BIOLOGIA (PAKISTAN)
June, 2018, 64 (1), 129-134

PKISSN 0006 – 3096 (Print)
ISSN 2313 – 206X (On-Line)

Comparative study of effect of Shohl's solution in pediatric patients with Renal Tubular Acidosis

USAMA SARDAR GORSI[1], UMAR FAROOQ GOHAR[2], AAMIR MUSHTAQ*[3], BASHIR AHMAD[1] & ASAD MEHMOOD[4]

[1]Riphah Institute of Pharmaceutical Science, Riphah International University Lahore
[2]Institute of Industrial Biotechnology, GC University Lahore
[3]Gulab Devi Institute of Pharmacy, Gulab Devi Educational Complex Lahore
[4]Faculty of Pharmacy, University of Central Punjab, Lahore

ABSTRACT

Renal Tubular Acidosis is characterized by the failure of kidney to excrete acid in urine by affecting the reabsorption of bicarbonate ion or excretion of ammonia. Different treatments are used to treat underlying cause but the first goal of treatment is to neutralize the acid in blood. Shohl's solution (bicitra, polycitra & polycitra K) is used to neutralize acid in blood. During the study 34 patients taking bicitra, polycitra and polycitra K were observed for 6 months and sodium, potassium, bicarbonate and pH values were measured at least twice during that period. It was observed that 44 % patients showed no change in prescription, 15 % patients showed change in medicine and 41 % patients exhibited change in dose. The changes in the observed parameters were due to bicarbonate level. Hereditary Factor was also observed and it was concluded that parents of 85 % patients had cousin marriages.

Key words: Renal tubular acidosis, Shohl's solution, Bicitra, Polycitra, Polycitra K

INTRODUCTION

Renal tubular acidosis (RTA) in children is either an inherited or acquired defect. The ability of the kidneys to reabsorb filtered bicarbonate ions or excrete ammonia or titratable acid is affected in renal tubular acidosis (Borthwick *et al.*, 2003). On the subject of epidemiology of renal tubular acidosis, the medical literature is evasive. The disease is less reported and the patients in which incomplete forms of RTA exists are often not diagnosed. These reasons restrict the exactitude of incidence and prevalence of RTA in children. Congenital disorders are fewer than acquired forms (Nash *et al.*, 1972).

Patients with renal tubular acidosis are usually presented with the following clinical features retardation in growth, polyuria (large volume of urine with greater urinary frequency), polydipsia (excessive thirst), persistent rickets, renal calculi (kidney stones), nephrocalcinosis (calcium levels are increased in kidney), other symptoms may include, dehydration, fatigue, weakness, pain in muscles, pain in bones or back or abdomen, increased heart rate, confusion, vitamin D deficiency (van Woerden *et al.*, 2003). Laboratory findings for renal tubular acidosis include, metabolic acidosis with hyperchloremia (high chlorine levels), metabolic alkalosis with or without hypokalemia (low potassium levels), hyponatremia (low sodium levels) along with hyperkalemia (high potassium levels), increased calcium in urine with normal serum calcium (Spector & McKhann, 1948).

In all cases and all types of RTA, the first aim of treatment is the neutralization of acid in the blood. Various therapies might also be required to treat the various underlying causes of renal tubular acidosis. Neutralization of acid in the blood is done by giving high doses of alkalis. Alkali therapy includes sodium bicarbonate, sodium or potassium citrate and citric acid. Kidney function is stabilized and formation of kidney stones is decreased with alkali therapies.

Author's Contribution: U.F.G., & B.A., Designed and supervised study; **U.S.G.** Performed experiments; **A.M.** Compiled data**; A.M.** Assisted in manuscript writing**;**
***Corresponding author**:aamir_mushtaq@hotmail.com

A solution of sodium and/or potassium citrate and citric acid is called Shohl's solution. Shohl's solution has to be given daily in divided doses for long term. Potassium replacement is also necessary in hypokalemic renal tubular acidosis (Coburn *et al.*, 1991; Izol *et al.*, 2013; Oduwole *et al.*, 2010)Shohl's solution is available in market by the generic names of bicitra, polycitra and polycitra K (Kalinowski & Kirsch, 2004).

