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International Children's Continence Society's Recommendations for Therapeutic Intervention in Congenital Neuropathic Bladder and Bowel Dysfunction in Children

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Purpose: We present a consensus view of members of the International Children's Continence Society on the therapeutic intervention in congenital neuropatic bladder and bowel dysfunction in children. **Material and Methods:** Discussions were held by a group of pediatric urologists and gastroenterologists appointed by the board. The following draft review document was open to all the ICCS members via the ICCS web site. Feedback was considered by the core authors and by agreement, amendments were made as necessary. The final document is not a systematic literature review. It includes relevant research when available as well as expert opinion on the current understanding of therapeutic intervention in congenital neuropatic bladder and bowel dysfunction in children. **Results:** Guidelines on pharmalogical and surgical intervention are presented. First the multiple modalities for intervention that do not involve surgical reconstruction are summarized concerning pharmacological agents, medical devices, and neuromodulation. The non-surgical intervention is promoted before undertaking major surgery. Indicators for non-surgical treatments depend on issues related to intravesical pressure, upper urinary tract status, prevalence of urinary tract infections, and the degree of incontinence. The optimal age for treatment of incontinence is also addressed. This is followed by a survey of specific treatments such as anticholinergics, botulinum-A toxin, antibiotics, and catheters. Neuromodulation of the bladder via intravesical electrical stimulation, sacral nerve stimulation, transcutaneous stimulation, and biofeedback is scrutinized. Then follows surgical intervention, which should be tailored to each individual, based on careful consideration of urodynamic findings, medical history, age, and presence of other disability. Treatments mentioned are: urethral dilation, vesicostomy, bladder, augmentation, fascial sling, artificial urinary sphincters, and bladder neck reconstruction and are summarized with regards to success rates and complications. Finally, the treatment on neuropathic bowel dysfunction with rectal suppositories irrigation and transrectal stimulation are scrutinized. *Neurourol. Urodynam. 31:615–620, 2012.* © 2012 Wiley Periodicals, Inc.

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INTRODUCTION

There are multiple modalities of intervention for infants and children with neuropathic bowel dysfunction (NBD) that do not involve surgical reconstruction. These treatment modalities include pharmacologic agents, medical devices, and neuromodulation. The non-surgical interventions should be promoted before undertaking major surgery. Indications for these non-surgical treatments depend on issues related to intravesical pressures, upper urinary status, prevalence of UTI, and degree of incontinence. While continence is usually addressed as the child reaches school age, issues such as elevated detrusor pressure, hydronephrosis and/or reflux, and chronic UTIs are treated at any time.

PHARMACOTHERAPY

Anticholinergics/Antimuscarinics

Anticholinergics are the mainstay of medical treatment for NBD. They are used to diminish DO and intravesical storage pressures when children have low detrusor compliance that places them at risk for renal compromise. There is excellent level 1 evidence for the efficacy of anticholinergics to reduce bladder storage pressure and DO.[1]

The clinical efficacy from anticholinergics depends on the receptor subtype present in the target organ. Several muscarinic receptors exist throughout the body that include the following receptor subtypes: M1, M2, M3, M4, and M5.[2] The predominant muscarinic subtype in the bladder is the M2

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receptor (66%); however it is the M3 receptor subtype (33%) that is responsible for the physiologic action of detrusor-mediated micturition.[3,4] Antagonism of M3 receptors result in detrusor smooth muscle relaxation; this reaction is similar for neurogenic and non-neurogenic patients.

Oxybutynin is the first modern anticholinergic agent; it has undergone extensive examination in children with NBD. It is the only FDA approved anticholinergic in the United States for pediatric use in NBD. The dosing of oral and intravesical oxybutynin is 0.2 mg/kg/dose every 8 hr. Many practitioners will use the formula 1 mg per year of age per dose, up to a maximum of 5 mg per dose. Despite its efficacy, oxybutynin has associated systemic effects that are related to the presence of muscarinic receptors in other organ systems. Side effects include: dry mouth, constipation, blurred vision, headache, tiredness (somnolence), impaired school performance, facial flushing, gastrointestinal discomfort, and dry itchy skin. Extended release oral formulations appear to be safe in children and may improve patient compliance while diminishing the incidence and severity of side effects seen with immediate release preparations.

