TO DETERMINE THE FREQUENCY OF HYPOKALEMIA IN CHILDREN WITH PERSISTENT DIARRHOEA

Rahida Karim, Jahanzeb Khan Afridi, Amjad Zaman, Umar Zada, Muhammad Younas

ABSTRACT

Introduction: Diarrhoea remains one of the leading causes of childhood morbidity and mortality worldwide. It results from infection of the intestinal tract by a wide range of enteric pathogens that can disrupt intestinal function. According to World Health Organization, persistent diarrhoea is an illness of proven or presumed infectious etiology that lasts 14 days or more. Diarrhoea is the major cause of hypokalemia that may be caused due to gastrointestinal loss of potassium. Hypokalemia is generally defined as a serum potassium level of less than 3.5 mEq/L (3.5 mmol/L) and severe hypokalemia is a level of less than 2.5 mEq/L. Hypokalemia is a potentially life-threatening imbalance that may be iatrogenically induced.

Materials and Methods: This study was conducted in the in the Department of Pediatrics Hayatabad Medical Complex, Peshawar from March 2014-August 2014. Through a Descriptive Cross Sectional Study Design, a total of 168 children between 1 month to 2 years of age having persistent diarrhea included in the study in a consecutive manner from OPD and serum potassium level was checked.

Results: The mean age group of our sample was 12.6 $\pm$ 6.5 months of which 54.2% male and 45.8% were females. Most of the children i.e. 39.9% were in the age group between 8-16 months. The mean duration of diarrhea in our sample was 19.4 $\pm$ 3.9 days with 81% presenting between >14 to 21 days and 19% presenting beyond 21 days. On testing for serum potassium, we observed that 28.6% of children had hypokalemia.

Conclusion: Hypokalemia is a common occurrence among children with persistent diarrhea. We recommend further research for its prevention and other studies regarding causes of persistent diarrhea as well as studies on knowledge of mothers with oral rehydration therapy.

Key Words: Persistent Diarrhea, Serum Potassium, Hypokalemia.

INTRODUCTION

Diarrhoea remains one of the leading causes of childhood morbidity and mortality worldwide. It results from infection of the intestinal tract by a wide range of enteric pathogens that can disrupt intestinal function.[1] The annual global burden of infectious diarrhoea is enormous, involving 3 to 5 billion cases and nearly 2 million deaths, with the latter accounting for almost 20% of all deaths in children younger than 5 years.[2] Of these diarrhoea-related deaths, acute watery diarrhoea is responsible for 35%, dysentery for 20% and persistent or chronic diarrhoea 45%.[1]

According to World Health Organization, persistent diarrhoea is an illness of proven or presumed infectious etiology that lasts 14 days or more. Persistent diarrhoea accounts for 3% to20% of all diarrhoeal episodes in children aged less than five years.[1,3] It is also directly responsible for 36% to 54% of all diarrhoea-related deaths according to community based studies. Thus, the main consequences of persistent diarrhoea are morbidity with an increased risk of hospital admission, death, and malnutrition.[3]

Diarrhoea is the major cause of hypokalemia,[4] that may cause due to gastrointestinal loss of potassium. Hypokalemia is generally defined as a serum potassium level of less than 3.5 mEq/L (3.5 mmol/L) and severe hypokalemia is a level of less than 2.5 mEq/L. Hypokalemia is a potentially life-threatening imbalance that may be iatrogenically induced. The frequency of hypokalemia in the general population is difficult to estimate. Potassium intake varies according to age, sex, ethnic background, and socioeconomic status. Whether these differences in intake produce different degrees of hypokalemia or different sensitivities to hypokalemic insults is not known.[5] A study reported the rate of hypokalemia is exceeding than 60% in children hospitalized with diarrhoea.[1] Gangaraj S. et al. found hypokalemia in 61.22% (30/49) children presented with diarrhoea and vomiting, and in 33% (9/24) presented with no diarrhoea and vomiting. The overall hypokalemia rate in this study was 51.53% (39/73).[6] In another study by Chisti MJ et al. hypokalemia was diagnosed in 31% children admitted with diarrhoea.[7]

Hypokalemia resulted from persistent diarrhoea is one of the leading causes of morbidity and mortality among children in developing countries. One reason

