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Role of Efonidipine in CKD Patients: A Study In North Bihar

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Abstract
The role of efonidipine, a calcium channel blocker in reducing the progression of chronic renal disease is well established by various studies. It also imparts beneficial effects in cardiovascular disease by reducing synthesis and secretion of aldosterone, it prevents hypertrophy and remodelling of cardiac myocytes. There is decrease in 24 hour urinary protein as efonidipine reduces glomerular capillary pressure. And overall there is improvement in GFR too. The aim of the study is to find the role of efonidipine in CKD patients.
Methods: *CKD patients (age >25 years, both gender) attending outdoor clinic and indoor CKD patients of Medicine department Darbhanga Medical College were selected by simple random method and advised efonidipine 40mg once daily. The statistical significance of improvement in proteinuria and GFR was measured.*
Result: *There was improvement in proteinuria in 52% patients taking efonidipine 40mg once daily. The GFR was increased in 54% patients taking drug.*
Out of 50 patients 29 were male and 21 were females. There was substantial decrease in 24 hour urinary protein in 26 patients out of 50 at the end of 6 months period. GFR also improved in 27 patients out of 50 at the end of study period.
Conclusion: *Our 24 weeks study period in CKD patients taking efonidipine a novel dihydropyridine calcium antagonist showed its beneficial effects. The outcome was measured by 24 hour urinary protein excretion and GFR. The beneficial effect on proteinuria was particularly apparent in patients with proteinuria 1 g/day. These effects of efonidipine would appear to make the drug more advantageous than other CCBs in terms of slowing the progression of renal dysfunction and preventing cardiovascular tissue and organ injuries in patients with hypertension and chronic kidney disease.*

Introduction

Efonidipine, is a new generation dihydropyridine (DHP) calcium channel blocker. It blocks both L and T type calcium channel. Calcium channel blockers are mainly used in hypertension, angina pectoris, cardiac arrhythmias, and hypertrophic cardiomyopathy. Efonidipine mainly have shown to have many beneficial effects on renal outcome in CKD patients. Renin angiotensin system have a major role in hypertension and renal function. Efonidipine suppresses renin secretion from the juxta glomerular apparatus in the kidneys and enhances sodium excretion from the kidneys by suppressing aldosterone synthesis and secretion from the adrenal glands. Aldosterone induced renal parenchymal fibrosis is also suppressed by Efonidipine. Efonidipine increases glomerular filtration rate without increasing intra-glomerular pressure and filtration fraction. This prevents hypertension induced renal damage. There are several studies which showed that efonidipine reduces proteinuria also.

Hypertension is a well known risk factor for kidney damage and that kidney damage can

increase blood pressure, thereby leading to a vicious cycle. Having a good blood pressure control in hypertensive patients can aid to prevent long term renal damage. Calcium channel blockers are widely used in hypertension. The main stratergy is to reduce Glomerular pressure so that proteinuria can be minimized.

There are many studies in the past providing ample data to confirm the beneficial effects of efonodipine in renal failure. The main aim of the study is to evaluate the effects of efonidipine in CKD patients.

Methods

The type of study was prospective showing the effects of efnodipine in CKD patients. The study was conducted over a period of six months (1st March to 31st August 2018) on patients attending outdoor and indoor clinic of darbhanga medical college and hospital (a government medical college of north Bihar).

The study group included all CKD patients above 20 years old of both genders receiving efonidipine. Seriously ill patients and patients having co morbid conditions such as cardiovascular disease, or any other disease except hypertension and diabetes was excluded from study.

The primary objective of study was to find the effects of efonidipine either beneficial or harmful on CKD patients. The patients were followed up and assessed at regular intervals and at the end of study period for outcomes. Proteinuria, and GFR was calculated to evaluate the effects of efonidipine. GFR was calculated by using the Cockcroft and Gault formula for both men and women whereas 24 hour urinary protein was estimated for proteinuria.

A sample size of 50 patients was taken. Paired student T test was used to determine the statistical significance. A p value of <0.05 was considered statistical significant.

No ethical committee issues were raised during the study.