MATERIAL AND METHODS

Study Design

It was a prospective study conducted to compare the effect of Shohls'solution (bicitra, polycitra&polycitra K) in pediatric patients with renal tubular acidosis. The number of patients observed, were thirty four. All these were taking Shohls' solution. These were observed for period of six months. Effect of Shohl's solution on laboratory values and in return change in prescription was observed. Parameters evaluated were sodium, potassium, bicarbonate and pH of the urine. These values were monitored twice during six months.

Data Collection

Patient's data was collected from the records of patients on prescribed form and laboratory reports of the patients were also observed for the collection of relevant findings. All the laboratory tests were conducted by the reputable, authentic and approved laboratories. Data collection form is given in figure 18.

Participants

Participants used in study were pediatric patients diagnosed with renal tubular acidosis

Inclusion & Exclusion Criteria

Pediatric patients less than 16 years of age both male and female were included in study.

Main Outcome Measures

Evaluation of the relationship between doses and lab values was done and clinical impact of treatment was also analyzed. Effect of Shohl's solution in management of renal tubular acidosis was also monitored.

Statistical Analysis

All data were analyzed by descriptive statistical analysis using phi Cramer's test on SPSS.

RESULTS AND DISCUSSIONS

Sample consisted of thirty four pediatric patients who were selected randomly with age limit less than 16 years suffering from renal tubular acidosis. These patients were prescribed Shohl's solution (bicitra, polycitra and polycitra K) for the management of renal tubular acidosis. It was observed that young estpatient was 0.25 years (3months) old while eldest patient was 15 years old.

Patients were divided into three groups on the basis of age i.e. group 1 contained patients up to 5 years of age, group 2 contained patients between 5 and 10 years age and group 3 contained patients above 10 years of age as shown in fig 1. 41% patients were from age group less than five years old, 53% patients were from five years to ten years of age and 6% patients had age above ten years. It was observed that maximum numbers of patients were from age group 2 followed by age group 1 and 3 respectively which is shown in Figure2.

The gender distribution of the patients into groups has been shown in the fig 3. The age group 1(AG-1) was further subdivided into two groups i.e. male and female. According to this age group 1 contained total of 14 patients and among them seven patients were male and seven were females. In age group 2 (AG-2) out of total eighteen patients number of males and females patients were twelve and six, respectively, whereas group 3 contained two patients and both were females. It was observed that maximum percentage of female in group 3 was 100% followed by 50% in group 1 and 33% in group 2 as shown in fig 4.

Data of patient weight showed that lightest patient had weight of 4.5 kilograms whereas heaviest patient was of 38 kilograms weight. On the basis of weight patients were divided in three groups i.e. weight group 1 (WG-1) contained patients with weight up to 15 kilograms, group 2 (WG-2) contained patients with weight between 16 to 30 kilograms and group 3 (WG-3) contained patients above 30 kilograms of weight. Figure 5 shows that maximum numbers of patients were from group 1 which constituted 65% of total patients followed by group 2 which contained 26% of total patients. Minimum number of patients was from group 3 which contained 9% of total patients. Figure 6 shows that according to weight Group 1 contained total of 22 patients and among them eleven patients were male and eleven were females. In group 2 out of total nine patients male and females were

seven and two, respectively, whereas group 3 contained 3 patients among which one was male and two were females.it was observed that maximum males to female ratio was in group 2 which was 78% to 22% followed by group 1which was 50% to 50% and group 3 containing 33% to 67% as shown in fig7.

Renal tubular acidosis was prevalent in both males and females. This was confirmed by the data collected from the patients. Figure 8 shows that out of total thirty four patients included in the study nineteen patients were male and fifteen were female so prevalence of disease was observed to be slightly higher in males as compared to females. The proportion of males and females was 56% and 44%,respectively.

Figure 9 revealed the prescription trends of patients at the start of the study. In the beginning of study fifteen patients were prescribed polycitra K, eleven were prescribed polycitra and eight were prescribed bicitra for management of conditions associated with renal tubular acidosis.

