Research Papers

Risk Factors for Renal Injury in Patients with Meningomyelocele

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Patients and Methods: *Thirty operated patients of myelodysplasia were clinically evaluated for the age at presentation, the extent of lesion and neurological deficit. Urological assessment was done with urine cultures, serum creatinine, radiological (ultrasound of kidney, ureters and bladder, voiding cystourethrogram) and urodynamic (water cystometry) parameters. An objective scoring for bladder (Galloway, et al.) was applied. Dimercapto-succinic acid (DMSA) scan was done in all the patients for evidence of renal scars. The results of above investigations were correlated with presence or absence of renal scars (renal injury) on DMSA scan. None of the patients had received any prior bladder care.* ***Results:*** *Twenty one patients had no renal scars and 9 patients had evidence of renal scarring. Patients with renal scars were older at presentation, they had greater degree of hydroureteronephrosis (P ≤0.001) and vesicoureteric reflux (P ≤0.005). The incidence of high leak pressures (>25 cm of water, P ≤0.05), unacceptable bladder volumes (maximum cystometric capacity <60% for age, P ≤0.005) and high risk Galloway's score (>5, P ≤0.05) was high in patients with associated renal scarring as compared to their nonscarred counterparts. Three of these patients had serum creatinine >1 mg/dL (P ≤0.005). The incidence of urinary complaints and positive urine cultures was also higher in these patients (NS).* ***Conclusion:*** *Increasing age, evidence of hydroureteronephrosis and vesicoureteric reflux, high leak pressures, low bladder volume and high combined Galloway score(>5) define a high risk bladder in our population and predispose to renal injury in patients of myelodysplasia. Early referral for bladder risk assessment and management of all myelodysplasia patients is recommended.*

Key words: *DMSA scan, Neural tube defects, Renal scarring, Urodynamics.*

MYELODYSPLASIA is a common disorder of multifactorial etiology. Though a intense campaign with prenatal ultrasound and folate prophylaxis in developed countries has been successful in reducing its incidence to 0.44/1000 live births(1), in India a large number of children are born each year with serious myelodysplasia(2). The neurological disability associated with myelodysplastic disorders is permanent and has far reaching implications, including those involving the urinary tract. This study analyzes the extent of urological involvement in children with neural tube defect (NTD) who have had no prior urological intervention. An attempt has been made to correlate these uroradiological and urodynamic changes of lower urinary tract with renal scarring.

Patients and Methods

Thirty operated cases of myelodysplasia, who presented between June 2004 to January 2006, were enrolled and evaluated for urological complaints. They were investigated with urine cultures, serum creatinine, ultrasound for kidneys, ureters and bladder, voiding cystourethrogram (VCUG) and fluid cystometry. Dimercaptosuccinic acid (DMSA) scan was done and interpreted by independent specialists who were unaware of the uroradiological and urodynamic findings. All urological investigations were done at least six weeks post-operatively after the effect of spinal shock had subsided. Vesicoureteric reflux (VUR) on VCUG (voiding cystouretherogram) was graded

as per the international classification(3). Urodynamic parameters including compliance, hyperreflexia, sphincter activity, maximum cystometric capacity (MCC) and leak pressures were measured using standard definitions(4). Any change in MCC was measured as a percentage of normal bladder volume: Per cent MCC = Bladder volume at end point of filling cystometry / MCC expected for age × 100. The end point of filling cystometry was taken as continuous pericatheter leak or pain or a strong urge to void or the cystometrogram showing a sharp rise in detrusor contraction. Leak point pressure below 25 cm of water and compliance >20 mL/cm of water was considered normal(4). An objective score (combination of radiological and urodynamic parameters) described by Galloway was evaluated used as a independent parameter for assessment of lower urinary tract changes(5). It uses five variables; bladder compliance, detrusor contractibility, VUR, leak pressure and sphincter behavior. Each was assigned a score from 0-2. A score of greater than five (>5) was correlated with occurrence of renal injury in our patients. Correlation of all observed radiological and urodynamic parameters independently to scar formation on DMSA was analyzed. Chi-square test and Mann Whitney U test were used for statistical analysis. P value ≤0.05 was considered significant. Other parameters like urinary complaints, incidence of positive urine cultures and serum creatinine levels at presentation (≥1 mg/dL) were also evaluated. Correlation of age with renal deterioration was established using Mann Whitney U test. Parameters having statistically significant correlation with renal injury were considered as indicators of high risk bladder.

Results

Of 30 patients (25 boys), 24 (80%) had a lumbar or lumbosacral lesion; 3 patients each had sacral and thoracic lesions. 21 patients had no scars on DMSA scan while 9 patients (30%) had scars. The age of the patients ranged from six months to eighteen years (median age = 4.5 yr). The median age of patients was higher in scar positive patients as compared to scar negative patients. (7 vs 4 yr). All patients irrespective of the age at presentation had received no prior urological care for neurogenic bladder. Of the 9 patients with scars, 5 had bilateral and 4 had unilateral scars. Ultrasonographic evaluation showed hydroureteronephrosis in one patient without renal scar and 7 patients with renal scars (P ≤0.001, *Table I*). Three scar negative patients and 6 scar positive patients showed vesicoureteric reflux on VCUG (P ≤0.005, *Table I*).

