Original article:

A Prospective Study of Growth in Children with Renal Tubular Acidosis and the Effect of Treatment

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ABSTRACT:

Introduction: The present study was undertaken to evaluate complications in children adequately treated with distal renal tubular acidosis (RTA). Also study was extended to identify factors influencing their development and effect of treatment during the course of study.

Materials and Methods: The patients identified and diagnosed with primary distal RTA and suffering from more than 2 years at this hospital were reviewed and records were maintained. Case records were examined for age at onset of symptoms and at initiation of treatment, treatment protocols, follow-up and complications. The various parameters related to growth velocity like height, weight were expressed as standard deviation score (SDS) during the course of study and data have been assessed with regression analysis. P value of less than 0.05 was considered to be significant.

Results: Of 30 patients (ninteen boys), the diagnosis was established at the median (range) age of 6 yr (1.5-13 yr). These patients were followed up for an average period of 4 yr (2-18.5 yr). Short stature (height SDS< –2) was noted in all patients at the time of diagnosis with median (range) height SDS of –5.2 (–7.5 - –0.4). All patients had failure to thrive with median (range) weight SDS of –3 (–5.7 - –1.5). Height SDS increased by median (range) of 2 (1.2-5.5) to become –2.7 (–4.8 - –1.1) at last follow-up. Weight SDS increased by median (range) of 0.9 (–0.6 - 2.8) to become –2.4 (–4 - –0.5). Median (range) growth velocity SDS decreased from 3 (1-16) during first year of treatment to 1 (–0.3 - 7) at four years with an increase in mean height SDS by 1.3 during the first two years of treatment. The incidence of rickets overcomes without treatment with vitamin D in twenty five patients after a median (range) period of 4 month (1-12 month). 7 patients (24.4%) had nephrocalcinosis at diagnosis. Twenty-four hour urine calcium excretion was higher in those with nephrocalcinosis (P = 0.01).

Conclusions: There is a need for early diagnosis, appropriate treatment and regular follow-up of patients with distal RTA for improving outcome.

Keywords: Distal Renal Tubular Acidosis, Growth, Nephrocalcinosis.

INTRODUCTION

The renal tubules are an important organ in homeostasis and regulation of body fluid, electrolyte, and acid-base. Any impairment in its regular function leads to a number of complications and disorders.[1,2] These complications may be inherited or acquired. In the developing countries like India and China, the data is spreading with alarming rate. Renal tubular acidosis (RTA) is characterized as a systemic metabolic acidosis pointing to a decrease in glomerular filtration rate. Renal tubular acidosis (RTA) is a group of transport defects secondary to

reduced proximal tubular reabsorption of bicarbonate (HCO_3^-), the distal secretion of protons (hydrogen ion, H^+) or both, resulting in decreased capacity for net acid excretion and persistent hyperchloremicmetabolic acidosis.[3,4] Specially in the hyperchloremic metabolic acidosis the patients are diagnosed to have distal RTA when there is normal anion gap, low urine Hydrogen ion concentration, positive urine net charge, normal excretion of bicarbonate, low urinary CO_2 and hypercalciuria. The most accepted mechanism is due to damaged or dysfunctioning of one or more transporter proteins involved in the buffering of pH. This include the Hydrogen ion/ATPase,the carbonate ion/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.[4-6] 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.[7] Wasting of Phosphate and consequent Rickets is seen in Fanconi Syndrome. Besides bicarbonaturia, aminoaciduria, glycosuria, and uricosuria are also present.[8] Fifteen percent bicarbonate is normally excreted in urine at normal bicarbonate levels. Generally the acidic components are excreted through urine and thus the net urine-plasma pH remains buffered which do not lead to metabolic acidosis. Prompt diagnosis and quick therapeuticinterventions can improve the overall clinical outcome of these children. On the other hand the metabolic acidosis results to bone dissolution andserious effects on growth. The plasma and urine pH can also be restored by sufficient bicarbonate administration which 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. Also children suffering with hypercalciuria need thiazide diuretics. Type IV patients need chronic treatment for hyperkalemia beside treatment of specific aetiology. Prognosis is dependent on nature of underlying disease.