Figure shows that at the beginning maximum numbers of patients were prescribed polycitra K followed by polycitra and bicitra. Levels of sodium, potassium, bicarbonate and pH were observed at least twice during the period of 6 months to monitor the deviation from normal range of above mentioned laboratory findings. Out of these four findings at least three levels were monitored. Change in prescription was observed with change in laboratory values. At the end of the study number of patients who were prescribed bicitra and polycitra increased whereas decrease in number of patients prescribed polycitra K was observed. Figure 10 shows that at the end of study patients on bicitra increased from 24% to 27 %, those on polycitra increased from 32% to 35 % and on polycitra k decreased from 44% to 38 %. Although percentage of patients on bicitra, polycitra and polycitra K had changed but maximum percentage of patients were still taking polycitra k followed by polycitra and bicitra respectively. During the study period few patients showed changes in prescriptions whereas prescriptions of others remained unchanged. Figure 11 depicted that 44 % of patients did not show any change in prescription where as 56 % patients showed change in prescription either in form of dose or formulation. These changes in prescriptions of patients during the study period were to keep the laboratory findings within normal range. Change in prescription was observed in nineteen patients. This change in prescription was divided into two categories. First were those who showed change in formulations while second were those who showed change in doses as shown in Figure 12.

According to method of Srinivas *et al*., (2001), on the basis of changes in prescription trends patients were divided into three groups i.e. patients who showed no change in prescription, patients whose doses were changed and patients whose formulation was changed. Figure 13 showed following trends during the study.

a) Prescription of 44% patients remained un-changed. These remain unchanged because bicarbonate level of patients after taking medicine remained within the normal values i.e. 18- 22 and as a result of which no change in prescription wasseen.
b) Prescription of 15% patients showed change in medicine. Patients switched from polycitrato polycitra K, polycitra K to polycitra and polycitra to bicitra. Patients on polycitra K, polycitra and bicitra changed from 47%, 29% & 24% to 41%, 32% & 27%, respectively.
c) Prescription of 41% of patients showed change of dose. These doses were either increased or decreased to adjust the bicarbonate level between 18 and 22 mEq/L When bicarbonate level was less than normal dose was increased while dose was reduced when bicarbonate level was increased.

Figure 14 showed mean levels of bicarbonate, potassium and pH of patients as 18.12, 3.535 and 7.311 mEq/L, respectively. Change of doses caused these levels to be changed to 21.44, 3.77 and 7.348, respectively. This showed that change of dose caused the rise inbicarbonateslevelby18.257%.Similarly levels of potassium and pH were raised by 6.64% and 0.5% respectively. Pre and post change levels of Sodium have been shown in Figure 15. It shows that level of sodium was changed from 136.37 to 136.28. It is observed that sodium level is decreased by 0.06% with changed dose. Effective management required regular follow-ups. During initial period of diagnosis more frequent follow-ups were needed to adjust bicarbonate level. Once levels were adjusted laboratory findings should be checked at least once after every three months so that necessary adjustments can be made in formulation, dose or both to keep laboratory findings within normal range (Baehner *et al.,* 1968). The effect of bicarbonate after first

Test on change pattern of medicine was statistically significant with Cramer value 0.639, p = 0.001. The effect of bicarbonate after second test, effect of potassium after first test and effect of potassium after second test on change pattern of medicine showed no statistically significant relationship with Cramer values 0f 0.353, 0.164, 0.238 and p values of 0.120, 0.634, 0.383respectively.

Impact of genetics on the prevalence of disease was also observed by observing the marriage history among the parents of patients and existence of disease in the family. It was observed that out of total thirty four patients twenty nine patients were those whose parents had cousin marriage among themselves. Figure 16 shows that ratio of these two were 85% and 15% respectively.

It was observed that from total thirty four patients siblings of fourteen patients were suffering from same disease which is 41% of total patients while twenty were those who do not have same disease among their siblings. History of parents' marriage was compared with the prevalence of disease in the family to establish its genetic linkage. Figure 17 shows that among the 14 patients who had existence of the disease in their family 86% patients were those whose parents had cousin marriages and parents of 14 % patients didn't have cousin marriage among their parents. This indicated the association of genetic factor in existence of renal tubular acidosis. According to their findings over 70% of pediatric kidney diseases (Seedat, 1964) had genetic causes(Borthwick *et al.*, 2003).

.

