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INHIBITION OF RENIN-ANGIOTENSIN-ALDOSTERONE ANTAGONIST IN DECREASING DIABETIC KIDNEY DISEASE

PRIYANKA.G., HARSHINI.D. (PHARM D STUDENTS), YESURATNAM.M. (ASSISTANT PROFESSOR), DEPARTMENT OF PHARMACY,

AM REDDY MEMORIAL COLLEGE OF PHARMACY, NARASARAOPET

ABSTRACT:

Diabetic kidney disease is an emerging epidemic of hypertension, diabetes mellitus, and obesity. It usually occurs slowly and gets worse for many years. The RAAS system is a hormone system that regulates blood pressure, fluid and electrolyte balance, and systemic vascular resistance. A Renoprotective effect is exerted that is independent of the blood pressure reduction caused by RAAS inhibition. Combination of ACE and AT II receptor antagonists to maximize RAAS inhibition and reduce proteinuria and GFR decline in diabetic and nondiabetic renal disease. According to recent trials, there is a benefit in slowing nephropathy progression in the presence of albuminuria. An approach including lifestyle modifications may achieve remission of proteinuria and stabilization of renal function in a substantial proportion of patients with proteinuria renal disease with RAAS inhibition combined with intensified amelioration of dyslipidemia. Independent of blood pressure reduction, a renal protective effect is exerted by RAAS inhibition using proteinuria as an endpoint compared to the effects of ARBS or ACE-1 as monotherapy or with a combination of both ACE-1 and ARB therapy. Most studies suggest that combination therapy provides a greater antiproteinuric effect than monotherapy, despite the methodological limitations, because of more prolonged and complete RAAS inhibition. Combination therapy has higher efficiency than monotherapy and is also associated with a higher incidence of adverse effects.

KEYWORDS:

Diabetic kidney disease, Renin angiotensin aldosterone antagonist (RAAS), Angiotensin converting enzyme (ACE), Angiotensin receptor blockers (ARBS), Diabetes, Blood pressure, Monotherapy, Dual therapy, Direct renin inhibitors (DRI), End stage renal disease (ESRD), Proteinuria, Albuminuria.

INTRODUCTION:

A major public health problem chronic kidney disease in the world has consequences mainly in the form of an emerging epidemic of hypertension, diabetes mellitus, and obesity. Diabetic kidney disease is caused by diabetes, which is a leading cause of kidney disease. It usually occurs slowly and gets worse for many years. The RAAS system is a hormone system that regulates blood pressure, fluid and electrolyte balance, and systemic vascular resistance.

EPIDEMIOLOGY:

According to current estimates, nearly 15% of the population has some degree of renal damage, with risk groups reaching 50%. Diabetic kidney disease affects approximately one-third of all diabetic patients.

THE ACTION OF THE RENIN-ANGIOTENSIN-ALDOSTERONE-ANTAGONIST (RAAS) ON THE KIDNEY:

The agents of choice to control hypertension, representing RAAS inhibition, reduce urinary albumin excretion, thereby preventing renal function deterioration. A Renoprotective effect is exerted that is independent of the blood pressure reduction caused by RAAS inhibition. Comparing the effects of angiotensin-converting enzyme (ACE) and angiotensin II is used in many studies. RAAS plays an important role in blood pressure regulation, fluid volume, and sodium (NA+) balance. A variety of clinical conditions associated with CKD contribute to the overactivity of RAAS. Blood pressure regulation and determinant of target organ damage The RAAS system is a well-known pathway. Controlling fluid and electrolyte balance through coordinated effects of the heart, blood vessels, and kidneys AT-II AND ACE INHIBITORS: The main effector of RAAS is AT II, which exerts vasoconstrictor effect mainly on the post