A significant concern with any anticholinergic is its impact on the brain. This potential side effect is important because all five muscarinic subtypes are expressed in the brain.[2] M1 receptors are particularly important in higher cognitive processes such as learning and memory. Subsequently, anticholinergics that spare the M1 receptor are desirable. Only one trial has assessed the impact of anticholinergic medications on cognitive function in children.[5] This small, double blinded cross-over trial demonstrated that long-acting oxybutynin and tolterodine for NBD do not appear to cause a deleterious effect on a child's short-term memory attention. Further studies are needed to elucidate these potential issues.

If children are unable to tolerate oral oxybutynin, other modes of delivery can help diminish side effects. The intravesical route is one alternative that does not rely on gastrointestinal absorption and therefore largely avoids the first pass hepatic metabolite, N-desethyloxybutynin that is generated from the portal venous system.[6] It is an active metabolite that shares similar pharmacologic properties with oxybutynin, thus increasing the potential for adverse effects. Advocates for intravesical oxybutynin therapy tout a reduction in oral oxybutynin-related side effects; however, there has not been a single randomized controlled study investigating intravesical oxybutynin. Published studies are primarily non-comparative case reports with small sample sizes. A recent meta-analyses involving intravesical oxybutynin in children with NBD supports its efficacy in lowering the mean maximum detrusor pressure while increasing bladder capacity, but side effects are nevertheless present, although less than with oral oxybutynin.[7] The incidence of side effects of oral oxybutynin ranges from 6% to 57%[8] whereas side effects from intravesical oxybutynin are approximately 9%.[7] Another consideration for using the intravesical route is the composition of the oxybutynin solution and its durability. Crushing the oxybutynin tablets has been cited as a deterrent to patient compliance but reconstituting the purified oxybutynin into a physiologic pH balanced sodium chloride solution seems to counteract this hurdle and ensure more consistent dose delivery.[7,9]

Transdermal oxybutynin is another alternative to oral oxybutynin that has the same benefits as intravesical treatment as it avoids the initial first pass metabolite *N*-desethyloxybutynin that is supposed to reduce side effects. These advantages were noted in a recent report using transdermal oxybutynin in children with neurogenic DO.[10] The pharmacokinetics, dosing and efficacy have yet to be established with transdermal oxybutynin. There are inherent limitations with transdermal delivery such as local skin site irritation and the necessity for continual skin adherence. Nevertheless, transdermal oxybutynin appears to be a reasonable alternative to oral oxybutynin in the treatment of NBD in older children.

Besides oxybutynin, there has been an emergence of new selective anticholinergic medications that are designed to diminish side effects by either targeting specific muscarinic receptor subtypes or by altering the structural compounds so that they are less likely to cross organ barriers. Tertiary amines (oxybutynin, tolterodine, darifenacin, solifenacin, and propiverine) are more likely to cross the blood–brain barrier (BBB) than quaternary amines (propantheline and trospium).[1] Other factors such as lipophilicity, molecular size, and molecular charge are also responsible for determining permeability of an anticholinergic crossing the BBB. Despite emergence of new anticholinergics, few have been studied in children. Tolterodine is the only other anticholinergic besides oxybutynin that has undergone a trial in children with NBD by the FDA. Study design limitations, however, prevent therapeutic labeling for tolterodine in the treatment of children with NBD. Nevertheless, in small case studies of children with NBD, tolterodine appears to have similar efficacy and tolerability as oxybutynin.

Botulinum-A Toxin (BTX-A)