Nine (42.9%) patients without scars and eight (88.9%) with scars had leak pressures >25cm of water (P ≤0.05, *Table I*). The mean bladder volume in scar positive patients (30.9 ± 16.2 mL) was lower than scar negative counterparts (64.2 ± 39.0 mL). All patients with scars had a MCC less than 60% of expected, compared to 43% of patients without scars (P ≤0.005, *Table I*). Other urodynamic parameters including compliance, bladder hyperreflexia and sphincter activity did not differ significantly between the two groups. Eight patients without scars and seven (77.8%) patients with scars had a high risk bladder score (P ≤0.05, *Table I*). Serum creatinine levels >1 mg/dL was noted in 3 patients with scars and none of the patients without scars (P ≤0.005, *Table I*). The

TABLE I–*Statistical Comparison of Biochemical, Uroradiological and Urodynamic Parameters in Patients with Scars and Without Scars*

Total patients (n = 30)	Serum creatinine > 1 mg%	Hydroureteronephrosis	Vesico-ureteric reflux	Leak pressure (>25 cm.water)	MCC* <60% for age	Combined score (>5)
Scar negative (n = 21)	Nil	1	3	9	9	8
Scar positive (n = 9)	3	7	6	8	9	7
P value	≤0.005	≤0.001	≤0.005	≤0.05	≤0.005	≤0.05

* MCC = Maximum cystometric capacity.

What this Study Adds

- Renal injury in myelodysplasia is related to increasing age, presence of hydroureteronephrosis on USG KUB region, demonstrable VUR on VCUG, leak pressures >25 cm of water, <60% MCC, Galloway's score >5 and serum creatinine >1mg/dL on presentation.

difference in incidence of positive urine cultures and urinary complaints however was not found to be statistically significant. All urologically symptomatic patients (n = 24) were started on a bladder management programme.

Discussion

Myelodysplasia is a progressive neurological disease resulting in progressive urological damage(6). Though many children may have no scars at birth they develop scars as they grow. It implies that these patients require a long term follow-up. Two general management options are available *viz*., starting early CIC (proactive) or starting CIC after development of radiological features of back pressure (retrospective). Good results have been reported after treating children in either fashion(7-9). The higher scarring rate found in the present study as compared to West emphasizes the need for a strict follow-up protocol and early intervention(8). Thirty per cent of our patients had a DMSA scan evidence of scars at the time of referral to us. This may be because of lack of urological intervention and increasing damage with age. 77.8% of these patients had demonstrable hydroureteronephrosis on ultrasound of the KUB (kidney, ureter, bladder) region and 66.7% demonstrated vesicoureteric reflux on VCUG.

There has been lack of consensus amongst experts to establish uniform urodynamic criteria to define high risk bladder. In our work hyperreflexic detrusor contractions were not found to be a significant threat to the upper tracts and this was also reported by Galloway, *et al.*(5). Sidi and associates considered compliance and leak pressures as the most predictive urodynamic parameters(10). In our study also eight of nine patients with scars had unacceptable leak pressures (>25 cm of water). Majority of our patients with leak pressures greater than 40 cm of H_2O had associated radiological changes. Low compliance however, was not found to be a statistically significant parameter associated with renal scarring by us. Galloway's score could pick up 77.8% of the patients with positive scars on DMSA scan in our study, a combination of radiological and urodynamic parameters is, therefore, a better correlate to renal injury rather than either of them individually(5).

All patients with scars were found to have <60% MCC and would eventually require bladder augmentation if no improvement is noticed after initiating a bladder management program. Failure of improvement in bladder volumes post imipramine was taken to be a decisive parameter for management decisions in high risk bladders in a recent study by Puri, *et al.*(11). Most children born with myelodysplasia will require CIC to achieve social continence by the time they are 5 to 7 years old. As noted by Klose, *et al*. the indications to institute CIC before this age have been hydronephrosis and/or vesicoureteric reflux in addition to an inability to empty the bladder (retrospective group)(12). An early start of CIC in all patients of spina bifida after neurosurgical closure as practiced by some European groups (proactive group) however decreases the incidence of scar formation in their patients(9).

In our country patients hardly receive any bladder management and hence constitute an uncontrolled group. While some workers would consider radiological surveillance as adequate others would use urodynamics as the basis for bladder management. Regardless of the approach, these children need close surveillance in the first few years of life. It is necessary to start a spina bifida association in India as a patient support group to help and support these families in order to limit the urologic disability. The State should also support these families and the patient support

groups. At present in India a retrospective bladder management program appears more feasible due to constraints of manpower and money.

We conclude, patients of myelodysplasia are susceptible to progressive renal damage. Hydroureternephrosis on ultrasound, demonstrable vesicoureteric reflux on VCUG, leak pressures >25 cm of water, MCC <60% for age, Galloway score >5 and serum creatinine >1 mg/dL at presentation were recognized as statistically significant parameters which correlate with higher risk of renal injury and can be considered as indicative of high risk bladder. We recommend early institution of a bladder management program and a long term follow up in these patients.

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