Pediatr Nephrol
DOI 10.1007/s00467-006-0034-5

ORIGINAL ARTICLE

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Neuropathic bladder as a cause of chronic renal failure in children in developing countries

Received: 23 September 2005 / Revised: 5 November 2005 / Accepted: 6 November 2005

Abstract Neuropathic bladder is considered a threat to the kidneys if not managed appropriately. In this study, we report our experience with neuropathic bladder at King Abdulaziz University Hospital (KAUH) as a cause of chronic renal failure (CRF) in the pediatric age group. This retrospective study included all children diagnosed with neuropathic bladder who presented with moderate or severe CRF over a 4-year period from December 2000 to December 2004 [glomerular filtration rate (GFR) at presentation <50 ml/min per 1.73 m^2]. Fifteen patients were diagnosed with neuropathic bladder; group A consisted of ten patients with spina bifida and one with sacral agenesis and group B consisted of four patients with nonneurogenic neurogenic bladders (NNNB). The mean age±SD at presentation was 6.2±3.8 years, GFR was 24.2± 12.4 ml/min per 1.73 m^2, and creatinine was 289.9± 253.2 μmol/l. There were no differences in the age at presentation to a pediatric nephrologist or the degree of renal failure at presentation between the two groups. Clean intermittent catheterization (CIC) was not started in all patients before presentation to KAUH, except in two children. Five children required dialysis as they were in end-stage renal failure (ESRF). All except one received peritoneal dialysis (PD). Their mean age at the start of dialysis was 10.8±1.7 years. Neuropathic bladder due to spina bifida or NNNB is an important cause of CRF in developing countries. There was a considerable delay in the diagnosis of NNNB and a significant delay in starting CIC in all neuropathic patients.

Keywords Neuropathic bladder · Chronic renal failure · Children

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Introduction

Neuropathic bladder is considered a major risk factor for chronic pyelonephritis and progressive renal damage [1, 2]. There are numerous causes of neuropathic bladder including open and closed spina bifida, sacral agenesis, spinal cord tumor, trauma, transverse myelitis, and autonomic neuropathy [3, 4]. Furthermore, no anatomical or neurological defect could be found in a small group of children who manifested signs of bladder sphincter incoordination and intravesical functional obstruction. The latter condition is called nonneurogenic neurogenic bladder (NNNB) or occult neuropathic bladder (Hinman syndrome) [4, 5] and it carries the same risks to the kidneys [6]. The usual presentation of NNNB is incontinence with daytime wetting as a result of impaired bladder sensation and poor bladder emptying [7, 8] or recurrent urinary tract infection (UTI) [4].

The aim of the management of neuropathic bladder is to preserve renal function and to improve continence [4, 9]. The best way of preserving renal function is by keeping the bladder empty, at low pressure, and free of infection [4, 9]. Clean intermittent catheterization (CIC) has made a tremendous difference to the management of such patients, with an improvement in continence, reduction of renal problems, and UTI [4, 10]. However, CIC has psychosocial impact on the treated children and their families [11, 12] and probably the rejection of this form of treatment is more common in Arab cultures like ours. With the recent modalities of treatment, chronic renal failure (CRF) is rarely seen in children with neuropathic bladder; however, there is a risk that this may merely be postponed into adulthood [1].

Spina bifida remains a problem in Saudi Arabia as the incidence of neural tube defects (NTD) appears to be nondeclining over the years [13, 14], despite a recent folic acid food fortification. Furthermore, high prevalence of consanguinity of the parents in Saudi Arabia was reported as a significant risk factor for spina bifida. Consanguinity of the parents was found in 89% of the spina bifida parents and in only 67% of the controls (p<0.0005) [14].

In this study we report our experience at King Abdulaziz University Hospital (KAUH) with children with neuropathic bladder who presented with CRF. We discuss the possible causes of their presentation early in life with CRF.

Patients and methods

This retrospective study covered all pediatric cases diagnosed with neurogenic bladder who presented with chronic renal failure (CRF) to the pediatric nephrology clinic over 4 years from December 2000 to December 2004. Only children with glomerular filtration rate (GFR) of less than 50 ml/min per 1.73 m^2 were included in the study. GFR was measured using diethylenetriaminepentaacetic acid (DTPA) scan or calculated using the Schwartz formula.

The patient's notes were reviewed for demographic data, age at presentation to a pediatric nephrologist, clinical presentation, radiological investigations, and laboratory data of kidney function.

Results are expressed as mean+SD or median (range). The *t*-test assuming equal variance was used to compare groups A and B.

Results

Fifteen patients presented with a variable degree of CRF [six moderate CRF (GFR 49–30 ml/min per 1.73 m^2), four severe CRF (GFR 29–15 ml/min per 1.73 m^2), and five end-stage (GFR <15 ml/min per 1.73 m^2)]. All were of Arab ethnic origin (67% Saudi) and the female:male ratio was 1:4. Ten patients had spina bifida, one patient had sacral agenesis, and four had occult or nonneurogenic neurogenic bladder.

