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# MODIFIED INTRAVESICAL OXYBUTYNIN CHLORIDE THERAPY IN CHILDREN WITH NEUROGENIC BLADDER: A TEN-YEAR FOLLOW-UP

Hypothesis / aims of study
Children with spinal cord disorders can present with neurogenic bladder, a condition in which the bladder partly or completely loses its ability to store urine and void at low pressure. A bladder with low compliance may cause urinary incontinence, which negatively impacts quality of life and renal function. Long-term high pressure neurogenic bladder can increase the risk of deterioration in renal function. Anti-muscarinic pharmacotherapy with clean intermittent catheterization (CIC) is currently considered one of the most effective treatments for these patients. However, some patients do not respond to oral medication or have unacceptable adverse events, e.g., dry mouth, constipation, drowsiness, and cognitive dysfunctions, which may result in medical withdrawal for these patients. Intravesical oxybutynin is an effective treatment with less adverse events compared with oral medication. There is increasing evidence that intravesical oxybutynin is an effective therapy against neurogenic bladder [1]. However, an important issue with this treatment is retention of the solution in the bladder. A previous study reported that intravesical oxybutynin with hydroxypropylcellulose (HPC) can effectively treat children with neurogenic bladder [2]. In the present study, we report on the efficacy, safety, and side effects of long-term modified intravesical oxybutynin therapy in children with neurogenic bladder.

Study design, materials and methods
The study protocol was approved by the institutional ethics committee for clinical trials. Modified intravesical oxybutynin was administered to four paediatric patients (three males and one female) with neurogenic bladder, who were previously unresponsive to or experienced intolerable adverse events from oral medication (Table 1). Three patients had myelomeningocele and one had a neurogenic bladder due to resection of a pelvic teratoma. Parents of the patients were advised about the risks and possible adverse events of treatment before joining the study and signed an institutional ethics committee-approved informed consent form. All patients underwent general urological examinations as well as urodynamic studies to verify the diagnosis of neurogenic bladder. All patients were using CIC. The oxybutynin solution was prepared in the pharmacy division of our hospital. The solution consisted of oxybutynin chloride 2.5 mg, sodium chloride 58 mg, HPC 100 mg, sodium dihydrogen phosphate 52.6 mg, disodium hydrogen phosphate 8.7 mg, and water 10 mL (pH 5.85). The catheter for bladder emptying was used to instill the solution twice daily, at a dosage of 5 mL each time. There were no changes in frequency or dosage of oxybutynin during the course of the study. Results of pretreatment cystometrograms were compared to those from follow-up urodynamic studies. Urodynamic studies were performed according to the standard methods of the International Continence Society. We also carefully monitored adverse events, occurrence of urinary tract infection and degree of urinary incontinence during treatment.

Results
Follow-up durations were 118 months, 126 months, 127 months, and 128 months for the four patients. After 1 year, bladder compliance improved in all patients, and detrusor overactivity was undetectable in two of four patients (Table 2). At 3 years, detrusor overactivity was not observed in three of the patients. Bladder compliance at 3 years and 10 years after initiation of therapy were similar for three patients, and modified intravesical oxybutynin therapy is currently ongoing. One patient discontinued therapy at 118 months due to worsening of bladder compliance and upper urinary tract infection. Significant improvement in the degree of urinary incontinence was achieved. None of the patients had systemic adverse events related to intravesical treatment.

Interpretation of results
Although the number of patients in this study was small, all showed improved bladder compliance and reduced degree of urinary incontinence. Our data suggest that modified intravesical oxybutynin is an effective treatment option for children with neurogenic bladder. To our knowledge, this study is the first to assess the efficacy of the ten-year use of modified intravesical oxybutynin for children with this disorder. The mechanism of action of intravesical oxybutynin is highly disputed. Because systemic adverse events are rare, it has been suggested that intravesical oxybutynin is not absorbed into the bloodstream and its efficacy results from an intense local effect. Based on previous reports, difficulty retaining solutions in the bladder is an important issue to address. Since HPC is an agent that enhances drug retention in the bladder [3], including it in the regimen may reduce the absorption of oxybutynin from bladder mucosa, allowing for oxybutynin to be retained in the bladder for longer, and may also reduce anticholinergic adverse events compared to a regimen without HPC.

Concluding message
Our results suggest that long-term use of modified intravesical oxybutynin in children with neurogenic bladder with detrusor overactivity and/or high intravesical pressure during the filling phase could be an important option for improving continence and bladder compliance.

**Table 1** Patient profiles

| Patient | Age | Sex | Disease |
|---|---|---|---|
| 1 | 3y7m | Male | Pelvic teratoma |
| 2 | 1y6m | Male | Myelomeningocele |
| 3 | 1y6m | Female | Myelomeningocele |
| 4 | 2y5m | Male | Myelomeningocele |

y, years; m, months.

**Table 2** Bladder compliance and urinary incontinence before and after treatment with modified intravesical oxybutynin chloride

| Patient | Bladder compliance ($cmH_2O/mL$) | | | | Urinary incontinence | | | |
|---|---|---|---|---|---|---|---|---|
| | Before | 1 year later | 3 years later | 10 years later | Before | 1 year later | 3 years later | 10 years later |
| 1 | 1.7 | 6.7 | 6.5 | 3.7 [a] | 3 times/month | None | None | 2.3 times/day [a] |
| 2 | 0.2 | 3.5 | 4.7 | 10.5 | 4.6 times/day | 3 times/month | None | None |
| 3 | 0.1 | 10.0 | 9.3 | 9.7 | None | None | None | None |
| 4 | 2.5 | NP | 5.9 | 11.8 | 4.5 times/day | None | None | None |

[a] at 118 months; NP, not performed.


References

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Disclosures

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