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Effect of Renin-Angiotensin System Blockers on Serum Potassium Levels in Hemodialysis Patient in the Year 2019-2020

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Abstract:- Background: Renin-angiotensin system blockers (ACE-I or ARBS) is well known to be associated with hyperkalemia in patients with advanced chronic kidney disease (CKD) who are not on dialysis. However, few studies have investigated the relationship between renin-angiotensin system blockers (RASB) and hyperkalemia in chronic HD patients, and the results remain controversial. Methods: The research sample included 111 patients from hemodialysis patients in the hemodialysis division at Tishreen University Hospital in Latakia,Syria .The research sample was divided into two groups : the first group takes RASB and the second group was not taking these medications in order to study the effect of these medication on serum potassium levels .A blood potassium analysis was conducted monthly for 6 months during the time period 2019-2020. Resuls: there was no statistically significant difference in the mean values of serum potassium between the two research groups , but it was lower in the case group.Where the mean values of serum potassium were between the group that was taking RASB and the group that did not take RASB:(K serum with RASB= 4.44±0.3 VS K serum without RASB 4.85±0.4 mmol/l , p=0,08). Conclusion: there is no relationship between RASB and hyperkalemia in chronic hemodialysis patient, but close potassium monitoring is mandatory.

Keywords:- *Renin-Angiotensin System Blockers , Angiotensin-Converting Enzyme Inhibitor, Angiotensin II Receptor Blocker, Hyperkalemia , Hemodialysis.*

I. INTRODUCTION

Hyperkalemia is a serious medical condition that can cause severe cardiac electrophysiology alterations, such as cardiac arrhythmias , and sudden death, hyperkalemia is defined as a serum potassium more than 5 mmol/l, Patients with chronic kidney disease (CKD) (especially advanced CKD) are at high risk for hyperkalemia, especially when other factors and comorbidities that interfere with renal potassium excretion are present. The prevalence of hyperkalemia in CKD patients is considerably higher than in the general population. A recent review reports hyperkalemia frequency as high as 40-50% in the CKD population compared to 2-3% in the general population. [1]

Those at highest risk are patients with diabetes and advanced CKD, kidney transplant recipients, and patients treated with renin-angiotensin aldosterone system (RAAS) inhibitors. Moreover, an episode of hyperkalemia in patients with CKD increases the odds of mortality within one day of the event.[2] Patients undergoing PD have a lower risk of developing hyperkalemia than those on HD because of the continuous nature of PD treatment,[3] and the fact that many patients on PD retain residual kidney function for longer than those on HD and receive high-dose diuretics, which increases the urinary excretion of K.[4]

Cardiovascular diseases are the main cause of morbidity and mortality in patients with chronic renal failure and occur in 50-60%.[5]

The renin-angiotensin-aldosterone system (RAAS) plays key roles in the regulation of blood pressure, blood volume and cardiovascular function. Therapeutic manipulation of the RAAS by the use of angiotensin converting enzyme inhibitors (ACEi) and/or angiotensin receptor blockers (ARBs) is an important treatment strategy for hypertension, heart failure, and diabetic patients.[6] In recent years, ACEi and ARB have been increasingly used in patients with ESRD with the aim to reduce fatal and nonfatal cardiovascular events and left ventricular mass.[7] However, recent evidence suggests that ACEi and ARB may not be superior to other antihypertensive agents in reducing cardiovascular risk in advanced kidney disease.[8] In contrast with those patients before the start of maintenance hemodialysis, renin–angiotensin system (RAS) blockades are not likely to have major effects on the serum potassium levels in patients on maintenance dialysis because the removal of potassium is achieved mainly by hemodialysis and renal excretion plays a minor role in those patients .[9] However, their effect on serum potassium (sK) concentrations in patients on chronic HD treatment is still controversial.

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II. MATERIALS AND METHODS

The research sample included 111 patients from hemodialysis patients in the hemodialysis division at Tishreen University Hospital in Latakia whose started hemodialysis since three months or more .The research sample was divided into two groups : the first group was taking RASB (44 patient) and the second group was not taking these medications (67 patient) in order to study the effect of these medication on serum potassium levels . (figure 1)

The first group was divided into two group : the first group was taking ACEI (17 patient) and the second group was taking ARBS these medications (27 patient). (table 1).

