61(7): 483-490. https://doi.org/10.1007/s00228-005-0961-2

[24] De Cesaris R, Ranieri G, Andriani A, et al. Effects of benazepril and nicardipine on microalbuminuria in normotensive and hypertensive patients with diabetes. Clin Pharmacol Ther. 1996; 60(4): 472-478. https://doi.org/10.1016/S0009-9236(96)90204-0

[25] Hayashi K, Wakino S, Sugano N, Ozawa Y, Homma K, Saruta T. Ca^{2+} channel subtypes and pharmacology in the kidney. Circ Res. 2007; 100(3): 342-353. https://doi.org/10.1161/01.RES.0000256155.31133.49

[26] Hayashi K, Homma K, Wakino S, et al. T-type Ca channel blockade as a determinant of kidney protection. Keio J Med. 2010; 59(3): 84-95. https://doi.org/10.2302/kjm.59.84

[27] Dietz JR, Davis JO, Freeman RH, Villarreal D, Echtenkamp SF. Effects of intrarenal infusion of calcium entry blockers in anesthetized dogs. Hypertension. 1983; 5(4): 482-488. https://doi.org/10.1161/01.hyp.5.4.482

[28] Abe Y, Komori T, Miura K, et al. Effects of the calcium antagonist nicardipine on renal function and renin release in dogs. J Cardiovasc Pharmacol. 1983; 5(2): 254-259. https://doi.org/10.1097/00005344-198303000-00015

[29] Roy MW, Guthrie GP Jr, Holladay FP, Kotchen TA. Effects of verapamil on renin and aldosterone in the dog and rat. Am J Physiol. 1983; 245(4): E410-E416. https://doi.org/10.1152/ajpendo.1983.245.4.E410

[30] Steinhausen M, Baehr M. Vasomotion and vasoconstriction induced by Ca agonist in the split hydronephrotic kidney. Prog Appl Microcirc. 1989; 14: 25–29.

[31] Hansen PB, Jensen BL, Andreasen D, Skøtt O. Differential expression of T- and L-type voltage-dependent calcium channels in renal resistance vessels. Circ Res. 2001; 89(7): 630-638. https://doi.org/10.1161/hh1901.097126