BTX-A is an attractive treatment for NBD because it inhibits acetylcholine neurotransmitter release at the neuromuscular junction. In addition, there is evidence suggesting that BTX-A modulates both sensory and motor pathways by inhibiting the release of "other" neurotransmitters (adenosine triphosphate, and substance P) and down-regulating the expression of purinergic and capsaicin receptors on afferent neurons within the bladder.[11,12] Intravesical BTX-A is considered an alternative to improving continence and urodynamic parameters of NBD in children. Neither the FDA or the European Medicines Agency (EMEA) has approved the use of BTX-A for the treatment of NBD; thus BTX-A use is off-label requiring informed consent. A recent review using BTX-A was conducted that provided a current summary of the efficacy and safety profile of BTX-A in children with NBD.[13] Collectively, these small, uncontrolled studies demonstrate a significant improvement in clinical and urodynamic parameters as evidenced by complete continence in approximately 65% to 87% of children and a reduction in maximum detrusor pressure and an increase in detrusor compliance in the majority of those treated. The youngest child was 2 years old, which corresponds to the minimal age that has been approved by the FDA and the EMEA for the treatment of spasticity from cerebral palsy. In most published studies, the dose of BTX-A is 10 U/kg up to a maximal dose of 300 U involving 30 trigone-sparing injections of 10 U/kg/ml in the detrusor. BTX-A appears to reach efficacy levels at 2 weeks and maximum effects within 4–6 weeks. Duration of the BTX-A effect ranges from 3 to 8 months depending on short-term versus long-term repeated injections.[13] Clarification, optimization, and standardization of follow-up of BTX-A in the treatment of NBD remains open for future clinical trials. Furthermore, collecting detailed safety data will be necessary to support the reported excellent tolerability of BTX-A.

Antibiotics

Antibiotic administration in children with NBD requires special consideration because CIC is commonly relied on for bladder emptying and the resultant frequent colonization of

the bladder with bacterial flora is quite innocuous. The incidence of asymptomatic bacteriuria in children who perform CIC ranges from 42% to 76%.[14,15] The incidence of bacteriuria is higher still when correlated with the presence of periurethral bacterial flora—93% when *Escherichia coli* is present on the periurethral skin.[16] Studies have shown that expression of specific bacterial virulence factors do not reliably predict infection in children with NBD[17,18] and antibiotic prophylaxis does not significantly alter the rate of symptomatic UTIs in comparison with no antibiotic prophylaxis.[17]

One concern when using continuous antibiotics is more virulent organisms may be selected that result in development of complicated UTIs. Two randomized, placebo-controlled studies have examined the efficacy of antibiotic prophylaxis in reducing the incidence of symptomatic UTIs in children who perform CIC for management of their NBD.[19,20] Neither study found any difference in the rate of symptomatic or total UTIs using trimethoprim/sulfamethoxazole prophylaxis compared to placebo or nitrofurantoin prophylaxis versus placebo. Antibiotic prophylaxis did result in the selection of more virulent bacterial isolates such as *Klebsiella* and *Pseudomonas*.[20]

In the setting of recurrent UTIs, intravesical antibiotic instillations have been used successfully to address UTIs in children who perform CIC.[21–23] Most report use gentamycin instillation with good safety and few adverse events. Unfortunately, selection bias, study design, and data are limited, which prevents drawing any definitive conclusion with regard to efficacy of intravesical antibiotic treatment.

In summary, there appears to be level-1 evidence as demonstrated by several controlled and placebo-controlled trials that there is no medical benefit to using antibiotic prophylaxis in children with NBD who perform CIC. Additionally, antibiotic prophylaxis appears to alter the normal skin and bladder flora; this finding may lead to potential complications related to antibiotic usage.

CATHETERS

As mentioned previously, CIC has had a profound impact on the management of NBD in children. Given the high prevalence of latex sensitivity in the NBD population, non-latex catheters are employed exclusively. There have been a wide variety of material-modifications to catheters that facilitate CIC but these are typically employed in individual cases.

Hydrophilic-coated catheters are helpful in the setting of painful catheterization or in the presence of urethral strictures and/or false passages in boys. In two recent randomized trials comparing hydrophilic-coated catheters to uncoated catheters, there was a reduction in microscopic hematuria and better overall satisfaction with the hydrophilic coated catheters.[24,25] The drawbacks of these hydrophilic catheters include: single use, more expense, and lack of proven, efficacious benefit over standard catheters. Other useful modifications include a coudé tip catheter that allows passage over a high bladder neck and pre-packaged, lubricated catheters for simplicity of use.

