International Journal of Children and Adolescents

Original Article
IJCA, Vol. 1, No. 2, Oct, 2015.16-19.

Neurologic manifestations in children and adolescents with chronic kidney diseases

Ladan Afsharkhas: *MD. Assistant Professor of Pediatric Neurology Department, Ali-Asghar Children's Hospital, Iran University of Medical Science, Tehran, Iran. drafshar1@yahoo.com*
Nasrin Hoseininajad: *Assistant Professor of pediatric Respiratory diseases, Ali-Asghar Children's Hospital, Iran University of Medical Science, Tehran, Iran. nasrnejad@rocketmail.com*
Zohreh Kalbassi: (**Corresponding author*) *MD. Assistant Professor of Pediatric Department, Ali-Asghar Children's Hospital, Iran University of Medical Science, Tehran, Iran. z_kalbassi@yahoo.com*

Received: 11 April 2015 Accepted: 19 May 2015

Abstract

Background and Objective: Chronic renal failure (CRF) may have many effects on nervous system and manifest as headache, seizure, dialysis disequilibrium syndrome, cerebral hemorrhage, hypertensive encephalopathy, uremic neuropathy, and some neurologic complications of transplantation. In this present study we investigate neurologic disorders in children with CRF.

Methods: In this descriptive, cross sectional study, we evaluated 60 cases. Thirty normal cases compared with thirty patients with CRF admitted in nephrology ward in Aliasghar Children Hospital between April and December 2014.Two groups were matched for age and gender. Data were recorded on age, sex, causes of CRF, renal transplantation and neurologic manifestations.

Results: Thirty patients had CRF and mean age was 10.86±5.25 years. Seventeen cases (56.7%) were male. Fourteen (46.7%) of cases had been transplanted. Twelve (40%) of patients had neurologic findings including seizures 7(23.4%), tension type headache 3 (10%), and developmental delay 2(6.6%). Causes of CRF were included congenital anomalies (46.6%), glomerulopathies (26.6%), tubulopathies (10%) and idiopathic cases (16.8%). Neurologic complications was significantly seen more in male patients (P=0.01).There was not significant relationship between age, causes of CRF, history of seizure in relatives, renal transplantation and neurologic findings. Two (7%) cases died of which both had seizures. In control group, neurologic findings was detected in two cases and there was significant differences between occurrence of seizure and neurologic findings in two groups (P=0.01, P=0.005).

Conclusion: Some neurologic manifestations such as seizure, headache and developmental delay in patients with CRF are seen especially in childhood period. It is recommended to evaluate neurologic disorders and treated properly in these cases.

Keywords: CRF, Manifestation, Neurologic disorder

Introduction

Incidence of chronic renal disease in children may be as high as 32.4 per million in developed countries. Sixty four percent of these children are 9-15 years of age (1). Neurologic complications that may be observed in chronic renal failure (CRF) are water intoxication, hyponatremia, hypo and hyperkalemia, uremic and hypertensive encephalopathy, posterior reversible encephalopathy syndrome (PRES), dialysis disequilibrium syndrome, uremic neuropathy and transplantation complications. Hyponatremia can result in brain edema and increased neuron excitability (2). Hyperkalemia provokes weakness in smooth and striated muscles and slows velocity of conduction in peripheral nerves and hypokalemia may lead to periodic paralysis as a manifestation in renal tubular acidosis (3). Uremia is a serious complication in CRF and -with increasing of parathyroid hormone and disturbances in calcium homeostasis - has negative effect on cerebral excitability and neurotransmission. In earlier phases of uremic encephalopathy patients have inattention, irritability, speech disorders and lethargy. In more severe cases, tremor, cranial nerve palsy -especially abdusence nerve-loss of vision or hearing, muscle

twitching, seizures and EEG abnormalities may be detected. Most of these complications are removed by dialysis. Although, in early phase of dialysis headache, seizure, muscle cramps and loss of consciousness may be occurred as dialysis disequilibrium syndrome (3,4). Hypertensive encephalopathy is a very important complaint in patients with CRF and some of its causes, are including renovascular thrombosis (because of cyanotic heart diseases), disseminated intravascular coagulopathy, Wilms' tumor, neuroblastoma, hemolytic–uremic syndrome (HUS), nephritis, polycystic kidney disease, inflammatory and infectious diseases, renal structural anomalies. More common inflammatory diseases are glomerulonephritis and collagen vascular diseases (5). Neurologic manifestations are related to severity and rapidity of rising blood pressure. Severe headaches, visual disturbances, papilledema, irritability, loss of consciousness and seizures are common presentations (6). PRES is a leukoencephalopathy due to abnormal cerebral autoregulation especially in hypertensive cases with severe headache, confusion and loss of vision (7). However, any neurologic complication that may occur in patients with chronic kidney diseases should recognize and manage appropriately as soon as possible to reduce morbidity and mortality in these cases. This study was designed to determine neurologic manifestations in children and adolescents with CRF.