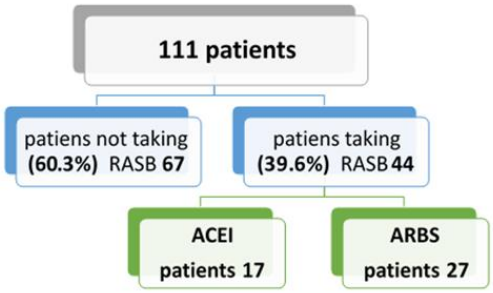

Fig 1:- Shows Those included in the research in the Hemodialysis Division at Tishreen University Hospital in Lattakia during the time period 2019-2020.

In addition to recording the demographic characteristics (age, gender, cause of renal failure) for the patients of the research sample, each of the following was carried out: an average of one value per month for a period of 6 months in the time period 2019-2020:Potassium and sodium analyzes before dialysis, measuring the rate of weight gain between sessions, measuring arterial pressure values before dialysis. exclusion criteria were Hemodialysis patients taking potassium-reducing drugs: sodium polystyrene sulfonate (Kayexalate) or calcium polystyrene sulfonate (calcium resonium) ,or hemodialysis patients who have gastrointestinal bleeding and who have had blood transfusions or who have been admitted to the hospital for a period of two weeks , or Chronic hemodialysis patients who have irregular dialysis

Patients on ACEi	**17**	
Drug	patients, n	dose, mg
Fosinopril	4	(10-2)
Enalapril	5	(10-40)
Ramipril	8	(5 -10)
Patients on ARBS	**27**	
Drug	patients, n	dose, mg
Valsartan	18	(80-160)
Telmisartan	9	(40-80)

Table 1:- Shows Type and dosage of renin-angiotensin-aldosterone system blocker drugs in the 111 patients under study

III. RESULTS

The ages of the study sample patients ranged from 22 to 90 years old. The mean age was 54.49 ± 15.2 years. 58.2% of the studied research sample was male with Sex Ratio(M:F)=1.4:1 (table 2)

Research sample	**The number**	**Percentage**
Male	**63**	**58.2%**
Female	**48**	**41.8%**
The total	**111**	**100%**

Table 2:- Shows Distribution of a sample of 111 patients by gender.

The most common causes of renal insufficiency were the presence of diabetes mellitus with a rate of 39.6%, followed hypertension with a rate of 26.1% (figure 2).

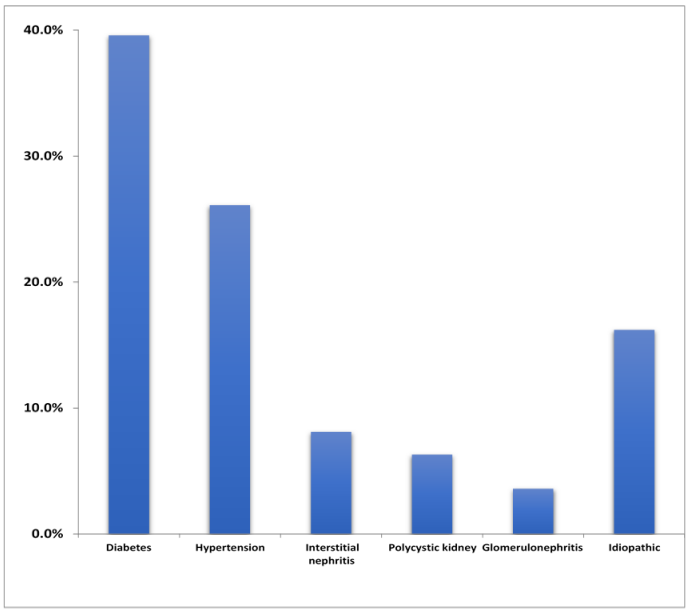

Fig 2:- Shows Distribution of a sample of 111 patients according to the cause of renal failure

There was no statistically significant difference in the mean values of serum potassium between the two research groups , but it was lower in the case group.

Where the mean values of serum potassium were between the group that was taking RASB and the group that did not take RASB:

(K serum with RASB= 4.44±0.3 VS K serum without RASB 4.85±0.4 mmol/l , p=0,08). (table 3).