One concern expressed by families and primary care providers is the risk of re-using the same catheter for CIC and the incidence of bacteriuria. This concern was addressed in a small, prospective, randomized, crossover trial comparing new, sterile catheters versus reusing clean catheters for CIC.[15] There was no difference in the frequency of bacteriuria in patients with NBD on CIC with a 73% incidence of bacteriuria in the new, sterile catheter cohort and a 76% incidence in the clean catheter group. A Cochrane review examined sterile versus clean catheterization technique, coated (pre-lubricated) versus uncoated (separate lubricant) catheters, single (sterile) or multiple use (clean) catheters, self-catheterization versus catheterization by others, and any other strategies designed to reduce UTIs with respect to incidence of symptomatic UTI, hematuria, other infections, and user preference, in adults and children using CIC.[26] This review found a lack of evidence to state that the incidence of UTI is affected by using sterile or clean technique, coated or uncoated catheters, single (sterile) or multiple use (clean) catheters, self-catheterization or catheterization by others, or by any other strategy. Additionally, current research evidence is weak and design flaws are significant. Therefore, it is not possible to state that one catheter type, technique, or strategy is better than another. In summary, modification of catheters and catheter regimens should be made on an individual basis for children with NBD.

NEUROMODULATION TREATMENTS

Intravesical Electrical Stimulation of the Bladder

Intravesical electrical stimulation of the NBD is labor intensive and controversial. In a large single, institutional 22-year experience, there was favorable results with a 20% or greater increase in bladder capacity after treatment and attainment of safe detrusor pressures <40 cm H_2O.[27] In a multi-institutional report, the efficacy of intravesical electrical stimulation was less impressive.[28] Finally, in the only reported randomized, placebo-controlled trial, there was no efficacy demonstrated in children with NBD.[29]

Sacral Nerve Stimulation

Sacral nerve stimulation has primarily been reported in the treatment of patients with a non-neuropathic bladder. The procedure is FDA approved and indicated in individuals with urinary retention and/or symptoms of DO who have failed or could not tolerate more conservative treatments. The safety and effectiveness have not been established for children <16 years of age or for patients with neurological disease. The only report of sacral nerve modulation conducted in children with NBD had mixed results and the study design was limited.[30] Comparison of urodynamic variables disclosed no significant statistical difference except that functional bladder capacity was better in the oxybutynin group and leak point pressure was better in the sacral neuromodulation group. Evaluation of inter-individual variations in the sacral neuromodulation group revealed significant improvement in compliance and functional bladder capacity at 6 and 9 months but not at 12 months. In summary, sacral nerve stimulation is considered investigational at this time.

Transcutaneous Neuromodulation

There is little written about transcutaneous neuromodulation in the treatment of children with NBD. A recent report evaluated the efficacy of percutaneous tibial nerve stimulation (PTNS) for different types of lower urinary tract dysfunction in children.[31] A majority of the 44 patients were non-neurogenic but 7 had NBD. All were resistant to conventional therapy and underwent PTNS weekly for 12 weeks. Objective symptomatic improvement was significantly greater in non-neurogenic than in neurogenic cases (78% vs. 14%, $P < 0.02$); it was noteworthy that results in 5 of 7 NBD (71%) were unsatisfactory as expressed by parents after the first six-weekly sessions.

Biofeedback

The role of biofeedback has been explored extensively in children with functional disorders but no significant studies of biofeedback have been reported in children with NBD.

SURGICAL INTERVENTION

NBD encompasses a wide variety of presentations depending on the degree of lower urinary tract involvement and the interplay between bladder storage capability and sphincter function. No specific universal surgical procedure is suitable for everyone. Surgical management has to be tailored to each individual case, based on careful consideration of urodynamic findings, medical history, age, and presence of other disability. The mainstay of current NBD management is non-surgical with anticholinergics and CIC in the majority of children. A small subgroup that fails to respond to treatment may need to undergo surgery.

ATTAINING SAFE BLADDER STORAGE PRESSURE AND CAPACITY

Urethral Dilatation

This procedure aims at lowering the pop-off pressure of a hostile neuropathic bladder by lowering DLPP to below 40 cm. H_2O.[32] It has been employed primarily in younger age groups. Dilatation is carried out under general anesthesia using sounds up to 36 Fr in infants and Hegar dilators in those older than 6–8 years.[33] Technically, it is best suited for females. In males, dilating the external sphincter using a balloon or by sounds is feasible via a perineostomy.[34]

