

Clinical and Radiological Changes after use of Alpha-1 Blocker Therapy in Patients of Posterior Urethral Valve with Bladder Neck Hypertrophy

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ABSTRACT

Background: We evaluated the effects of alpha-1 blocker therapy on clinical and radiological abnormalities in patients of posterior urethral valve with bladder neck hypertrophy.

Materials and Methods: A total of 74 patients with posterior urethral valves were seen at our department between 2003 and 2007. Out of these 24 had radiological evidence of bladder neck hypertrophy. Those patients with bladder neck hypertrophy who were seen before June 2006 and did not receive alpha-1 blocker (prazosin) therapy after valve ablation were assigned to group 1 (n=10). Group 2 consisted of 14 age matched patients with bladder neck hypertrophy and comparable prognostic factors who received alpha-1 blocker therapy after valve ablation (n=14). Micturating cystourethrography (MCU) was done periodically and a novel method used to calculate bladder neck hypertrophy. Trends in symptoms and radiological changes were evaluated throughout follow-up.

Results: Mean patient age at presentation was 3.02 ± 2.68 years in group 1 and 3.12 ± 3.4 years in group 2. Bladder neck hypertrophy decreased from 2.3 ± 1.0 to 2.0 ± 0.5 in a mean time of 52.0 (34-52) weeks in group 1 where as it decreased from 2.2 ± 0.5 to 1.6 ± 0.3 in a mean time of 32.0 (22-52) weeks. Symptomatically patients in group 2 who received alpha-1 blocker therapy after valve ablation were better and had quick resolution of bladder neck hypertrophy.

Conclusions: Use of alpha-1 blocker therapy in patients of posterior urethral valve with bladder neck hypertrophy helps in quick resolution of bladder neck hypertrophy. (*J Med Sci* 2009; 12(1):3-7)

Key Words: Urethra, Urinary bladder, Bladder neck hypertrophy, Posterior urethral valve, Alpha blocker

Introduction

Posterior urethral valves (PUV) are the most common cause of congenital urethral obstruction in boys.^{1,2} Most urologists now agree that primary endoscopic valve ablation is the treatment of choice for PUV, with urinary diversion reserved for severely ill infants in whom valve ablation is technically impossible.³ Although endoscopic valve ablation is effective in resolving the anatomical

obstruction and upper tract dilatation, the sequelae in the bladder and kidneys remain (and sometimes worsen) after valve ablation during childhood and through adolescence.⁴ The prevalence of bladder dysfunction is estimated to be 75% to 80% in boys studied urodynamically after PUV ablation, and a third of boys with PUV have progression to renal failure.^{4,5} There is also a strong association between bladder dysfunction and deterioration of renal function in patients with PUV.⁴ Many adjuvant therapeutic modalities are suggested to achieve treatment goals in children with PUV. These consist of use of anticholinergics drugs, clean intermittent catheterization (CIC), timed voiding etc. Some authors have used even transurethral incision of the bladder neck (BNI) for primary bladder neck obstruction.

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However, the fear of possible retrograde ejaculation postoperatively has limited the number of such procedures in children with PUV. Alpha-1 blocking drugs represent a good alternative to relieve the bladder neck obstruction without the side effects of a radical procedure like BNI. We used alpha blocker in a group of patients with radiological evidence of bladder neck hypertrophy and studied the clinical and radiological changes with time.

Patients & Methods

Seventy four patients of posterior urethral valve followed our clinic from Jan 2003 to Dec 2007. Out of these a subgroup of patients (n=24) with radiological evidence of bladder neck hypertrophy were selected for study. All new cases (n=14)with bladder neck hypertrophy from Jun 2006 were treated with a selective alpha 1 blocker (prazosin) after valve ablation starting with a dose of 20 mcg /kg/day in three divided doses and increasing to 50 mcg/kg/day over 1 week monitoring blood pressure daily. Rest of the cases who were seen before this who had not received alpha-1 blocker were treated as control group (n=10). Patients were followed with micturating cystourethrogram (MCU), urodynamic studies, ultrasonography, radionuclide scans and renal function tests. Symptoms were recorded at each follow up and especially the presence of straining at micturation. MCU was done at 6 weeks, 6 months, and 1 year. We measured the bladder neck hypertrophy objectively by a novel method finding the ratio between diameter of posterior urethra and the bladder neck (Figure 1) in a good oblique micturating film under fluoroscopy at each study. Urodynamic studies were done within 1 week after ablation and 6 months, and 1 year using a double lumen 7 Fr catheter using Albyn Phoenix medical system. Ultrasound was obtained at 3, 6 and 12 months. Renal dynamic scans and GFR was measured after fulgration and during follow up as required. Serial renal function tests were also obtained as required. Renal function was taken as normal if GFR was 100ml/min/1.73 meter square of body surface area in patients of age more than 2 years and above 80/min/1.73 meter square of body surface area in patients of age less than 2 years and serum creatinine was normal for the age.