Result

A total of 50 patients were selected randomly who fulfilled the inclusion criteria for the study. All patients were selected from outdoor n indoor admissions in Darbhanga Medical College. 32 patients had diabetes and hypertension both whereas 18 patients had only diabetes as a comorbidity.

Out of 50 patients 29 were male and 21 were females. There was substantial decrease in 24 hour urinary protein in 26 patients out of 50 at the end of 6 months period. GFR also improved in 27 patients out of 50 at the end of study period.

T-Test

Paired Samples Statistics

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	proteinuria1	3.8606	50	.81116	.11472
	proteinuria2	2.8461	50	1.21555	.17191

Paired Samples Correlations

		N	Correlation	Sig.
Pair 1	proteinuria1 & proteinuria2	50	.496	.000

Paired Samples Test

		Paired Differences					t	df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference Lower	Upper			
Pair 1	proteinuria1 - proteinuria2	1.01453	1.07540	.15208	.70890	1.32015	6.671	49	.000

There was improvement in proteinuria in 52% patients taking efonidipine 40mg once daily at the end of the study. The p value came to be .000 which was significant.

T-Test

Paired Samples Statistics

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	GFR1	50.1600	50	11.46665	1.62163
	GFR2	58.5600	50	12.31584	1.74172

Paired Samples Correlations

		N	Correlation	Sig.
Pair 1	GFR1 & GFR2	50	.848	.000

Paired Samples Test

		Paired Differences					t	df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference Lower	Upper			
Pair 1	GFR1 - GFR2	-8.40000	6.59932	.93328	-10.27551	-6.52449	-9.000	49	.000

The GFR was calculated prior to the starting of the study and at the end of the study. It was found that patients on efonidiopine 40mg daily improved. The GFR was increased in 54% patients taking drug. Statistically p value came to be significant.

Discussion

Diabetes and hypertension are leading causes of chronic renal failure worldwide. As we know these patients are also at risk of cardiovascular complications. To prevent such complications certain drugs which selectively improve the progression and improve the prognosis should be used.

To protect the kidneys from diabetic and other renal diseases, it is important to prevent the increase in glomerular capillary pressure. The drugs acting on rennin angiotensin system, such as ACE inhibitors and ARBs, are known to improve glomerular hypertension by reducing the constrictive effect of angiotensin II on the efferent arterioles. With regard to the Ca channels in the glomerular arterioles, the afferent arterioles express the L- and T-type Ca channels, while the efferent arterioles express only the T-type Ca channel. This distribution of Ca channels may explain the experimental observation that efonidipine, the L- and T-type CCB, dilates both the afferent and efferent arterioles in the isolated perfused kidney, while the L-type CCB preferentially dilates the afferent arterioles. The elevated glomerular hydraulic pressure promotes ultrafiltration of plasma proteins, resulting in proteinuria.

It has been found in many large scale studies that the amount of urinary protein excretion was predictive for the rate of deterioration of renal function in patients with diabetic and non diabetic renal diseases. Proteinuria itself is detrimental to the kidney because ultrafiltration of proteins across the glomerular basement membrane brings about mesangial and tubular protein overload, which provokes inflammation and ultimately results in glomerulosclerosis and tubulo-interstitial fibrosis. Proteinuria is also know to be a risk factor for cardiovascular disease.

Efonidipine, a dihydropirydine calcium channel blocker, has been shown to dilate the efferent glomerular arterioles as effectively as the afferent arterioles. It increases glomerular filtration rate without increasing intra-glomerular pressure and filtration fraction. This prevents hypertension induced renal damage. It also prevents Rho-kinase induced renal parenchymal fibrosis and provides long term renal protection.

Efonidipine is unique among clinically available CCBs. Its antihypertensive efficacy is superior or

at par with other CCBs. But, in terms of pleiotropic effects leading to enhanced cerebral, cardiac and renal protection, Efonidipine scores over the other CCBs.

This study showed the effectiveness of efonidipine in providing renal protection in patients of chronic renal failure.

Conclusion

A substantial proportion of patients advised efonidipine showed improvements in renal status. The reno protective benefits of efonidipine was imparted largely due to decrease in proteinuria and improvement in GFR.

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