Several studies have proven urethral dilatation effective in lowering DLPP to safe limits and improving bladder capacity and compliance.[33–36] With careful patient selection, durable positive outcomes can be expected in about 70%.[33,35] A major concern raised in connection with this procedure has been the potential risk of causing or aggravating urinary incontinence; however, these concerns have proven unfounded.[33]

Vesicostomy

Vesicostomy effectively reduces bladder storage pressures to safe levels in NBD. This procedure has been useful in infants. Additionally, it can be considered if parents are noncompliant with CIC or where urethral catheterization is difficult. Vesicostomy is easily performed. It has been shown to effectively reverse hydronephrosis, VUR, and to decrease the incidence of UTIs.[37,38] Complications are minor and readily managed; they include bladder mucosal prolapse, stomal stenosis, stone formation, and peri-stomal dermatitis. Although intended as a temporizing procedure in the majority, stomas can be left functional as a permanent solution in children who lack the mental acuity or social support to ensure reliable compliance with CIC.[39] Its greatest drawback is the inability to easily fit and maintain a collecting appliance over the stoma in older individuals.

BLADDER AUGMENTATION

Enterocystoplasty

Augmenting the bladder using segments of small intestine, colon, or gastric patches represents the definitive method of creating a safe, low-pressure capacious organ for storage, albeit at the cost of incurring a multitude of short- and long-term complications.

Reported outcomes of enterocystoplasty have generally been favorable with respect to increasing bladder capacity, decreasing storage pressures, and improving upper urinary tract drainage.[40,41] Up to 90% achieve socially acceptable urinary continence with or without an additional bladder outlet procedure.[40,42,43] Notwithstanding, enterocystoplasty has potential serious implications, especially for children with an anticipated longer residual life span than adults because enteric tissue, although incorporated into the bladder, retains its absorptive and secretory properties. Mucus formation is especially bothersome as it tends to block catheters and requires regular irrigation, and may predispose to stone formation.[44] The hematuria dysuria syndrome is a recognized entity following gastric augmentation, which is believed to be caused by acidic secretions from gastric mucosa.[45] Additionally, reconstruction entails intraperitoneal surgery with its risks of subsequent adhesions, bowel obstruction and the need for lengthy postoperative hospital stays. Reports of surgical complications in up to 40% of patients are not unusual.[41,44,46,47] Another long-term complication is stone formation (approximately 15% of augmented bladders).[44,46] Finally, in a recent review of 500 children undergoing enterocystoplasty, a failure rate of 9.4% was reported.[47]

Long-term metabolic complications are also common, and are particularly worrisome in children as these may interfere with growth and development. Hyperchloremic metabolic acidosis is the most common disturbance encountered, and may lead to demineralization of bone and stunted linear growth.[48,49] Bowel resection may lead to malabsorption of vitamin B_{12} and chronic diarrhea, which may also impair normal development.[49] Finally, there is the potential for malignant transformation in 0.6%, which is a serious and often fatal consequence of enterocystoplasty. Therefore, these patients need to be followed indefinitely with regular cytology and endoscopy, starting 5–10 years after augmentation,[46,47] although efficacy of these surveillance parameters has yet to be proven.[50,51]

Autoaugmentation

This technique involves partial detrusorectomy or detrusor myotomy, leaving the underlying mucosa intact and bulging, as a wide mouthed diverticulum, leading to an increase in bladder capacity and compliance. The technique is appealing because it precludes the use of intestinal tissue.[52]

Conflicting outcomes and modest success rates in children with NBD has hampered widespread application of autoaugmentation. There have been discrepancies between studies, but it remains that autoaugmentation is a safe simple procedure with low morbidity that may avert the need for formal enterocystoplasty in a select group of children.[53,54]

INCREASING BLADDER OUTLET RESISTANCE

Fascial Sling

The technique involves suspension of the bladder neck with an autologous fascial strip or artificial material secured to the rectus fascia or the pubic symphysis. It is believed the mechanism of action involves co-aptation of the bladder neck due to traction, and/or elevation of the urethra to an intra-abdominal position, which increases tension on the bladder neck with abdominal straining. In a review regarding slings in children with NBD, Kryger et al.[55] found continence rates ranged

between 40% and 100%. It is difficult to compare results as techniques and concomitant augmentation rates vary between studies. Complication rates are modest and include difficult catheterization and rectal injury.[55]

