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Research Article

# Early use of Bladder Relaxant (Oxybutynin) in Posterior Urethral Valve Patients. Is it Justified?

**Sajad Ahmad Wani*, Narindra Babu, Mir Faheem, Viney Jadhav, Ramesh S, Deepak J**

*Department of Paediatric Surgery, SKIMS Soura Srinagar, Jammu and Kashmir, India*

## ABSTRACT

**Introduction:** Posterior Urethral Valves (PUV) constitute the most common infravesical urinary obstruction in boys. Bladder dysfunction, the pattern of which changes with the age and is common cause of morbidity in PUV patients. Urodynamic study provides a useful tool to identify the bladder dysfunction and allow timely and appropriate management. The aim of this study was to determine the efficacy of early use of bladder relaxant (oxybutynin) on urodynamic parameters in PUV patients and to compare our results with other authors.

**Material and Methods:** Patients with posterior urethral valves more than 4 years of age were included in the study. After the diagnosis, oxybutynin was started prophylactically in all patients. Invasive urodynamic study was done in all patients minimum one year after start of oxybutynin. Bladder relaxant (oxybutynin) was stopped 48 hours before the study. Various urodynamic parameters which were noted in each patient include compliance, bladder stability (normal/overactivity), bladder capacity, detrusor pressure during voiding (sustained, waxing and waning or myogenic failure), detrusor sphincter dysynergia and post void residue.

**Results:** 47 patients were included in the study. Age of patients ranged from 4 years to 14.8 years with mean age of 8.4 years. Normal detrusor pressure during filling (stable bladder) was seen in 95.7% of patients, bladder overactivity in 4.3% of patients, compliance (compliance good in 89.4% and compliance poor in 6.4%), bladder capacity (normal (70.2%), decreased (10.6%) and increased (19.1%), detrusor pressure during voiding (sustained (68.1%), waxing and waning (21.3%) and myogenic failure (10.6%)).

**Conclusion:** Early use of oxybutynin immediately after the diagnosis of PUV, improves the urodynamic parameters in these patients possibly because of protective effect of oxybutynin on bladder function and structure.

**Keywords:** PUV; Oxybutynin; UDM

## INTRODUCTION

Posterior Urethral Valve (PUV) is the most common form of congenital urethral obstruction with an incidence ranging from 1/2500 to 1/5000 male births [1]. In recent years, the overall prognosis of PUV patients has improved. Several factors have been identified as predictors of long term outcome [2-6]. The bladder dysfunction is one of the important predictor of long term outcome in PUV patients, which is seen in about 75% in these patients [2,7].

A poor understanding and inappropriate management of bladder dysfunction can result in early onset renal damage and unnecessary morbidity. Urodynamic study provides a useful tool to identify the bladder dysfunction. It is used to test the efficacy of treatment and any refinement in the treatment that is necessary to improve the outcome in PUV patients [8,9].

The bladder dysfunction shows a changing pattern with the age of the child in PUV patients [10]. It is important to know if these changes in the bladder are reversible or can be modified after valve fulgration. Animal models have shown that oxybutynin decreases the intravesical pressure and detrusor overactivity. It protects the bladder against functional and structural changes and improves the compliance, bladder capacity and detrusor overactivity. The aim of this study was to determine the efficacy of early use of bladder relaxant (oxybutynin) on urodynamic parameters in PUV patients and to justify its prophylactic use in these patients.

## MATERIALS AND METHODS

This study was conducted in the Department of Paediatric Surgery and Pediatric Urology IGICH, Bangalore, INDIA. Patients with

**Correspondence to:** Sajad Wani, Department of Paediatric Surgery, SKIMS Soura Srinagar, Jammu and Kashmir, India, Tel: 07006749570; E-mail: wanisajad862@gmail.com

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posterior urethral valves more than 4 years of age were included in the study. After the diagnosis of PUV on micturating cystourethrogram, oxybutynin (0.2 mg/kg) was started prophylactically in all patients for a period of about 3 years. Invasive urodynamic study was done in all patients, minimum one year after start of oxybutynin using LABORIE URODYNAMICS.

