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Role of Alpha Adrenergic Blocker on Bladder Emptying In Children with Posterior Urethral Valves after Valve Ablation

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Original Research Article

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Abstract: Role of alpha adrenergic blocker in children with posterior urethral valves after valve ablation. Seventy one children with significant post void residual urine from January 2009 to December 2012, after confirming there was no residual valve on repeat VCUG, were taken for the study. Children less than 2 years of age and children more than 2 years of age, with significant post void residual urine were placed on 0.1 mg and 0.2 mg capsule Tamsulosin respectively. Post void residual urine (PVR) and uroflowmetry was done at the commencement of alpha blocker and at follow up. PVR was monitored with abdominal ultrasound by two different observers. We also look for breakthrough urinary tract infection in children during the study. Post void residual urine significantly reduced in 71 patients. Mean pretreatment PVR was 31.59+/- 1.30ml and mean PVR, at the last follow up was 7.62+/- 4.36 ml. (P =0.000) There was a reduction of 75.87% in the pretreatment post void residual urine volume. Mean pretreatment Qmax was 10.77 +/-6.57 ml/min and it was 13.78 +/-8.58 ml/min at the last follow up in toilet trained children. (P =0.000) 34 patients had history of recurrent urinary tract infection. At last follow up, there was resolution of breakthrough urinary tract infection. These children had reflux on micturating cystourethrogram. This may be due to decrease in PVR. Mean follow up was 36+/- 10.5 months. Alpha 1 adrenergic blocker therapy in children with posterior urethral valves results in significant improvement in bladder emptying. It reduces episodes of breakthrough urinary tract infection. Further research in form of randomized controlled trials and long-term follow up are necessary to further define the role of an adrenergic blocker therapy in children with posterior urethral valves.
Keywords: Post void residual urine (PVR), Tamsulosin, uroflowmetry

INTRODUCTION

The successful use of α-1 adrenergic blocker for overactive bladder sphincter in adult with prostatic hypertrophy has generated interest in its possible use in children with voiding dysfunction. Although α-1 adrenergic blocker has been used to treat children with neurogenic and non-neurogenic voiding dysfunction, its general use in patients with posterior urethral valves remains limited. We evaluate the role of alpha 1 adrenergic blocker in children with PUV. Androulakakis et al have found endoscopic evidence of prominent hypertrophic semi closed bladder necks in patients with PUV and myogenic failure [5]. 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 [5]. Although in normal bladder, alpha adrenergic stimulation is not very prominent, but studies have shown that under pathological condition, the adrenergic receptors density can increase [7, 8].

Stimulation of the adrenergic receptors will result in smooth muscle contraction and increases in outlet resistance; blockage will result in smooth muscle relaxation at the bladder base and decreases in bladder outlet resistance. [9] So we evaluate the role of alpha 1 adrenergic blocker in children with PUV after valve fulguration.

MATERIALS AND METHODS

Children who were treated for posterior urethral valves were followed up in the outpatient department on regular basis. VCUG was repeated after 3 months of valve ablation. Check cystoscopy was done if VCUG suggested incomplete valve ablation. In all patients where residual valves were ruled out were enrolled for the study. All children were followed up in the outpatient department between January 2009 and December 2012. Post void residual urine (PVR) was assessed with ultrasound by two different observer after a witnessed void in toilet untrained children and in toilet trained children at the time of uroflometry. This was done after 2 week of the valve ablation allowing time for the bladder neck and urethral spasm to subside after valve ablation, and catheterization. uroflowmetry

was done in toilet trained children (more than 3 years of age) [14]. Episodes of breakthrough urinary tract infection were seen in all children. Bladder capacity was determined by using the koff formula: expected capacity in ml = weight (kg) x 7 for children less than 2 years and [age (years) + 2] x 30 for children greater than or equal to 2 years [1]. Post void residual urine volume of greater than 10% of expected capacity for age was taken as significant. Children less than 2 years of age and children more than 2 years of age, with significant post void residual urine were placed on 0.1 mg and 0.2 mg of capsule Tamsulosin (in form of tablet veltam) respectively. It is a selective alpha 1 adrenergic blocker. This was given with milk. Adverse events were generally mild and included dizziness, rhinitis, postural hypotension and abnormal ejaculation. These side effects were increased in a dose-dependent manner. Such effects are similar to placebo at 0.2 mg but increasing to 16% with the 0.8-mg/day dosage [2]. We look for postural hypotension and rhinitis. First dose of this drug was given in the OPD to look for postural hypotension. Alpha blocker was stopped if PVR remained normal and maintained for 6 months. PVR values, uroflowmetry and episodes of urinary tract infection before initiating Tamsulosin and at the last follow up were compared for statistical significance with student's paired t test using SPSS version 16.