Artificial Urinary Sphincters

In 1973 Scott introduced the artificial urinary sphincter (AUS).[56] Reported continence rates after AUS implantation have been high with different series reporting success in 70% to 85%.[57–59] Many surgeons are reluctant to implant an AUS as it consigns patients to further revision surgery, and the potential risk of deterioration in bladder function and a concomitant deleterious effect on upper urinary tract drainage.[55] However, with improved durability of newer models that have an average life span of about 8 years, revision rates have become less of an issue.[58] The ideal patients for AUS implantation are post-pubertal males or females, who can void volitionally and empty the bladder completely.[57] It is important to recognize that CIC is feasible in patients with an AUS.

Complications specific to AUS include altered bladder compliance, and worsening DO. This has necessitated bladder augmentation, in approximately 50%.[58,59] Removal of an AUS due to erosion, infection, or mechanical malfunction occurs in at least 20%.[57,59] Revision rates for wear and tear have steadily been decreasing with ongoing refinements in AUS; the most recent long-term experience with the AMS 800 AUS has a revision rate of 0.03 revisions per patient-year.[59]

Bladder Neck Reconstruction

The optimal bladder neck procedure should increase bladder outlet resistance at minimal cost of decreasing bladder capacity, maintain easy catheterization and still allow some leakage at high pressure in order to protect the upper urinary tract. Different operative techniques with the aforementioned aims have been used with varying outcomes. The Young–Dees–Leadbetter bladder neck repair has been employed primarily in treating incontinence associated with exstrophy–epispadias complex yielding continence rates of about 70% to 80% but it seems to have little success in children with NBD.

TREATMENT OF THE NEUROGENIC BOWEL FUNCTION

The overall aim of treatment is to obtain regular bowel emptying, continence, and independence by establishing a bowel management program tailored to meet the needs of each child. Naturally, a normal healthy *diet* is recommended for these children. The diet should consist of small-portioned fiber foods and sufficient water intake to keep a good fluid balance.

Initially, the child will need *laxatives* and should be maintained on a laxative regimen until bowel regularity is obtained. As behavior modifications begin, it is important to encourage normal toilet training. Often *rectal suppositories* are introduced to enable the child to defecate once a day at a given time; however, some parents and children are comfortable using *digital stimulation* instead. Children with a weak anal sphincter may require a balloon catheter for instillation of enemas. A cone enema, or a colostomy irrigation set may be used as a continence enema. Because proper volume and retention are difficult as a result of poor sphincter tone, the balloon helps to seal the lower rectum as the enemas solution (often tap-water) is administered.

Transanal irrigation is the most important treatment for NBD today. Regular irrigation reduces the risk of fecal leakage and has a positive effect on sphincter tone and rectal volume. The majority of children need help from parents until they are older.

Children under five will have difficulty using transanal colonic irrigation because the procedure requires a cooperative child. In some instances, the retrograde transanal irrigation is too difficult and may not sufficiently stimulate the distal colon to empty, restricting the child from achieving independence. In the 1980s, the *MACE* (Malone Antegrade Continence Enema) procedure was introduced. It involves reimplanting the appendix into the cecum in a non-refluxing manner bringing the opposite end to the abdominal wall as a continent catheterizable stoma, so the channel can serve as an antegrade colonic washout. If the appendix is not available, a catheteriable channel can be fashioned from other parts of the intestine tract or the ureter. Tap water was used initially as an irrigant with good results,[60] but saline, Golytely, or macrogol 3350 has been shown to be effective and safe as well.[61] In a recent review of MACE management, 92% were using saline or Golytely irrigations and 35% required additives (biscodyl, glycerin, etc.) to achieve acceptable continence.[62]

Studies in adults suffering from neurogenic bowel dysfunction have shown good results with *transrectal anocutaneous electric stimulation* as well as *sacral nerve stimulation*. Studies on children are too few to provide meaningful recommendations.

The *anal plug* is of benefit in a majority of patients using it.[63] The plug is recommended in certain situations to avoid fecal incontinence, for example, while swimming, it will last for 12 hr and it is tolerable in some children.