Statistical analysis was done using paired t-test and multiple serial analysis using ANOVA test. *p* values less than 0.05 were considered significant.

Results

Mean patient age was 3.02±2.68 years in group 1 and 3.12±3.4 years in group 2. Clinical presentations are summarized in table 1. Both groups were comparable to each other except that the follow up period was longer in group 1.

On follow up, most of the symptoms improved but few patients persisted with straining and incontinence

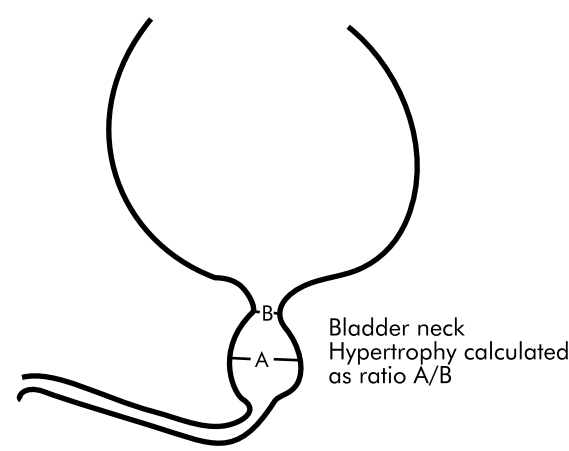


Figure 1: Calculation of bladder neck hypertrophy

which was mostly nocturnal. The symptoms of straining improved more in group 2 however statistically difference was not significant, where as other symptoms were comparable in both the groups.

Bladder neck hypertrophy was measured as the ratio depicted in figure 1. The comparison was done between the ratio obtained before the ablation (R1) and the ratio at the last follow-up (R 3). There was a statis-tically significant difference in the reduction of bladder neck hypertrophy in group 2 (*p*-valve <0.05) when compared before valve ablation and at last follow up.

Table 1: Clinical characteristics by treatment group

	Group 1	Group 2
No. of patients	N= 10	N= 14
Age (range)	1.5 months-8 years	1 month-10 years
Mean±SD (years)	3.02±2.68	3.12±3.4
< 1 year	3	3
> 1 year	7	11
Follow-up	1.5 year-2.5 years	3 months-1.5 years

Table 2: Presenting signs and symptoms by treatment group

	Group 1 (n= 10)		Group 2 (n= 14)	
	At presen-tation	Last follow-up	At presen-tation	Last follow-up
Straining	7 (70%)	3 (30%)	8 (57%)	2 (14%)
Poor stream	6 (60%)	-	9 (64%)	-
Fever	3 (30%)	1 (10%)	4 (28%)	1 (7%)
Retention	2 (20%)	-	-	-
Pyuria	2 (20%)	-	4 (28%)	-
Incontinence	3 (30%)	1 (10%)	4 (28%)	2 (14%)
Others	4 (40%)	1 (10%)	6 (42%)	1 (7%)

Table-3: Bladder neck hypertrophy in both groups

Group	Ratio 1# (mean±SD) at presentation	Time 1** (weeks)	Ratio 2 (mean±SD) at 1st follow-up	Time 2** (weeks)	Ratio 3 (mean±SD) At last follow-up	Time 3 (weeks)	P-value
I	2.3±1.0	23.0	2.1±0.9	52.0 (34-52)	2.0±0.5	73 (4-104)	0.716
II	2.2±0.5	9.0 (6-12)	1.8±0.4	32.0 (22-52)	1.6±0.3	41 (30-60)	<0.001*

Ratio was calculated from the MCU at each study; * P-value calculated between R1 and R3; ** T1 and T2 represent the time interval between the two studies



Figure 2: Serial MCU of patient (Group 1) at presentation

Figure 5: Serial MCU of a patient (Group 2) at presentation

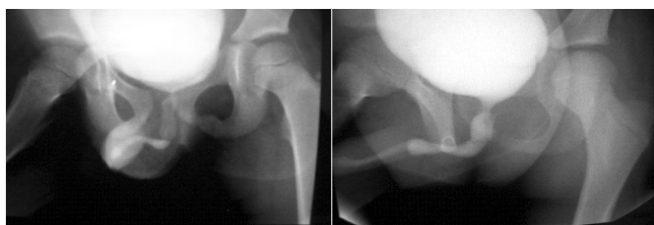


Figure 3: Serial MCU of patient (Group 1) at 1 year

Figure 6: Serial MCU of patient (Group 2) at 6 weeks

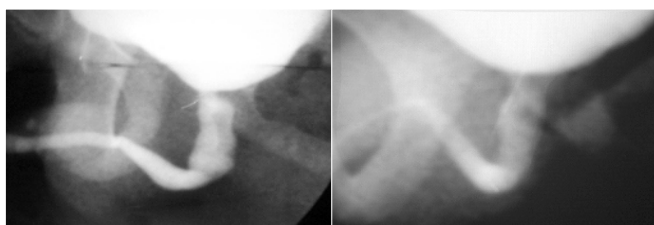


Figure 4: Serial MCU of patient (Group 1) at 2 year showing non-resolution of bladder neck hypertrophy