At presentation to our pediatric nephrology clinic, their mean age±SD was 6.2±3.8 years (range: 1.5–13), GFR was 24.2±12.4 ml/min per 1.73 m^2 (range: 5–44), and creatinine was 289.9±253.2 μmol/l (range: 69–925).

All children with spina bifida (except two) had hydrocephalus which required ventriculoperitoneal (VP) shunt. Similarly, all of them were paraplegic except two who had minimal neurological involvement of their lower limbs and were able to walk. All of them had operations to close the spina bifida in the first 2 days except one who underwent closure on the 10th day of age.

Table 1 summarizes the clinical and radiological data of group A consisting of children with spina bifida or sacral agenesis and the clinical and radiological data of group B consisting of children with occult or nonneurogenic neurogenic bladder. There were no differences in the age at presentation to a pediatric nephrologist or the degree of renal failure at presentation between the two groups.

All children with NNNB in group B presented with recurrent urinary tract infection (UTI) and two of them were also reported as wet during the day (the other two were young and in nappies).

The diagnosis of NNNB in group B was made on the bases of radiological investigations and urodynamic studies. All of them had radiological and urodynamic evidence of neuropathic bladder with no neurological abnormalities. All of them had normal magnetic resonance imaging (MRI) of the spine (Table 1).

Table 1 Clinical and radiological data of groups A and B. *GFR* glomerular filtration rate, *MCUG* micturating cystourethrogram, *VUR* vesicoureteral reflux, *PUJ* pelviureteric junction obstruction, *MRI* magnetic resonance imaging, *CIC* clean intermittent catheterization

	Group B (*n*=4)	Group A (*n*=11)	*p* value
Age at presentation	5±4.2 years [median (range): 4.3 (1.5–8.5) years]	6.6±3.7 years[median (range): 5 (1.5–13) years]	0.24
Sex (male:female)	All females	7 F, 3 M=2.3:1	
Nationalities	All Saudi	5 (50%) Saudi	
Ethnic origin	100% Arab	100% Arab	
GFR at presentation (ml/min per 1.73 m^2)	23.4±12.8	24.5±12.9	0.44
Serum creatinine at presentation (μmol/l)	238.3±126	304.5±289.2	0.36
Ultrasound	All had bilateral hydronephrosis and thickened trabeculated bladder	Bilateral hydronephrosis (8), right hydronephrosis and absent left kidney (1)	
MCUG	Bilateral VUR(2)	Bilateral VUR (5), left VUR (1)	
DTPA scan		Unilateral PUJ (2)	
Urodynamic study (6 patients only)	Contractile (3)	Contractile (2), acontractile (1)	
MRI spine	All normal	Sacral agenesis (1), leptomeningeal cyst (1)	
Age at which CIC started	5±4.2 years	6±3.4 years	0.33

CIC was started by the pediatric nephrologist in all patients except two patients in group A, in whom it was started by urologists before their presentation. Five children required dialysis as they were in end-stage renal failure (ESRF), four in group A and one in group B. All except one received peritoneal dialysis (PD), two with automated PD (APD) and two with continuous ambulatory peritoneal dialysis (CAPD). Their mean age at the start of dialysis was 10.8±1.7 years. Two children with shunted hydrocephalus were dialyzed peritoneally. One of them had no infections or other complications for 1 year, while the other one had peritonitis which was complicated by a staph epidermis shunt infection. The latter was changed to hemodialysis and required externalization of the VP shunt for few weeks. Only one patient was started on hemodialysis from the beginning because of social reasons. Three patients continued on CIC, while two stopped it, as they were continent and they felt that it was difficult to do both PD and CIC. All of them received anticholinergic agents while they were on dialysis.

The patients on dialysis were advised to have renal transplantation after correcting their lower urinary tracts. However, none of the patients had renal transplantation because of the unavailability of donors.

The rest of the patients were managed with CIC, anticholinergic drugs (oxybutynin), prophylactic antibiotics, and conservative measures for CRF (phosphate binders, active vitamin D, erythropoietin, iron, folic acid, sodium bicarbonate, antihypertensive agents if needed, and high calorie, low protein, low phosphate and potassium diet). Two of them were lost to follow-up, one died from nonrenal causes (toxic shock syndrome), and the remaining seven were followed up for 2.7±1.1 years. Five of them had fairly stable kidney function while the last two showed a slow worsening of their GFR.

Discussion

All the patients in our study group presented with a considerable degree of CRF at an early age. This finding is different from reports from Western countries [1, 2]. Although renal complications were reported as the most frequent cause of long-term morbidity in children with neuropathic bladder, CRF is rarely seen at an carly age [1, 2, 6]. This could be explained by the delay in the management as most of the children were not started on CIC until presentation to pediatric nephrology or urology clinics, which occurred after multiple scars and significant renal damage had already occurred. Similar reports of neurogenic bladder causing CRF were reported from other developing countries [15], and this could be attributed to the same lack of early awareness, early diagnosis, and appropriate treatment of the problem, which are vital to avoid chronic renal insufficiency in these patients.