(G-1 (age group); less than five years, AG-2; 6 to 10 years, AG-3; 11 to 15 years)

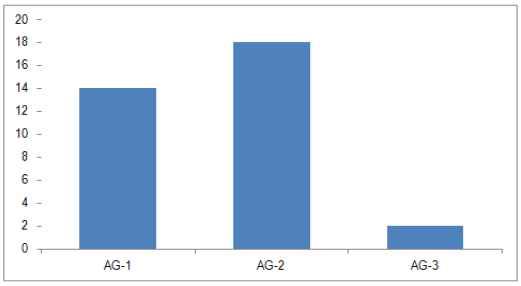

Fig. 1: No of patients in different age groups

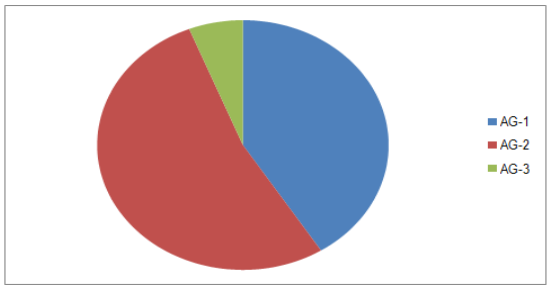

Fig. 2: %age of patients in different age groups

(G-1 (age group); less than five years, AG-2; 6 to 10 years, AG-3; 11 to 15 years)

