Original article

Study of growth in children with renal tubular acidosis and the effect of treatment

Dr. Maya Borle[1], Dr.Promod Jog [2]

[1]Associate professor, Department of Pediatrics, Dr.DY Patil Medical College, Hospital &Research Centre , Pimpri , Pune
[2]Professor, Department of Pediatrics, Dr.DY Patil Medical College, Hospital &Research Centre, Pimpri , Pune
Corresponding author: Dr. Maya Borle

Abstract:

Introduction: Renal Tubular Acidosis is Tubular disorder, characterized by normal anion gap metabolic acidosis. Growth is severely affected, mainly due to mobilization of organic components from bone to serve as buffers to counter the chronic metabolic acidosis.

Methods: A prospective Case Control and Comparative study was under taken in a Tertiary care hospital in Semi-Urban part of Pune.Out of 120 study subjects ,30 had Renal Tubular Acidosis(RTA) and 90 were normal children up to 15years of age.

Observations: Children with RTA presented at a median age of 6 years. Treatment resulted in significant improvement in growth parameters. We found serum Bicarbonate levels to be reliable indicators for drug compliance.

Results & Conclusion: Median age for presentation was found to be 6 years. Screening of children with Short stature helped in early diagnosis. Significant improvement in growth was seen on starting treatment with Bicarbonate ,though the results in those with Proximal RTA were less encouraging. Hypokalemia was seen to persist even after commencement of therapy -hence we recommend prolonged Potassium supplementation in such patients.

Key words: Renal tubular acidosis, Growth retardation, Alkali Treatment

Introduction

Renal Tubular Acidosis (RTA) is a disease state characterized by normal anion gap metabolic acidosis, resulting from either impaired bicarbonate reabsorption or defective urinary acid secretion within the renal tubule. Renal function test remain intact. Inherited and Acquired forms exist. There are four main types of RTA-Type II (Proximal(RTA),Type I(Distal RTA) and Type IV (Hyperkalemic RTA).Type III form has been seen to have features of both type I and type II. Patients RTA mainly present with Growth failure in infancy. Proximal RTA results from impaired bicarbonate reabsorption Additional symptoms may be polyuria, dehydration,anorexia,vomiting, constipation and hypotonia .Wasting of Phosphate and consequent Rickets is seen in Fanconi Syndrome. Besides bicarbonaturia, aminoaciduria, glycosuria, and uricosuria are also present. Fifteen percent bicarbonate is normally excreted in urine at normal bicarbonate levels. Normally acid loads are successfully excreted in urine and do not lead to metabolic acidosis.

Distal RTA results from impaired urinary acidification ie.hydrogen ion secretion. Mechanism is probably due to damaged or impaired functioning of one or more transporters or proteins involved in the acidification process. This include the H+/ATPase

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,the HCCO3-/Cl- anion exchangers or the components of aldosterone pathway. Due to the impaired hydrogen ion excretion the urinary pH cannot be reduced below 5.5 despite of severe metabolic acidosis.

Nephrocalcinosis and Nephrolithiasis may be present consequent to Hypercalciuria which is also a prominent feature of Distal RTA. In these children persistent acidosis may be critical leading to Growth retardation.[1,2,3] The logic says that indeed, if it is the metabolic acidosis which is reason for short stature and poor weight gain, then correction of metabolic acidosis by alkali therapy should be able to reverse these problems.[4,5,6] Bone disease is common resulting from mobilization of organic components from bone which serve as bone buffers for acidosis. Also it is seen that Metabolic acidosis interferes with action of growth hormone ,more specifically IGF 1.This leads to severe short stature. Severe Rickets is generally seen in Distal RTA,with initial signs and symptoms being failure to thrive,polyuria and increased intake of water. Due to hypokalemia (impaired H+ secretion), transient paralysis may be seen. Autosomal form of Distal RTA is associated with sensorineural deafness. Type IV(Hyperkalemic) RTA occurs due to Hypo-aldosteronism or impaired responsiveness to aldosterone .In addition to direct effect on H+ ATPase responsible for hydrogen ion secretion,aldosterone is a potent stimulant for Potassium secretion in collecting tubule. Loss of aldosterone effects leads to Hyperkalemic metabolic acidosis.