Department of Paeds HMC Peshawar

Address for Correspondence:
Dr. Rahida Karim
Senior Registrar
Department of Paeds HMC Peshawar.
Cell: 0333-9258790
E-mail: rahidakarim88@yahoo.com

may that the health workers in resource limited settings might miss the clinical signs in hypokalemic diarrhoeal children, delaying the initiation of appropriate antibiotics and potentially increasing the probability of deaths. It is thus very important to understand the influence of persistent diarrhoea on the clinical features of hypokalemia in children in order to develop guidelines for diagnosing hypokalemic diarrhoea in such population and initiate appropriate management to reduce probability of deaths, especially in resource constraint settings. Moreover, despite several attempts to estimate morbidity from hypokalemic diarrhoea over the past decades and in recent years, the uncertainty surrounding its current level, especially in Pakistan, remains unknown. The current study, in this regard, is designed to determine the frequency of hypokalemia in children presented with persistent diarrhoea at our local population.

OBJECTIVE

To determine the frequency of hypokalemia in children with persistent diarrhoea.

MATERIALS AND METHODS

Study Design: Cross-sectional descriptive study.

Setting: Department of Pediatrics, Hayatabad Medical Complex, Peshawar.

Sample size: Sample size was 168 using 31% proportion of hypokalemia in children7, 95% confidence interval and 7% margin of error, under WHO software for sample size determination.

Sampling Technique: Non probability consecutive sampling.

Sample Selection:

Inclusion criteria:

Children of both gender and age 1 month to 2 years. Children presented with persistent diarrhoea confirmed by clinical history and laboratory investigation (stool microscopy).

Exclusion Criteria:

Children with Leukemia, Spurious Hypokalemia i.e. High WBC count.

Children with transcellular shift i.e. Alkalemia, insulin, α-adrenergic agonists, drugs, hypokalemic periodic paralysis, thyrotoxic periodic paralysis, refeeding syndrome.

Children with decreased intake.

The above mentioned conditions in exclusion criteria will act as confounders and if included they will introduce bias in the study results.

Data Collection Procedure

This study was conducted after approval from the ethical board and research committee of the hospital. All patients with the inclusion criteria on the basis of clinical findings presenting to children OPD or emergency was included in the study. The purpose and benefits of study and complete procedure of clinical and pathological diagnosis was explained to the parents or guardian of the subject children and a verbal informed consent was obtained.

All patients was subjected to detailed history and examination by an expert pediatrician. The history of diarrhoea and any previous diagnoses was recorded from all patients. The clinical diagnosis of diarrhoea and hypokalemia was based on the history and laboratory test respectively. From all patients 3 cc blood samples were collected and were sent to the laboratory to find the serum potassium level.

Data Analysis Procedure

All the data collected was analyzed through SPSS 17 version. Mean +SD was calculated for continuous variable like age and duration of diarrhoea. The categorical variables were expressed as frequencies and percentages like gender and hypokalemia. The hypokalemia was stratified among age and gender to see the effect modification.

RESULTS

The study was conducted on 168 children presenting with persistent diarhoea. The mean age of the sample was 12.6 $\pm$ 6.5 months. We divided the age in 3 different groups. In age group up to 8.00 months we had 31% of children, in 8.01 to 16.00 months we had 39.9% children and in age group 16.01 to 24.00 months we had 29.2% children. (Table 1)

Out of 168 children included in the study, there were 54.2% male children and 45.8% female children.

According to our operational definition, we only included those children who presented with diarrhoea lasting for more than 14 days. The mean duration of diarrhoea in our sample was 19.4 $\pm$ 3.9 days with 81% presenting between >14 to 21 days and 19% presenting beyond 21 days.

As per operational definition of hypokalemia, we observed that hypokalemia was recorded in 28.6% of children. (Table 2)

On applying chi square test for stratifying hypokalemia with regards to duration of diarrhoea, we observed a statistically significant difference (p value 0.003) See Table 3.