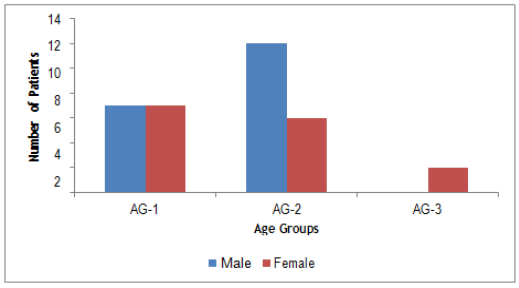

Fig. 3: Gender distribution (number) of patients age groups

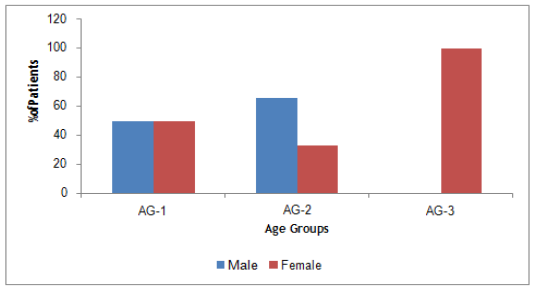

Fig. 4: Gender distribution (%age) of patients different of different age groups

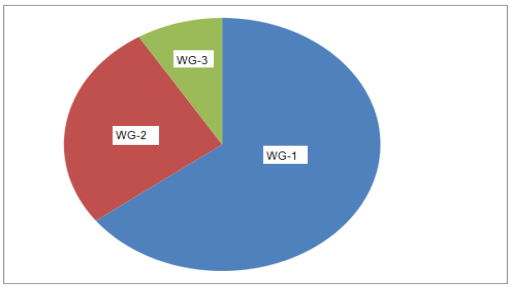

Fig. 5: Distribution (%age) of patients in different weight groups

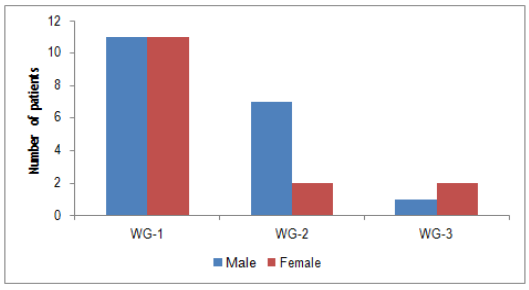

Fig. 6: Gender distribution of patients in different weight groups

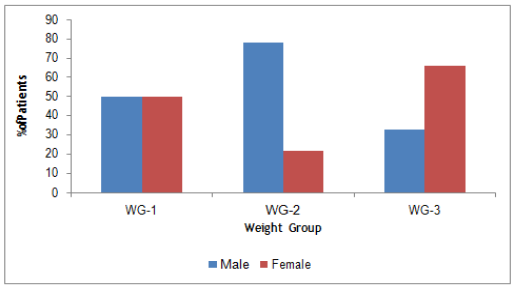

Fig. 7: Gender distribution of patients in different weight groups

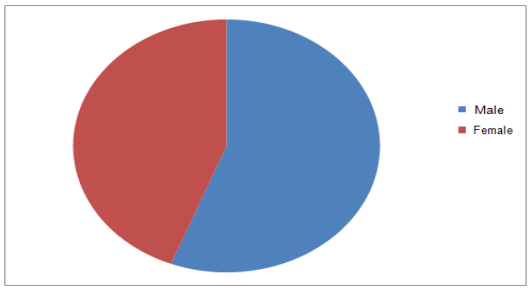

Fig. 8: %age of disease among male & females

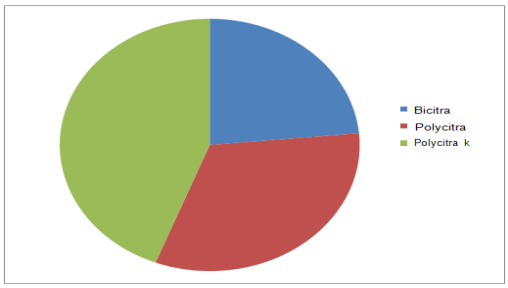

Fig. 9: Prescription trends of bicitra, polycitra and polycitra K at start of study

Fig. 10: Percentage of patients on bicitra, polycitra and polycitra K at the end of study

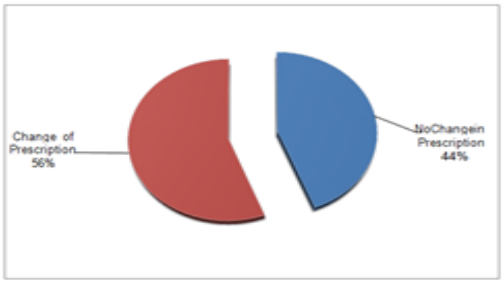

Fig. 11: Change in prescription trend

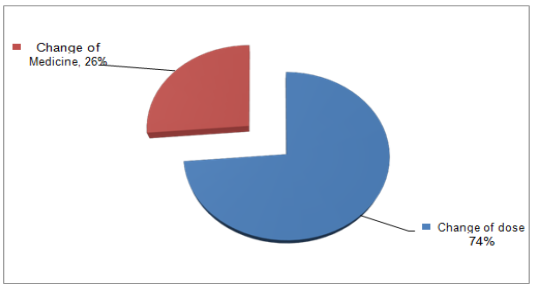

Fig. 12: Change of Percentage of various groups

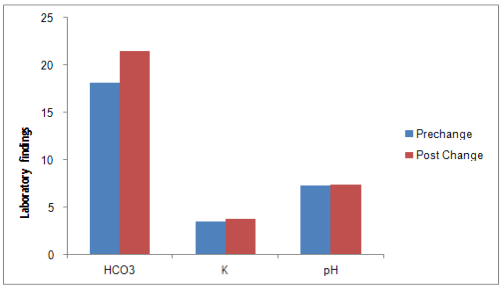

Fig. 13: Change in levels of HCO_3, K & pH before and after prescription of the Shohl's solution

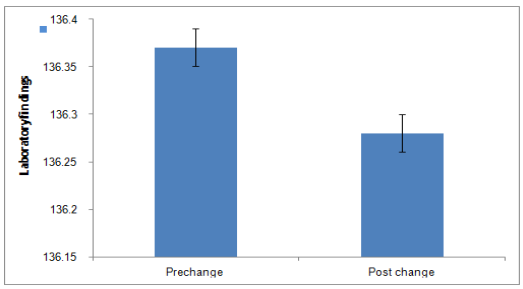

Fig. 14: Change in levels of Na before and after prescription of the Shohl's solution