Bladder relaxant (oxybutynin) was stopped 48 hours before the study. Various urodynamic parameters which were noted in each patient include compliance, bladder stability (normal/overactivity), bladder capacity, detrusor pressure during voiding (sustained, waxing and waning or myogenic failure), detrusor sphincter dysynergia and post void residue.

Cystometric capacity was calculated as [30+ (age in years × 30)] mL. Stable bladder was defined, when the pressure during the filing of bladder does not rise more than 6-10 cm $H_2O$ above baseline at the end of filling. Sustained detrusor pressure during voiding was defined when pdet is between 65 cm $H_2O$ to 110 cm $H_2O$. Waxing and waning of detrusor pressure (impending myogenic failure) was defined when pdet during voiding does not sustain between 65 to 110 cm $H_2O$ and drops down below the 50 cm $H_2O$ in between. Detrusor overactivity (hyperreflexia) was defined as an involuntary detrusor contraction >15 cm of water from baseline. Bladder underactivity (myogenic failure) was recognized in patients who are filled to >150% of their expected bladder capacity and have a poor (pdetmax <50 cm $H_2O$) or absent detrusor contraction during voiding. Poor compliance was defined when during filling; bladder pressure is equal to or more than 20 cm of water at expected bladder capacity.

Room temperature normal saline was used for filling the bladder at 5%-10% of the patients expected bladder capacity per minute. 7Fr urethral catheter was used for the catheterization. Before the urodynamic study, Uroflowmetery was done in all patients. After catheterization, any post void residue was noted. Post void residue was considered significant if the volume exceeds 15% of the total bladder capacity.

## RESULTS

47 patients were included in the study. Age of patients ranged from 4 years to 14.8 years with mean age of 8.4 years. The result of various urodynamic parameters were shown in Table 1.

**Table 1:** Urodynamic parameters.

| Urodynamic parameter | | No of patients (N=47) | Percentage (%) |
|---|---|---|---|
| Normal detrusor pressure during filling (stable bladder) | | 45 | 95.70% |
| Bladder overactivity | | 2 | 4.30% |
| Compliance | Good | 42 | 89.40% |
| | Poor | 3 | 6.40% |
| Bladder capacity | Normal | 33 | 70.20% |
| | Decreased | 5 | 10.60% |
| | Increased | 9 | 19.10% |
| Detrusor pressure during voiding | Sustained | 32 | 68.10% |
| | Waxing and waning | 10 | 21.30% |
| | Myogenic failure | 5 | 10.60% |
| Detrusor sphincter dysynergia | | 2 | 4.30% |

## DISCUSSION

During the normal fetal bladder development, bladder cycling generates stretch force on the bladder that results in decrease in collagen content in the bladder wall and decrease in the smooth muscle tension. In patients with Posterior Urethral Valves (PUV), normal bladder cycling fails that result in structural and functional alteration in the bladder. The severity of the bladder dysfunction depends on the duration and severity of the urethral obstruction.

In response to urethral obstruction, bladder is initially capable of generating higher voiding pressure and empties almost completely. There is increase in the deposition of extracellular matrix in the bladder wall hypertrophy of smooth muscles. The deposition of extracellular matrix between the muscle bundles and increase in the ratio of type-III to type-I collagen causes structural and functional damage to the bladder [11].

In PUV patients, there is progressive stretch injury to the bladder, which leads to a non-reversible changes in the cellular and extracellular characteristics of the bladder, leading to bladder dysfunction [12]. Due to over distension of the bladder wall, detrusor blood flow decreases resulting in ischaemia, shift to anaerobic metabolism and damage to nerves within the bladder wall [13,14]. In a rabbit model of over active bladder, there is free radical mediated ultrastructural damage and neurodegeneration [13,14]. Excess glycogen deposition within the detrusor in PUV patients results in bladder dysfunction with high pressures, bladder instability and poor compliance [15].

In Posterior Urethral Valves (PUV) patients with detrusor overactivity, there is histopathological and histomorphological changes in collagen and elastic system of the bladder leading to loss of strength and elasticity of the bladder wall and tissue fibrosis [16-18]. The end result of such changes in the bladder is gradual loss of bladder compliance, reduction in capacity and high storage pressures [19,20].