DISCUSSION

The term intractable diarrhea of infancy is defined as diarrhea of more than two weeks duration, occurring in the first three months of life, and resistent to stan-

Table 1: Age Wise Distriution of the Sample (n = 168)

Descriptive Statistics

	N	Range	Minimum	Maximum	Mean	Std. Deviation
Age of the child (Months)	168	20.50	3.50	24.00	12.6905	6.52381
Valid N (listwise)	168					

Age Groups

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Upto 8.00 Months				
	8.01 to 16.00 Months				
	16.01 to 24 Months				
	Total				

Table 2: Frequency of Hypokalemia (n = 168)

Hypokalemia

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Yes	48	28.6	28.6	28.6
	No	120	71.4	71.4	100.0
	Total	168	100.0	100.0	

Table 3: Duration of Diarrhea Wise Stratification of Hypokalemia (n = 168)

Crosstab

		Hypokalemia		Total
		Yes	No	
	Count	32	104	136
> 14 to 21 days	% within Duration of Diarrhea (Categories)	23.5%	76.5%	100.0%
Duration of Diarrhea (Categories)	Count	16	16	32
>21days	% within Duration of Diarrhea (Categories)	50.0%	50.0%	100.0%
	Count	48	120	168
Total	% within Duration of Diarrhea (Categories)	28.6%	71.4%	100.0%

P Value: 0.003

dard treatment resulting in a severe life threatening condition[8]. However, advances in nutritional support, and parenteral nutrition in particular, have improved survival and resulted in the replacement of the word intractable by the terms prolonged, protracted, or persistent diarrhea of infancy[9, 10]. In addition, the syndrome of intractable diarrhea of infancy is caused by many disorders that are heterogeneous and not specific for infants less than three months, making such designation rather controversial.

Nevertheless, the syndrome of protracted diarrhea in infancy may be primary (idiopathic) also called non- specific enterocolitis which is not to be confused with the term chronic nonspecific diarrhea (irritable bowel syndrome), a clearly more benign condition. On the other hand the syndrome may be secondary to any disease causing chronic diarrhea.

Intestinal water absorption is a passive process occurring in response to osmotic and hydrostatic pressure gradients across the intestine. Osmosis may be generated by active transport of electrolyte or non-electrolytes (Carbohydrates, aminoacids). Water and electrolytes cross the intestinal mucosa either passively by passing through the paracellular pathway (tight

junction) or actively through the apical and basolateral pathways. Sodium is absorbed by at least three mechanisms. The sodium pump (Na-K- ATP ase), located in the baso-lateral membrane of the cell, drives sodium out of the cell to the interstitial space (three sodium ions are exchanged for two potassium ions entering the cell). This process creates a low intracellular sodium concentration which drives more sodium into the cell. Similarly, the exchange of three sodium ions for two potassium ions results in intracellular electronegativity which drives more sodium from the intestinal lumen into the cell. The other mechanism of sodium absorption is neutral and occurs when sodium is in the form of sodium chloride or with sodium exchanged for hydrogen ion and parallel exchange of chloride in the cell and bicarbonate in the intestinal lumen. (This mechanism is lacking in congenital chloridorrhea). The last mechanism of sodium absorption occurs through transport proteins. In this Co-transport mechanism, sodium is linked to D-glucose, D-galactose. amino acids, dipeptids or tripeptids[11].

Sodium is efficiently absorbed by the colon primarily by an electrogenic mechanism through selective sodium pores. This process is regulated by aldosterone which stimulate sodium absorption and potassium excretion.

Chloride (Cl-), is the major ion that is actively secreted. This process is coupled with the Na-KATP ase pump, which accumulate Cl- in the cell. Cyclic AMP or increase in intracellular calcium stimulate Cl- secretion in the intestinal lumen. Similarly certain enterotoxins, bile acids, fatty acids, laxatives and hormones are capable of stimulating Cl- secretion. Potassium transport is primarily passive but active absorption and secretion have been demonstrated. Bicarbonate is usually absorbed in the jejunum and secreted by the duodenum, ileum and colon[12].

Unlike adult kidney function which maintains steady state by protecting against changing volume and composition of the extracellular fluid, the neonatal and younger infant kidney maintains a positive balance of many solutes to promote growth. Fluid spaces differ with age, and growth and organ maturation allow homeostasis despite apparent limitations of renal function[13].

Several factors appear to be involved in explanation of the low serum potassium children with persistent diarrhea. First, the diarrhea persisted for more than two weeks; thereby allowing for a great loss of potassium in the stools[14, 15]. Second, the average diet sufficient in calories will contain an adequate amount of potassium. The third factor which undoubtedly contributed to the depletion of the body's store of both sodium and potassium was the administration by hypodermoclysis of 2000 Ml. of 5% dextrose in distilled water. It is known generally that hypertonic glucose given into the peritoneal cavity will draw electrolytes into this compartment and some of the electrolytes so transferred will be excreted in the urine[16].