Methods

This is a case control study on 30 children and adolescents who were admitted with CRF in Aliasghar Children's Hospital, in Tehran, Iran, from April to December of 2014. They were compared with 30 healthy children and adolescents as control group who were visited as outpatients in general pediatric clinic or emergency room for upper respiratory or lower urinary tract infections. The project was approved by Committee of Ethics of Iran University of Medical Sciences. Collected data included age, gender, renal diseases as causes of CRF, neurologic findings such as headache, seizure, family history of seizure in first relatives, and history of kidney transplantation. All data obtained from medical records and collected through inventories. Statistical analysis was performed using SPSS for windows (ver. 18). The student t-test was employed for comparing variables in two groups and a Pearson correlation for association between variables. P values of less than 0.05 were considered significant.

Results

Over a period of 6 months, thirty patients with diagnosis of CRF admitted in our center. Mean±SD age was 10.86±5.25 years. Seventeen cases (56.7%) were male. Fourteen (46.7%) of cases had renal transplantation. Twelve (40%) of patients had neurologic issues including seizures 7 (23.4%), tension type headache 3 (10%), developmental delay 2 (6.7%) of cases. Seizures were due to epileptic syndromes, hypertension with posterior reversible encephalopathy syndrome, febrile convulsion, hyponatremia and increased intracranial pressure (ICP), in 3(9.8%), 1(3.4%), 1(3.4%), 1(3.4%) and 1(3.4%) of cases, respectively. A 12 years old boy, known case CRF due to focal sclerosis glomerulonephritis was admitted due to severe headache and hypertension. PRES was suggested because of brain MRI abnormal signals in bilateral subcortical regions of occipital lobes. Hypertension was controlled and headache removed by medications. Brain imaging was performed frequently and abnormalities removed after 3 months. Causes of CRF were included congenital and structural anomalies (46.6%), glomerulopathies (26.6%), tubulopathies (10%) and idiopathic cases (16.8%). Details are shown in Table 1. Neurologic complications was significantly seen more in male patients (P=0.016). There was not significant relationship between age, causes of CRF, history of seizure in relatives, renal transplantation and neurologic findings. Two (7%) cases died which both had seizures. In control cases mean±SD age was 8.87± 5.57years and 20 (66.7%) were male. There was not significant difference between age and gender in two groups (P=0.1 and P=0.4, respectively). Neurologic findings detected in two cases

Table 1. Causes of CRF

Variable	Number(%)
Congenital and structural anomalies	
Reflux nephropathy	3(10)
Neurogenic bladder	3(10)
Renal hypoplasia	2(6.6)
Multycystic Kidney	2(6.6)
Single Kidney	2(6.6)
Polycystic Kidney	1(3.4)
Hydronephrosis	1(3.4)
Glomerulopathies	
FSGS	3(10)
Nephrotic syndrome	2(6.6)
PSGN	1(3.4)
HUS	2(6.6)
Tubulopathies	
Cystinosis	1(3.4)
Bardet Biedl syndrome	2(6.6)
Idiopathic	5(16.8)

including febrile convulsion in 1(3.4%) and developmental delay in 1(3.4%) cases in control group. There was significant differences between occurrence of seizure and neurologic findings in two groups (P=0.01, P=0.005).

Discussion

Spectrum of CRF is from mildly asymptomatic renal dysfunction to severe end stage kidney disease with retention of salt, water and urea products in the body (9). Chronic renal diseases with metabolic, inflammatory, vascular, structural and toxin mediated disturbances can effect on function of nervous systems (1). Some of neurologic complications of CRF are including seizures, encephalopathies, neuropathies and cognitive problems (10,11). Some studies have detected that 30% of patients with uremic encephalopathy may have seizure (12). Although mechanism of seizure in CRF is unknown, it may be due to production of proconvulsive metabolites such as creatinine, creatine and guanidinosuccinic acid. However, seizure may occur in setting of electrolytes imbalance, hypertension, dialysis, kidney transplantation, cytotoxic drugs etc (13,14).

In our study 7 patients had seizure due to epileptic syndromes, febrile seizure, hyponatremia and increased ICP. In Scorza et al study (13) 5 cases (from 189 patients with CRF) had seizure related to dialysis and reminded that seizures in CRF are occasional events and should be manage among treatment of systemic disease.

PRES is a neurologic complication that occurs during acute hypertension particularly in patients who use acyclovir, cyclosporine, and high dose of methyl prednisolone (7).We found one case of PRES based on clinical and brain imaging findings. In Chen et al study (7) 14 patients with diagnosis of PRES were evaluated. Mean age was 11.6 years. Factors that precipitated to PRES were hypertension (100%), immunosuppressive agents (71%), antineoplastic drugs (21%), and hemodialysis (14%). Neurologic manifestations included seizures, mental change, headache and visual disturbance. In Gamie et al study (8), a 10 year old girl with recurrent vomiting was diagnosed as cyclic vomiting and hypertension. She had history of 15 times hospitalization over 3 year period. In recent admission brain imaging showed abnormal signals as PRES and these changes were removed after 3 months.