RESULTS

A total of 71 patients with significant PVR were taken for the study treated for posterior urethral valves. Pretreatment PVR, Uroflowmetry (Qmax) and episodes of breakthrough urinary tract infection was recorded and it was also recorded at last follow up. Mean age at last follow up was 7.45+/-3.88 years. Mean pretreatment PVR was 31.59+/- 1.30 ml and mean PVR, at the last follow up was 7.62+/- 4.36 ml (P =0.000).This was a reduction of 75.87% in the pretreatment post void urine volume.

Mean pretreatment Qmax was 10.77 +/-6.57 ml/min and it was 13.78 +/-8.58 ml/mint at the last follow up (P =0.000). 34 patients had history of recurrent urinary infection. At last follow up, there was no history of breakthrough urinary tract infection. These children had reflux on micturating cystourethrogram. Mean follow up was 36+/- 10.5 months.

Table- Comparison of different study

Study	No. of patients	Drug	Pre treatment PVR(ml)	Post treatment PVR (ml)	Response (%)	Follow up (months)	Side effect
Abraham *et al*. [12]	42	Terazocin	15.7	2.4	85	17	Hypotension - 1
Cain *et al*. [11]	55	Terazocin	65	8	88	2	Hypotension- 2
Present study	71	Tamsulosin	31.59	7.62	75.87	36	None
Androukakis *et al*.[5]	1	Tamsulosin	-	-	-	-	-
Misseri *et al*.[6]	3	Tamsulosin	-	-	-	-	-

DISCUSSION

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 [3, 4]. 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 [3, 5]. Androulakakis *et al.* have found endoscopic evidence of prominent hypertrophic semiclosed bladder necks in patients with PUV and myogenic failure [5]. 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 [5]. Moreover, accumulating data have shown the efficacy of alpha-blockers in improving voiding dysfunction and upper tract dilatation in patients with PUV, presumably through decreasing intravesical pressure and outlet resistance [3, 6].

Although alpha adrenergic stimulation is not very prominent in normal bladder, studies have shown that under pathological condition, the adrenergic receptors density can increase. This may be responsible for the hyperactivity observed in a variety of obstructive uropathy [7, 8]. Alpha 1 adrenergic receptor blocker therapy may potentially act to facilitate relaxation of the bladder base and proximal urethral sphincter which may be a secondary area of functional obstruction due to chronic over stimulation and up regulation of alpha

adrenergic receptors [8]. Stimulation of the adrenergic receptors will result in smooth muscle contraction and increases in outlet resistance; blockage will result in smooth muscle relaxation at the bladder base and decreases in bladder outlet resistance [9]. Alpha 1 adrenergic receptor blocker selectively relaxes the trigone and proximal urethra without peripheral vasodilatation.

Androulakakis *et al.* put one patient on tamsulosin and found to have improvement in post void residue although there were no formal measurements of flow rate. When they reevaluated, his bladder neck appeared more open, and they felt their flow had improved. [5]

Misseri *et al*. who also treated three boys with secondary bladder neck obstruction with tamsulosin. They also found a positive effect on bladder empting, substantially lowering the PVR. Alpha adrenergic antagonists are effective in improving uncoordinated voiding in patients with a history of PUV, their use after valve ablation could possibly avert myogenic failure and bladder decompensation [6].

Austin *et al.* have demonstrated the potential benefits of alpha 1 adrenergic blocker in obstructed, neurologically intact as well as neurogenic bladders in children, although there were only two patients with posterior urethral valves in their heterogeneous population of patients. Alpha blocker used in their study was Doxazocin with better result [10, 11].

This present study shows 75.87% reduction in post void residual urine with the use of Tamsulosin; this is comparable to 88% reduction in Cain's report [11]. Advantage with Tamsulosin is no dose titration as seen with terazosin.

Abraham *et al*. put their PUV patients on Terazosin, these patients had significant PVR. Mean PVR before commencing alpha blocker was 15.7 ml and mean PVR at the last follow-up was 2.4 ml (P = 0.000). The median follow-up period was 17 months (range 6– 75 months). There was 85% reduction in PVR [13].

Limitation of the study include- no urodynamic study was done to locate obstruction at bladder neck, mean age of children enrolled in the study were higher, no randomization

CONCLUSION

Alpha 1 adrenergic blocker therapy in children with posterior urethral valves results in significant improvement in bladder emptying. It reduces episodes of breakthrough urinary tract infection. Further research in form of randomized controlled trials and long-term follow up are necessary to further define the role of an adrenergic blocker therapy in children with posterior urethral valves.

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