Our study showed 70.8% cases were within 16 months of age. Similar age group was seen by Purohit and Joytsna[17]. Incidence of diarrhea is highest in this age group.

Hypokalemia was observed in 28.6% cases in this study. In a study done by Purohit and Joytsna, 75 cases out of 100 cases showed low serum values of sodium and potassium[17]. Rothrock et al.[18] had shown 28% cases with electrolyte abnormality in acute gastroenteritis. Shah et al.[19] found 80% patients presenting with diarrhea and dehydration had electrolyte abnormality with 46% hypokalemic.

The incidence of hypokalemia was higher in the present study as compared to other reports where the authors observed hypokalemia frequency of around 14%[20,21]. However, the authors included a variety of conditions including diarrhoea in their study. In diarrhoeal disease, the same authors[22] observed hypokalemia in 20% cases. The hypokalemia noted in our patient could be due to increased potassium loss through diarrhoea. The bicarbonate loss is also partly responsible for hypokalemia in those patients. But in our study bicarbonate level was not done. Zaman et al[23] showed higher prevalence of hypokalemia. They found mild, moderate and severe hypokalemia in 39%, 26% and 2% cases respectively. They showed significantly higher level of hypokalemia in malnourished children relatively healthy children.

Singhi et al[20] showed no statistically significant difference in the duration of hospital stay and hypokalemia as compared to normokalemia. Singhi et al showed 19% mortality rate[22]. They showed overall mortality increased with lowering of serum sodium concentration.

There is no direct evidence of when serum electrolytes should be measured in a child with diarrhea. Nevertheless, if feasible, children requiring intravenous rehydration should have their serum electrolytes measured.[24] Furthermore, because rates of hypokalemia can exceed 60% in children hospitalized with diarrhea, these children should also have their serum electrolytes and glucose measured, especially if they are malnourished, have impaired conscious state or seizures, are younger than 3 months, or are dehydrated or suffering from persistent diarrhea.[25] Similarly, when dysentery is present, stools should be examined for enteric pathogens and, if diarrhea is persistent, the stools should be tested for reducing sugars.

Hypokalemia is a common problem among PICU patients. Early detection through regular monitoring and rapid correction may help in improving the outcome.

In a study, 14.8% patients had 54 episodes of hypokalemia. Predisposing factors included the nature of primary disease (renal disease 19%, septicemia 19%, acute diarrhea 14%, heart disease with congestive failure, and meningoencephalitis 12% each), malnutrition (weight for age less than 80% in 72%) and therapy

with drugs (diuretics, corticosteroids and antiasthma drugs)[26].

Management of hypokalemia depends upon its severity and underlying condition. Some authors do not recommend treatment of mild hypokalemia[27], while other favor oral supplements [28] or rectal administration of potassium chloride solution[29]. Intravenous potassium infusion is generally recommended for severe hypokalemia[29]. Even here there is no unanimity regarding concentration of potassium solution to be used and the rate and duration of therapy.

CONCLUSION

Hypokalemia is common electrolyte abnormalities found in children having chronic diarrhea in this study. There are studies reported in the past suggesting increase mortality and duration of hospital stay of children who had lower potassium levels and certain risk factor leading to hypokalemia. We further recommend more robust research on children with hypokalemia regarding its risk factors, hospital stay and complications before suggesting future recommendations.