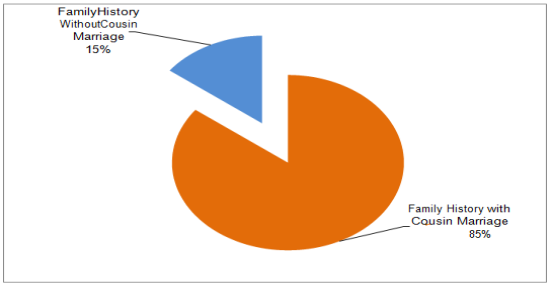

Fig. 15: Pie chart showing marriage history of parents

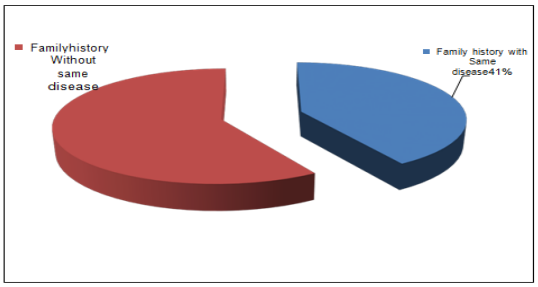

Fig. 16: Disease history of the patients

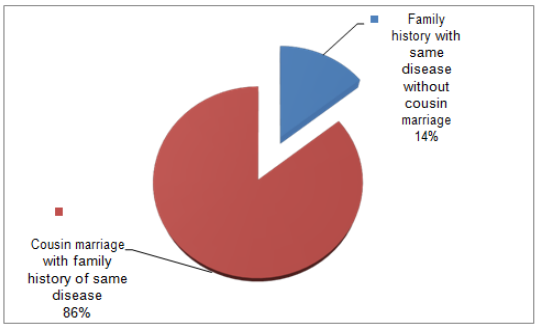

Fig. 17: Pie chart showing relationship between marriage history and family history of disease

REFERENCES

Baehner, R. L., Gilchrfist, G. S. & Anderson, E. J., (1968). Hereditary elliptocytosis and primary renal tubular acidosis in a single family *Am. J. Dis.Child*.,**115(4)**: 414-419.

Borthwick, K., Kandemir, N., Topaloglu, R., Kornak, U., Bakkaloglu, A., Yordam, N., Ozen, S., Mocan, H., Shah, G. & Sly, W., (2003). A phenocopy of CAII deficiency: a novel genetic explanation for inherited infantile osteopetrosis with distal renal tubular acidosis. *J. Med. Genet*.,**40(2)**: 115-121.

Coburn, J. W., Mischel, M. G., Goodman, W. G. & Salusky, I. B., (1991). Calcium citrate markedly enhances aluminum absorption from aluminum hydroxide. *Am. J. Kidney Dis*.,**17(6)**: 708-711.

Izol, V., Aridogan, I. A., Karsli, O., Deger, M. & Satar, N., (2013). The effect of prophylactic treatment with Shohl's solution in children with cystinuria. *J. Pediatr. Urol*.,**9(6)**: 1218-1222.

Kalinowski, C. P. H. & Kirsch, J. R., (2004). Strategies for prophylaxis and treatment for aspiration. *Best Pract. Res. Cl. Anaes*.,**18(4)**: 719-737.

Nash, M. A., Torrado, A. D., Greifer, I., Spitzer, A. & Edelmann, C. M., (1972). Renal tubular acidosis in infants and children: clinical course, response to treatment, and prognosis. *J. Pediatr*.,**80(5)**: 738-748.

Oduwole, A. O., Giwa, O. S. & Arogundade, R. A., (2010). Relationship between rickets and incomplete distal renal tubular acidosis in children. *Ital. J. Pediat*.,**36(1)**: 54.

Seedat, Y., (1964). Some observations of renal tubular acidosis-a family study. *S. Afr. Med. J.*,**38(28)**: 606-610.

Spector, S. & McKhann, C. F., (1948). Respiratory acidosis and alkalosis in children. *J. Pediatr*.,**32(3)**: 227-245.

Srinivas, K., Want, M. A., Freigoun, O. S. & Balakrishna, N., (2001). Methylmalonic acidemia with renal involvement: a case report and review of literature. *Saudi J. Kidney Dis. Transplant*.,**12(1)**: 49.

Van Woerden, C. S., Groothoff, J. W., Wanders, R. J., Davin, J. C. & Wijburg, F. A., (2003). Primary hyperoxaluria type 1 in The Netherlands: prevalence and outcome. *Nephrol. Dial. Transpl*.,**18(2)**: 273-279.