NNNB was not reported as a cause of CRF in the pediatric literature. Patients with NNNB present with symptoms similar to those with a neurogenic bladder, but no neurological or anatomical lesions can be identified. These children have diurnal wetting and recurrent urinary infections. Radiologically, a trabeculated, enlarged bladder with a thickened wall is usually found. Urodynamic studies usually reveal detrusor sphincter dyssynergia. The etiology of this voiding disturbance remains unclear; however, it results from functional urinary tract obstruction and can initiate and perpetuate vesicoureteral reflux (VUR) as well as encourage UTI and renal damage [16].

NNNB has traditionally been believed to represent a disorder of older children; however, recently it has been recognized as a severe form of dysfunctional voiding that may be present even in the neonatal period [17]. In our series, the younger patient with NNNB was 1.5 years old. The radiological and urodynamic investigations (Table 1) revealed similar results to those previously reported in young children with NNNB [17]. These were thick-walled, poorly compliant bladders with incomplete bladder emptying causing significant upper tract pathology (VUR and hydronephrosis). Boys with trisomy 21 may be at particular risk for NNNB [18]. However, none of our patients with NNNB had Down syndrome.

It is interesting to observe that all the patients with spina bifida had received attention to their neurological problems as all of them had operations for the myelomeningocele and the hydrocephalus. In contrast, most of them were not advised about the risk to their kidneys from the associated neuropathic bladder. This delay in the management also explains the high percentage of VUR in our cohort in both groups (A and B), as regular emptying of the bladder was not commenced early and anticholinergic drugs were not instituted to reduce intravesical pressure. Furthermore, the lack of good medical follow-up and management including early diagnosis and treatment of acute pyelonephritis could also have contributed to the bad outcome in these patients. A multidisciplinary approach in a specialized spina bifida clinic would help to reduce this observed delay in commencing the appropriate management to protect the kidneys.

One-third of our cohort required renal replacement therapy (RRT) at a rather young age. PD was the main modality of RRT as it is the dialysis of choice in the majority of pediatric patients. However, the presence of VP shunt makes it more complicated as those children are prone to develop shunt infection as was the case in one of our patients and has been reported by others [19]. More recent reports demonstrated that PD under close monitoring is not contraindicated in children with myelomeningocele, regardless of the presence of VP shunt or any stoma [2, 20]. However, if cerebrospinal fluid diversion is needed simultaneously or after starting PD, an extraperitoneal site would be a better choice than VP shunt. This may avoid the risk of intra- and postoperative infection in the PD catheter, secondary to surgical intervention for VP shunt insertion. Loss of peritoneal function is a potential late risk related to exposure to cerebrospinal fluid and PD. Furthermore, spina bifida patients on PD present specific diagnostic challenges due to overlapping symptoms (e.g., vomiting, abdominal tenderness, fever) secondary to PD- or VP shunt-related complications (e.g., peritonitis, visceral injury by devices)

or primary disease (e.g., neurogenic bladder, pyelonephritis) with potential risks of delaying adequate treatment. Early evaluation by a pediatric surgeon and a neurosurgeon is required for effective management of complications and selection of more efficient individualized therapeutic alternatives [20].

Although renal transplantation is now considered the optimal treatment for ESRF in all age groups, doubts remain however about the risks of transplantation when the patient has an abnormal lower urinary tract, because it is logical to assume that the bladder that contributed to the destruction of native kidneys would also threaten subsequent renal allograft [2]. Therefore, the general recommendation is to correct inefficiencies and deficiencies of the lower urinary tracts of these patients before transplantation [2]. Recent data demonstrate the feasibility of renal transplantation in patients with spina bifida and ESRF [21, 22]. The current recommendation is that these patients should not be deprived of the benefits of renal transplantation [19–22]. Similarly, renal transplantation in children with severe bladder dysfunction due to other causes can achieve similar results to those obtained in the general population [2]. Meticulous selection of patients and surgical reparative techniques ensuring voiding as well as adequate control of urinary infections are mandatory. Augmentation cystoplasty and intermittent catheterization are appropriate techniques currently used for achieving this outcome [23].

Conclusion

Neuropathic bladder due to spina bifida or NNNB is an important cause of CRF in the developing countries. There was a considerable delay in the diagnosis of NNNB and a significant delay in starting the appropriate management in all neuropathic patients. More awareness is required among pediatricians about NNNB and about the risk to the kidneys caused by neuropathic bladder. Specialized spina bifida clinics with a multidisciplinary approach will help to reduce the observed delay in commencing appropriate management of these patients.

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