Water intoxication and hyponatremia associated eurologic manifestations usually occur during acute or chronic renal failure. It is more prevalent to become symptomatic in serum sodium levels lower than 120 meq/L and its symptoms includes headache, vomiting, weakness, confusion and seizure especially during brain edema (15). In our study one case with hemolytic uremic syndrome, had hyponatremia and seizure and died due to brain edema and DIC. Another patient died with hypertension, seizure and brain edema.

In children with CRF balance of sodium, potassium and acid-base and vitamin D metabolism are disturbed, appetite decreases and anemia develops. All these events have role in developmental delay. Polinsky et al (16) evaluated 85 patients after age of 12 months with diagnosis of CRF at birth or during neonatal period. There was developmental delay in 63.2% of patients. Causes of developmental delay were under nutrition, psychosocial problems and hyperparathyroidism. In present study, developmental delay was detected in two cases with diagnosis of Bardet Biedl syndrome and renal hypoplasia. Lower rate of this finding in present study may be due to our different background diseases, small sample size and age of onset of CRF.

Conclusion

In patients who have chronic renal failure some neurologic manifestations such as seizure, headache and developmental delay may be detected. It is recommended to evaluate neurologic disorders and treated properly in these cases for decrease of morbidity and mortality.

Acknowledgment

We would like to thank Dr. Hoseini – nephrologist of our center- and personnel of the Medical Records Division of Aliasghar Hospital.

Conflicts of interest: None declared.

References

1. Seikaly MG, Ho PL, Emmett L, Fine RN, Tejani A. Chronic renal insufficiency in children. Pediatr Nephrol. 2003;18(8):796-804

2. Moritz ML, Carlos A, Yus JC. New aspects in the pathogenesis, prevention, and treatment of hyponatremic encephalopathy in children. Pediatr Nephrol. 2010; 25:1225–1238

3. Chan JCM, Williams DM, Roth KS. Kidney Failure in Infants and Children. Pediatr Rev. 2002; 23(2):47-60

4. Zepeda-Orozco D, Quigley R. Dialysis disequilibrium syndrome. Pediatr Nephrol. 2012; 27:2205–2211

5. Flanigan JS, Vitberg D. Hypertensive emergency and severe hypertension: what to treat, who to treat, and how to treat. Med Clin North Am. 2006; 90(3):439-51

6. Flynn JT, Tullus K. Severe hypertension in children and adolescents: pathophysiology and treatment. Pediatr Nephrol. 2009 Jun; 24(6):1101-12.

7. Chen TH, Lin WC, Tseng YH, Tseng CM, Chang TT, Lin TJ. Posterior Reversible Encephalopathy Syndrome in Children: Case Series and Systematic Review. J Child Neurol. 2013;28(11):1378-1386

8. Gamie Z, Rizwan A, Balen FG, Clarke M, Hassoon MM. Posterior reversible encephalopathy syndrome in a child with cyclical vomiting and hypertension: a case report. J of Med Case Rep. 2011;5:137.

9. Meyer TW, Hostetter TH. Uremia. **N** Engl J Med**.** 2007;357:1316-1325.

10. Murray AM. Cognitive impairment in the aging dialysis and chronic kidney disease populations: an occult burden. Adv Chronic Kidney Dis. 2008;15;123-132

11. Krishnan AV, Kiernan MC. Uremic neuropathy: clinical features and new pathophysiological insights. Muscle Nerve.2007**;**35:273-290

12. Gobbi G, Bertani G, Pini A. Electrolyte, sporadic, metabolic, and endocrine disorders. In: Epilepsy**:** A Comprehensive Textbook. Engel J, Pedley TA (Eds). Lippincott–Raven, Philadelphia, PA, USA, 1998; 2605–2627.

13. Glenn CM, Astley SJ, Watkins SL. Dialysis associated seizures in children and adolescents. Int J Pediatr Nephrol. 1992;6:182-186

14. Scorza FA, Albuquerque MD, Arida RM, Cysneiros RM, Henriques TMG, Scorza CA, et al. Seizure Occurance In Patients With Chronic Renal Insufficiency In Regular Hemodialysis Program. Arq Neuropsiquiatr 2005;63(3-B):757-760

15. Bhananker SM, Paek R, Vavilala MS. Water intoxication and symptomatic hyponatremia after outpatient surgery. Anesth Analg. 2004;98(5):1294-6, table of contents.

16. Polinsky MS, Kaiser BA, Stover JB, Frankenfield M, Baluarte HJ. Neurologic development of children with severe chronic renal failure from infancy. Pediatr Nephrol. 1987 Apr;1(2):157-65.