Treatment of urethral obstruction and detrusor hyperactivity should occur as early as possible that may reverse or even interrupt the deterioration of the structural and functional properties of the bladder and prevent the dysfunctioning of the bladder. The main purpose of the study was to address the effect of early use of bladder relaxant (oxybutynin) on bladder dynamics in posterior urethral valve patients.

Oxybutynin is used to lower intravesical pressure and detrusor overactivity. It inhibits stretch induced bladder smooth muscle cell proliferation. Oxybutynin has a protective effect on bladder function and structure. It improves compliance and decrease the collagen infiltration in the detrusor. Prevention of hypertrophic and ischemic bladder changes in the bladder is an argument for an early start of oxybutynin treatment in children with urethral valves [21]. Early use of anticholinergic therapy (oxybutynin) in infants with high voiding pressures and/or small bladder capacity after primary posterior urethral valve ablation has beneficial effects on bladder function.

Oxybutynin improves the compliance, bladder capacity and detrusor overactivity [22]. Oxybutynin prevent collagen and elastin alteration induced by outlet obstruction. It has anticholinergic and spasmolytic properties, which together form the basis for its use as a therapeutic option in patients with overactive detrusor function either idiopathic detrusor instability or detrusor overactivity [23].

Oxybutynin protect the bladder against functional and structural changes.

It prevents the abnormal increase in the amount of collagen and fibers in the detrusor that leads to a loss of strength and elasticity of the bladder wall and tissue fibrosis. Oxybutynin improves the bladder compliance, increases the bladder capacity and decreases the storage pressure [13]. Hamilto et al. [24] have noticed that oxybutynin has pprotective action on bladder ultrastructure with detrusor overactivity. It increases the bladder capacity and decreases the pressures. Inappropriate use of anticholinergic medications may induce iatrogenic myogenic failure. However, this drug-induced myogenic failure is reversible on stopping treatment [25,26].

In our study as shown in Table 2, normal detrusor (stable bladder during filling) with good compliance with normal bladder capacity and sustained detrusor pressure (pdet) during voiding was seen in more number of patients than other authors [27-29].

**Table 2:** Comparison of urodynamic findings with other authors.

| UDM parameter | Our results | Lal et al. [27] | Kumar et al. [28] | Mazen et al. [29] |
|---|---|---|---|---|
| Normal detrusor with good compliance with normal capacity with sustained pdet during voiding | 68.10% | 9.10% | 24% | 31% |
| Normal detrusor with good compliance with normal capacity with myogenic failure | 2.10% | 36.40% | 9% | - |
| Normal detrusor with good compliance with increased capacity with myogenic failure | 8.50% | 9.10% | - | 16% |
| Normal detrusor with good compliance with increased capacity with waxing and waning pdet. | 10.60% | - | - | 13 |
| Normal detrusor poor compliance with decreased capacity with waxing and waning pdet | 6.40% | - | 65% | 12% |
| Unstable bladder/ overactivity with decreased capacity with waxing and waning pdet. | 4.30% | 9.10% | 2% | 16% |

Poor compliance and overactivity was seen in less number of patients as compared to other authors [27-29]. As compared to other authors [27-29], improved bladder dynamics (better compliance, less bladder instability, good pdet during voiding and less myogenic failure) in our patients was possibly due to early use of oxybutynin which has protected the bladder against structural and functional changes and also changes in the collagen and elastic system of the bladder. However, it needs randomised studies to validate the effect of oxybutynin on urodynamic parameters in Posterior Urethral Valve (PUV) patients.

The weakness in our study was that there is no control group, no randomization and no pre and post treatment comparison. But, we are confident that better urodynamic parameters in our study as compared to other authors is due to early and prolonged use of oxybutynin in such patients. The age group in our study and other studies [27-29] was similar, however they have not used oxybutynin in their patients.

## CONCLUSION

After the diagnosis of PUV, early use of oxybutynin improves the bladder dynamics in these patients possibly because of protective effect of oxybutynin on bladder function and structure.

It increases the bladder capacity, decreases the bladder storage pressures and improves the compliance.

Early use of oxybutynin in PUV patients decreases the incidence of bladder overactivity, detrusor hypo contractility and myogenic failure.

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