Figure 7: Serial MCU of patient (Group 2) at 6 months showing resolution of bladder neck hypertrophy

Discussion

Despite early detection and intervention, one third of children with PUV ultimately have progression to ESRD.⁷ The nature of renal damage in these children is still debatable and may be due to a variety of factors, including renal dysplasia, bilateral reflux, early presentation and recurrent UTI. However bladder dysfunction has been recognized as the major risk factor for the development of renal failure in patients with PUV.⁸

Previous studies have demonstrated the association of bladder dysfunction with late onset renal failure, persistent VUR and poor allograft survival in trans-

planted patients with PUV.⁹ Ghanem *et al* reported that the combination of detrusor over activity and poor compliance was associated with the worst long-term prognosis of renal function in patients with PUV.¹⁰ The most frequent urodynamic patterns found in patients with PUV are bladder instability, poor compliance and myogenic failure. Some investigators believe that the dysfunctional bladder dynamics change with time, since the predominant findings during infancy are hypertonia and bladder instability, whereas myogenic failure gradually sets in with increasing bladder capacity and post-void residual after puberty.¹¹⁻¹³

Although primary valve ablation is considered the ideal initial treatment for PUV, resecting the valve is not a cure, since a broad spectrum of symptoms usually remains after the procedure.¹⁴ Thus, many adjuvant therapeutic modalities have been proposed to treat bladder dysfunction and postpone renal deterioration in patients with PUV. Misseri *et al* recommended early aggressive anticholinergic therapy and timed voiding for management of bladder dysfunction in children with PUV.¹⁵ Anticholinergic therapy effectively eliminates bladder instability. However, it may increase bladder capacity and decrease voiding detrusor pressure, which can lead to myogenic failure.¹⁶ Koff *et al* recommended overnight catheter drainage in place of (or in addition to) CIC and repeated voiding.¹⁷ Additionally, Kajbafzadeh *et al* suggested oral desmopressin therapy for these patients.⁶ These studies support the idea that valve ablation alone may not be sufficient for normalization of bladder function. The bladder neck was once recognized as the major cause of bladder outlet obstruction in patients with PUV. However, the concept was largely disputed by Glassberg and Waterhouse who reported that the bladder neck is not actually narrow.⁶ The bladder neck was recently revisited by some authors, who acknowledge that in some PUV cases there could be a persistent obstructive process secondary to bladder neck dyskinesia.¹⁸ Androulakakis *et al* have found endoscopic evidence of

prominent hypertrophic semiclosed bladder necks in patients with PUV and myogenic failure. They hypothesize that voiding under such circumstances may be obstructive at the level of bladder neck, and cause detrusor decompensation by a prolonged and increased bladder outlet resistance. Moreover accumulating data have shown the efficacy of α -blockers in improving voiding dysfunction and upper tract dilatation in patients with PUV presumably through decreasing intravesical pressure and outlet resistance.¹⁹⁻²²

It appears that this subset with bladder neck obstruction represents approximately 20% of the affected patient population. Potential therapy directed at persistent obstruction after primary valve ablation could include α -blockers or clean intermittent catheterization. Mac Kinnon²³ suggests a more aggressive medical approach or vesicostomy in non responders following simple valve ablation. His unpublished results have shown improved voiding and decreased upper tract dilatation in children treated with α -blockers following simple valve ablation which is in agreement with other reports.⁶

Kajbafzadeh, *et al* evaluated the effects of simultaneous bladder neck incision and valve ablation on urodynamic abnormalities in patients with posterior urethral valves. They demonstrated that valve ablation with bladder neck incision may result in better bladder urodynamic function in comparison to simple valve ablation. This study shows the importance of treating bladder neck in these patients.⁶

Use of α blockers represents a less invasive, approach to treat the bladder neck with added advantage of avoiding surgical complications.

We have used a novel method to measure radiologically the degree of hypertrophy at the bladder neck which reflects the degree of obstruction at this level. We found significant decrease in the BNH in patients who received α 1 blocker, over a mean follow up of 1 year and the symptoms of straining improved in these patients. No side effects were reported in our patients and α 1 blockers were found to be safe.

Conclusions

This study demonstrates that α 1 blockers have a definite beneficial role in patients with bladder neck hypertrophy in decreasing the hypertrophy. It is an ideal therapy for all these patients representing a midway between less aggressive medical and more aggressive surgical therapy like BNI. However, the long term effects need further evaluation.

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