MATERIALS AND METHODS

The present study entitled, “Study of growth in children with renal tubular acidosis and the effect of treatment” was conducted for a period of two years. Total of 120 children were enrolled out of which 30 had RTA and 90 were normal.

Inclusion Criteria

The normal healthy children up to 15years of age were treated as control which was 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 5.5- Type I
3. Normal Renal Functions.
4. Hyper or Hypokalemia

Exclusion Criteria

1. Patients suffering from chronic systemic illness
2. Failure to thrive due to other causes
3. Candidates not agree to participate

Methodology

The children with RTA were assessed with a detailed history for growth, failure to thrive and Blood and Urine analysis. The growth was mainly assessed by weight and height .The individual weight and heights was measured time to time and the standard deviation of height and weight was determined 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. Urine for pH, Glucose, proteins, haematuria, 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 with 95% CI. Interval data was summarized with mean, median and Standard Deviation.

RESULTS

Out of 120 children's enrolled for the study 90 were normal and healthy whereas 30 were diagnosed with distal RTA. Their average age was 6 years. The various complications and complaints registered from the patients is summarized in table 1. All the patients had complaint of failure to thrive, where as 76% cases were found to suffer from polyuria and anorexia. Other complains were regarding dehyderation (20%), vomiting (33%) and constipation (6%).

Table 1: 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)

Table 2: Distribution of weight in Cases Versus Controls at the beginning of the Study

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

Table 3: Distribution of weight in Cases Versus Controls at the End of the Study

End Values	Weight<-2SD	Weight>-2SD	P Value
Cases	2	28	<0.01
Controls	0	90	

Table 4: 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	<0.001
End of study	2	28	

Table 5: Distribution of Height Parameters in cases at the start of the Study

Initial Values	Height<-2SD	Height>-2SD	P Value
Cases	9	11	<0.001
Controls	0	90	

Table 6: Distribution of Height parameters in Cases at beginning and at the end of the Study

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

Table 7: Correlation Co-Efficient (r Value) for Height and Weight

Parameter	R Value
Height	0.99
Weight	0.98

DISCUSSION

120 children of approximately same age were taken into account where 30 children suffering from Renal Tubular Acidosis (RTA) whereas 90 were normal subject.The study was aimed to compare the rate of growth in children of normal and diagnosed groups. Further the study was subjected to evaluate the effectiveness of treatments in children with RTA by monitoring their growth at regular intervals. The average age of the studied population was 6 years which is in accordance to the previous study conducted by Bugga et al (254).[9] In present study the boys (male patients) were predominant (53.3%), the same study of Bugga et al showed 11 out of 18 children to be males. With a matter of fact before the start of treatment all the childrens were found to be poor weight and height. The various complains from the patients were recorded where Polyuria was seen in76% of the children in our study. Bugga et al had 100% patients with Polyuria. Similarly we observed76% cases of anorexia, constipation in 6%, and another 33% had history of vomiting. In the study by Santos F, 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%).[10] 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.[11] In another study by Elizabeth McSherry and R Morris involving 10 patients of RTA, it was seen that at the point of beginning alkali therapy was started 6 patients were stunted.[12] 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.

Dr. A Bugga study considered bicarbonate 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. In our study 4 patients were 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 regression coefficient 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.[13] The results were encouraging which is due to the treatment of chronic acidosis. Besides preserving the bicarbonate buffers thereby saving bone demineralization, hormonal influences may also contribute. The antianabolic 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 hormone and IGF I due to chronic metabolic acidosis which led to defective longitudinal growth of bones.[14] 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. In other words we need higher doses of alkali to get the patients growing, in cases of Proximal RTA. In another study[14] the investigators found that these patients, during the basal state excreted urine with low pH(5.5±0.18).

CONCLUSION

The 12o children taken to the study were having an average age of 6 years. Out of the diagnosed children (30) a slight male preponderance of 53.3% was seen. The most common symptom was failure to thrive followed by anorexia and polyuria. The height and weight of significant number of patients was retarded which improved with treatment protocol during the course of study. Also the gain in weight was more than that of height.

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