There were also no statistically significant differences regarding the mean values of serum potassium and they were lower in the case group compared to the control group and between the two groups of cases the mean values of serum potassium were close and without statistically significant differences with p-value = 0.8.

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	First group	Second group	p-value
serum potassium	**4.44±0.3**	**4.85±0.4**	**0.08**

Table 3:- Shows Comparison of the mean values of serum potassium between the two groups of patients.

We also studied the effect of RASB on the rate of weight gain in addition to its effect on serum sodium levels in patients with chronic hemodialysis. Our results showed that there was no difference between the mean rate of weight gain between patients placed on RASB and the control group, where the mean values of the rate of weight gain were : (IDWG,G= 2165.19±984.3 VS 2266.37±949.5 g, p=0.6). (table 4)

	First group	**Second group**	**p.value**
IDWG,g	2165.19±984.3	2266.37±949.5	0.6

Table 4:- Shows Comparison of mean values of weight gain between the two groups of patients**.**

In addition to the absence of a statistically significant difference between the two groups of patients in the study sample with regard to the mean values of serum sodium : (Serum Na with RASB= 137.74±0.9 mmol/l vs Serum Na without RASB = 137.65±0.7 mmol/l , p=0,6). (table 5)

	First group	**Second group**	**p.value**
serum sodium	137.74±0.9	137.65±0.7	0,6

Table 5:- Shows Comparison of the mean values of serum sodium between the two groups of patients.

The results of our study showed that there were no statistically significant differences between the two groups of patients in the research sample with regard to the mean values of arterial pressure, whether systolic or diastolic, where the mean values were: (Pre HD SBP with RASB = 13.01±1.02 vs Pre HD without RASB = 12.77±0.9,P=0,2) . Pre HD DBP with RASB = 6.92±0.5 vs Pre HD without RASB = 7.16±1.7, P=0,4)) . (table 6)

	First group	**Second group**	**p. value**
PAS, mm Hg	13.01±1.02	12.77±0.9	0.2
PAD, mm Hg	6.92±0.5	7.16±1.7	0.4

Table 6:- shows Comparison of the mean values of arterial pressure between the two groups of patients.

IV. DISCUSSION

RASB is frequently indicated in renal failure patients. The relationship between RASB and hyperkalemia in patients with end-stage renal disease (ESRD) receiving chronic HD remains controversial.

In this study, there was no difference in mean potassium levels among three groups, i.e. no exposure to any RAS blockades, or ACEI, or ARB, during the 6-month study period.

As a result, in our prospective study of patients receiving maintenance hemodialysis,the use of an ACEI or an ARB did not result in increased risk of hyperkalaemia.

One study found that the use of ACEIs or ARBs significantly increased serum potassium from the baseline values in anuric hemodialysis patients.[6] The authors suggested that interference with the RAS in patients on maintenance dialysis might impair intestinal potassium excretion or block tissue potassium redistribution. The authors claimed that aldosterone plays an important role in increasing potassium excretion via the intestinal tracts and in potassium redistribution in many cell types. In patients with chronic renal failure, gut elimination of potassium is shown to be increased, and appears to be mediated by increased colonic secretion of potassium .[10] In either case, RAS blockades in chronic renal failure would interfere with potassium homeostasis. However, increased fecal potassium excretion as an extrarenal adaptation of potassium homeostasis in chronic renal failure has not been convincingly demonstrated .[11]

Furthermore, recent studies have shown that a high dose of the non-selective aldosterone antagonist, spironolactone does not produce hyperkalemia in chronic hemodialysis patients.[12]

However, another one published in 2007 found that neither monotherapy (ACEI or ARB) nor combination therapy (ACEI plus ARB) was associated with the risk of hyperkaliemia in chronic HD patients.[9] However, there were several limitations of this study. First, although all patients were educated about a low potassium diet before blood sampling, some patients might not follow the diet accurately, and the potassium content of the patients food were not measured. Second Potassium values were routinely performed only monthly, without measurement of these values in emergency rooms or before additional dialysis sessions, which are more likely to hyperkalemia in these cases.

V. CONCLUSIONS

Our findings show that renin-angiotensin system blockade is not associated with hyperkalemia in chronic hemodialysis patients.

In addition, there was no statistically significant relationship between RASB and rate of weight gain, serum sodium levels, and diastolic or systolic arterial tension values in chronic hemodialysis patients.

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