REFERENCES

1. Grimwood K, Forbes DA. Acute and persistent diarrhea. Pediatr Clin North Am. 2009;56(6):1343-61.
2. Boschi-Pinto C, Velebit L, Shibuya K. Estimating child mortality due to diarrhea in developing countries. Bull World Health Organ. 2008;86:710-7.
3. Bernaola Aponte G, Bada Mancilla CA, Carreazo Pariasca NY, Rojas Galarza RA. Probiotics for treating persistent diarrhoea in children. Cochrane Database Syst Rev. 2010;11:CD007401.
4. Glancy DL, Wilklow FE, Rochon BJ. Electrocardiogram after 2 weeks of diarrhea. Proc (Bayl Univ Med Cent). 2010;23(2):173-4.
5. Lederer E. Hypokalemia. [Online]. [Cited on April 27, 2014]. Available at
6. http://emedicine.medscape.com/article/242008-overview
7. Gangaraj S, Das G, Madhulata S. Electrolytes and blood sugar changes in severely acute malnourished children and its association with diarrhoea and vomiting. Int J Pharma Sci Invent. 2013;2(5):33-6.
8. [Guideline] Walker-Smith JA, Sandhu BK, Isolauri E, et al. Guidelines prepared by the ESPGAN Working Group on Acute Diarrhoea. Recommendations for feeding in childhood gastroenteritis. European Society of Pediatric Gastroenterology and Nutrition. J Pediatr Gastroenterol Nutr. May 1997;24(5):619-20.
9. Avery GB, Villavicenio O, Lilly JR et al. Intractable diarrhea in early infancy. Pediatrics 1968; 41:712-22.
10. Keating JP, Ternberg JL. Amino-acid hypertonic glucose treatment for intractable diarrhea in infants. Am J Dis Child 1971; 122:226.
11. Lloyd-Still JD, Shwachman H, Filler RM. Protracted diarrhea of infancy treated by intravenous alimentation: 1. Clinical studies of 16 infants. Am J Dis Child 1973; 125:358.
12. Chopra S, Trier JS. Diarrhea and malabsorption. In: Pathophysiology of gastrointestinal diseases. Chopra S, May RJ (eds). Boston, Little Brown and Company 1989; 125-69.
13. Grasset E. Transport intestinale del'eau et des electrolytes. In: Gastroenterologie pediatrique. Navarro J., Schmitz J (eds). Paris, Flammarion 1986:54-6.
14. Herrin JT. Management of Fluid and Electrolyte Abnormalities in Children. In Core Concepts in the Disorders of Fluid, Electrolytes and Acid-Base Balance 2013:147-170.
15. Darrow DC. Retention of electrolyte during recovery from severe dehydration due to diarrhea, J. Pediat. 2000;28:515.
16. Holt LE, Angelia M, Helen LF. Chemical composition of diarrhealas compared with normal stools in infants, Am. J. Dis. Child. 1985;9:213.
17. Schechter AJ, Cary MK, Carpentieri AL, Darrow DC. Changes in composition of fluids injected into the peritoneal cavity, Am. J. Dis. Child. 1983;46:1015.
18. Purohit KR, Jyotsna PSR. Electrolyte disturbances in acute diarrhea. Indian Journal of Pediatrics 1971;38(10): 393-95.
19. Rothrock SG, Green MS, McArthur CL, Delduca K. Detection of electrolyte abnormalityies in children in children presenting to the emergency department. A multicentre Prospective analysis. Academic Emergency medicine 1997;4(11):1025-31.
20. Shah GS, Das BK, Kumar S, Singh MK, Bhandari GP. Acid base and electrolyte disturbance in diarrhoea. Kathmandu Univ Med J 2007; 5(1): 60-62.
21. Singhi S, Gulati S, Prasad SVSS. Frequency and significance of potassium disturbances in children. Indian Pediatr 1994; 31: 460-63.
22. Singhi S, Murudkar A. Hypokalemia in pediatric intensive care unit. Indian Pediatr 1997; 33: 9-14.
23. Singhi S, Prasad SVSS, Chug KS. Hyponatremia in sick children, a marker of serious illness. Indian Pediatr 1994; 31: 19-24.
24. Zaman K. Islam MR, Baqui AH, Yunus M. Hypokalemia in children with diarrhea in rural Bangladesh. Indian J Med Res 1981; 85: 169-74.
25. Australian Health Ministers' Advisory Council. Aboriginal and Torres Strait Islander health performance framework report 2008 summary. Canberra: AHMAC; 2008.
26. Building better communities for children: community preparation and implementation guide. A partnership between the Centre for Community Child Health, The Royal Children's Hospital Melbourne, and the Telethon Institute for Child Health

Research. Perth.

27. Singhi S, Marudkar A. Hypokalemia in a pediatric intensive care unit. Indian pediatrics, 1996;33(1):9-14.

28. Linshaw MA. Potassium homeostasis and hypokalemia. Pediatr Clin North Am 1987;34: 649-678.

29. Satlin LM, Schwartz CJ. Disorders of potassium metabolism. In: Pediatric Text Book of Fluids and Electrolytes, Ed. Ichikawa I. Baltimore, Williams and Wilkins, 1990, pp 218-236.