glomerular arterioles, thereby increasing the glomerular hydraulic pressure and the ultrafiltration of plasma proteins, which contribute to the beginning and progression of chronic renal damage and can also accelerate renal damage by sustaining cell growth, inflammation, and fibrosis. The activity of RAAS is inhibited by the interventions, which are Renoprotective and may slow or even stop the progression of chronic nephropathies. Combination of ACE and AT II receptor antagonists to maximize RAAS inhibition and reduce proteinuria and GFR decline in diabetic and nondiabetic renal disease. According to a recent study, adding an aldosterone antagonist improves renoprotection but increases the risk of hyperkalemia.: In the presence of albuminuria, there is a benefit to slowing nephropathy progression, according to recent trials. The RAAS system plays a central role in the pathogenesis and progression of renal and cardiovascular damage. Inhibition of this system by using multiple agents has been proposed in the past, especially in the presence of proteinuria. Taking into consideration the high cardiovascular risk burden associated with DKD, a multifactorial therapeutic approach is traditionally recommended in which glucose and blood pressure control play an important role. In non-albuminuria patients, whether strict blood pressure and pharmacological RAAS inhibition entail a favorable renal outcome is still unclear. In the management of DKD, this aspect has become an important issue since non-albuminuria DKD is currently the prevailing phenotype. Due to these reasons, the management of blood pressure should be tailored to each patient's renal phenotype as well as related comorbidities. A multimodal approach including lifestyle modifications may achieve remission of proteinuria and stabilization of renal function in a substantial proportion of patients with proteinuria renal disease with RAAS inhibition combined with intensified amelioration of dyslipidemia. Novel RAAS inhibitors, such as renin inhibitors or Vaso peptidase inhibitors, may provide additional benefits to those who do not respond or respond only partially to this multimodal regimen, according to ongoing research. Blocking of RAAS either by the combined use of multiple drugs or by supramaximal doses of a single agent may provide greater renal protection. To advocate for this therapeutic approach in CKD patients. There is insufficient evidence to execute.

DUAL THERAPY VS. MONOTHERAPY:

- RAAS inhibition has a Renoprotective effect independent of blood pressure reduction when compared to the effects of ARBS or ACE-1 as monotherapy or in combination with both ACE-1 and ARB therapy. Most studies suggest that combination therapy provides a greater antiproteinuric effect than monotherapy, despite the methodological limitations, because of more prolonged and complete RAAS inhibition. In COOPERATE, combination therapy resulted in significantly longer times for doubling serum creatinine or developing ESRD than trandolapril or losartan monotherapy. In the secondary target, compared with ramipril or telmisartan alone, it was found that combination therapy significantly increased the risk of renal dysfunction. In AVOID, a combination with Aliskiren, a direct renin inhibitor, and losartan resulted in a 20% greater protein excretion decrease than losartan monotherapy. It also suggests that combination therapy should include direct renin inhibitors to benefit renoprotection. The use of RAAS inhibitors as dual or monotherapy is beneficial at various stages of renal disease. RAAS inhibitors play a protective role both in the early and late stages of kidney disease by preventing proteinuria, kidney fibrosis, and the slow decline of renal function found in experimental and clinical studies. Combination therapy has higher efficiency than monotherapy and is also associated with a higher incidence of adverse effects. Aside from the ACE and ARBS, more mechanism research for the use of mineralocorticoids as receptor antagonists is needed.

CONCLUSIONS:

The choice of drugs to control HTN is RAAS inhibitors which reduce urinary albumin excretion and thereby delay renal function deterioration. Proteinuria is used as an endpoint in many studies to compare the effects of ace and arb's monotherapy with a combination of ACE and ARB therapy. The use of RAAS inhibitors as dual or monotherapy is beneficial at various stages of renal disease. RAAS inhibitors play a protective role both in the early and late stages of kidney disease by preventing proteinuria, kidney fibrosis, and the slow decline of renal function found in experimental and clinical studies. Most of the studies suggested that combination therapy provides a great antiproteinuric effect than monotherapy because of more prolonged and complete RAAS inhibition. A more favorable renal outcome in non-albuminuric patients is unclear.

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