Mainstay of therapy in all forms of RTA is Bicarbonate replacement. Bone has Calcium carbonate .It is a buffer for the acid in blood.The presence of metabolic acidosis thus will lead to dissolution of bone, affecting growth. Administration of sufficient bicarbonate to reverse acidosis stops bone dissolution and Hypercalciuria. Proximal RTA is treated with bicarbonate an oral phosphates supplements. Vitamin D is indicated to offset secondary Hyperparathyroism. Patients with Fanconi Syndrome also require phosphate replacement. Those children with hypercalciuria may also need thiazide diuretics. Type IV patients need chronic treatment for hyperkalemia beside treatment of specific aetiology. Prognosis is dependent on nature of underlying disease.

Aims and Objectives

1.To study the Growth Parameters in children withRTA.

2.To study the symptoms at presentation in RTA.

3.To Co-relate the the serum bicarbonate levels with improvement in Growth.

Material and Methods

A prospective Case Control Study was undertaken for a period of two years. 120 children were enrolled out of which 30 had RTA and 90 were normal.

Inclusion Criteria: Controls were normal children up to 15years of age irrespective of racial or ethnic bias, after informed consent.

Cases were diagnosed as RTA depending on presence of the following and started on therapy after taking their anthropometric measurement:

1.Hyperchloremic normal anion gap metabolic acidosis

2.Blood bicarbonate levels <20meq/L with Urine pH<5.5- type II,or >5.5- Type I

3. Normal Renal Functions.

4.Hyper or Hypokalemia

Exclusion criteria:

1.Children with chronic systemic illness

2..Failure to thrive due to other causes

3.Unwilling candidates

Methodology:

The children with RTA were assessed with a detailed history for growth, failure to thrive and Blood and Urine analysis .In this study the growth was assessed by weight and height .The standard deviation of height and weight was calculated by using the NCHS charts(National Centre for Health Statistics)-Centre for disease control and Prevention).Less than 2SD in Height and weight was taken as Short Stature and Failure to Thrive respectively. Hb,VBG,S.Na,S.K,S.Ca,S.P,Blood Urea,S.creatinine Urine for pH, Glucose, proteins, hematuria,

aminoaciduria.For every case, three controls of the same sex and age were taken.All data was analyzed for statistical significance. Descriptive statistics was used for categorical and interval data. Categorical data was summarized with95%CI.Interval data was summarized with mean, median and Standard Deviation.

Results Observations

- For RTA Median age was found to be 6 years.
- There was male predominance with 53.3%(16 children).

Table I: Symptoms at Presentation of all the children with RTA:

Symptoms	%(number of children)
Failure to thrive	100%(30)
Polyuria	76%(23)
Dehydration	20%(6)
Anorexia	76%(23)
Vomiting	33%(10)
Constipation	6%(2)

TableII: Distribution of weight in Cases Versus Controls at the beginning of the Study:

Initial Values	Weight<-2SD	Weight>-2SD	P Value
Cases	15	15	
Controls	0	90	<0.001

TableIII: Distribution of weight in Cases Versus Controls at the End of the Study:

End Values	Weight<-2SD	Weight>-2SD	P Value
Cases	2	28	
Controls	0	90	<0.09

Table IV: Distribution of weight parameter in cases at the Start and the End of the study:

Weight of Cases	<-2SD	>-2SD	P Value
Initial	15	15	
End of study	2	28	<0.001

Table V: Distribution of Height Parameters in cases at the start of the Study:

Initial Values	Height<-2SD	Height>-2SD	P Value
Cases	19	11	

| Controls | 0 | 90 | <0.001 |

Table VI: Distribution of Height parameters in Cases at beginning and at the end of the Study:

Height(Cases)	<-2SD	>-2SD	P Value
Initial	19	11	<0.001
End	4	26	

Table VII: Correlation Co-Efficient (r Value) for Height and Weight:

Parameter	R Value
Height	0.99
Weight	0.98

Table VIII: Correlation Co-Efficient (r Value) for Height and Weight with Bicarbonate Therapy:

Parameter	R Value
Height to Bicarbonate	-0.225
Weight to Bicarbonate	-0.225

Discussion

30 children suffering from Renal Tubular Acidosis (RTA) were compared with 90 normal subjectS ,who were matched for age and sex .This study intended to compare the growth parameters in children of the two groups and to see the effectiveness of therapy in children with RTA by monitoring their growth.In our study, the median age of diagnosis was 6 years. This is comparable to the study of Bugga et al(254).[7]While our study had male preponderance of 53.3%, the same study of Bugga et al showed 11 out of 18 children to be males. Symptomatically before treatment, all children (100%) had poor weight and height gain. Polyuria was seen in76% of the children in our study. Bugga et al had 100% patients with Polyuria. In the present study, anorexia was present in 76% of subjects, constipation in 6%, and another 33% had history of vomiting.

In the study by SantosF, Chan JC on children with type I RTA, the presenting signs and symptoms were Failure to thrive (50%), Vomiting or Diarrhea (37.5%), Dehydration(12.5%),and poor feeding(8.3%).[8]

When our study was started 50% of the children had a weight <-2SD.In the study by A Bajpai,A Bagga all subjects had Failure to thrive and Short Stature was also present in 100% children. [7] In another study by Elizabeth McSherry and RMorris involving 10 patients of RTA ,it was seen that at the point of beginning alkali therapy was started 6 patients were stunted. [9] When comparing the initial and end weights of the cases, the growth was significant with a P value of <0.001.This comparable to the study by A Bagga in which the increase in weight was analyzed and was found to be 0.0001.Similarly for height ,the growth was good with P value of <0.001 in our study while in Dr. Bugga study it was <0.0001.[7] The results of the study by McSherry et al showed that with sustained alkali therapy each patient attained and maintained normal stature. The mean height of the 10 patients increased from 1.4±4 to the 37.0±33 percentile (of the normal age and gender matched population).The mean height reached the 69th perce-ntile in 8 patients(80%).[9] In yet another study by Santos F et al the percentile weight (mean +/-SD) increased from

the initial 11.8±7.5 to the final 27.6±31.3(P value<0.003) and the the length /height perc-entile increased from 11.5±7.3 to 29.7±24.2(P Value<0.003). [8] Dr.A Bugga s study considered bicar-bonate levels >20meq/l as adequate. Of their 18 patients ,2 showed persistent metabolic acidosis-one patient had poor compliance and another one had renal insufficiency.[7] In our study 4 patients remained below -2SD for height -out of which 2 were noncompliant(Distal RTA) .The bicarbonate levels values of these were 18meq/l .The other two had Proximal RTA.

There was good correlation of catch up growth with corrected acidosis (Bicarbonate values).The r values were -0.225 for height and -0.225 for weight. In the study by Bajpai et al ,they correlated with Base excess-the weight and height correlated negatively with base excess.[7] The encouraging result is due to the treatment of chronic acidosis. Besides saving the bicarbonate buffers thereby saving bone dissolu-tion, hormonal influences may also contribute. The anti-anabolic effect of chronic metabolic acidosis was shown in the study of Green et al. They found that there was a state of partial resistance to Growth horm-one and IGF I due to chronic metabolic acidosis which led to defective longitudinal growth of bones. [10] In our study we found 2 patients with acidic urine in face of metabolic acidosis .These were Proximal RTA cases. The study by Soriano et al had two patients of Proximal RTA .Both these patients were unable to respond normally to metabolic acidosis with excretion of very acidic urine. The conclusion was that Proximal RTA requires inordinately high doses of bicarbonate to maintain bicarbonate levels within normal range.[11]In other words we need higher doses of alkali to get the patients growing, in cases of Proximal RTA. In another study[12] the investigators found that these patients ,during the basal state excreted urine with low pH(5.5±0.18).

Conclusion

The median age is found to be 6 years at diagnosis with a slight male preponderance of 53.3%.

The commonest symptom was failure to thrive followed by anorexia and polyuria.

Significant number had growth retardation which improved with medication;weight gain being better than height gain.

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