In conclusion, proactive treatment of patients with spina bifida has been shown to be effective in reducing the need for augmentation cystoplasty and in reducing the development of ESRD by minimizing the effects of high-pressure reflux on the upper urinary tract. Postponing treatment until upper urinary tract dilation is seen on ultrasound or until symptomatic pyelonephritis occurs is not acceptable in modern times.

Bowel management in children with neurologic conditions can be challenging. There is a lack of research into efficacious management and often the clinician has to rely on clinical experience instead of randomized controlled trials. It is very important to realize that children and adolescents who experience bowel dysfunction require patience and sensitive support from their health care providers.

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REFERENCES

1. Andersson KE, Chapple CR, Cardozo L, et al. Pharmacological treatment of overactive bladder: Report from the International Consultation on Incontinence. Curr Opin Urol 2009;19:380–4.
2. Abrams P, Andersson KE, Buccafusco JJ, et al. Muscarinic receptors: Their distribution and function in body systems, and the implications for treating overactive bladder. Br J Pharmacol 2006;148:565–78.
3. Eglen RM, Choppin A, Watson N. Therapeutic opportunities from muscarinic receptor research. Trends Pharmacol Sci 2001;22:409–14.
4. Hegde SS, Eglen RM. Muscarinic receptor subtypes modulating smooth muscle contractility in the urinary bladder. Life Sci 1999;64:419–28.
5. Giramonti KM, Kogan BA, Halpern LF. The effects of anticholinergic drugs on attention span and short-term memory skills in children. Neurourol Urodyn 2008;27:315–8.
6. Buyse G, Waldeck K, Verpoorten C, et al. Intravesical oxybutynin for neurogenic bladder dysfunction: Less systemic side effects due to reduced first pass metabolism. J Urol 1998;160:892–6.
7. Guerra LA, Moher D, Sampson M, et al. Intravesical oxybutynin for children with poorly compliant neurogenic bladder: A systematic review. J Urol 2008;180:1091–7.

8. Franco I, Horowitz M, Grady R, et al. Efficacy and safety of oxybutynin in children with detrusor hyperreflexia secondary to neurogenic bladder dysfunction. J Urol 2005;173:221–5.
9. Buyse G, Verpoorten C, Vereecken R, et al. Intravesical application of a stable oxybutynin solution improves therapeutic compliance and acceptance in children with neurogenic bladder dysfunction. J Urol 1998;160:1084–7.
10. Cartwright PC, Coplen DE, Kogan BA, et al. Efficacy and safety of transdermal and oral oxybutynin in children with neurogenic detrusor overactivity. J Urol 2009;182:1548–54.
11. Apostolidis A, Dasgupta P, Fowler CJ. Proposed mechanism for the efficacy of injected botulinum toxin in the treatment of human detrusor overactivity. Eur Urol 2006;49:644–50.
12. Chapple C, Patel A. Botulinum toxin—New mechanisms, new therapeutic directions? Eur Urol 2006;49:606–8.
13. Game X, Mouracade P, Chartier-Kastler E, et al. Botulinum toxin-A (Botox) intradetrusor injections in children with neurogenic detrusor overactivity/neurogenic overactive bladder: A systematic literature review. J Pediatr Urol 2009;5:156–64.
14. Joseph DB, Bauer SB, Colodny AH, et al. Clean, intermittent catheterization of infants with neurogenic bladder. Pediatrics 1989;84:78–82.
15. Schlager TA, Clark M, Anderson S. Effect of a single-use sterile catheter for each void on the frequency of bacteriuria in children with neurogenic bladder on intermittent catheterization for bladder emptying. Pediatrics 2001;108:E71.
16. Schlager TA, Hendley JO, Wilson RA, et al. Correlation of periurethral bacterial flora with bacteriuria and urinary tract infection in children with neurogenic bladder receiving intermittent catheterization. Clin Infect Dis 1999; 28:346–50.
17. Guidoni EB, Dalpra VA, Figueiredo PM, et al. E. coli virulence factors in children with neurogenic bladder associated with bacteriuria. Pediatr Nephrol 2006;21:376–81.
18. Schlager TA, Whittam TS, Hendley JO, et al. Expression of virulence factors among *Escherichia coli* isolated from the periurethra and urine of children with neurogenic bladder on intermittent catheterization. Pediatr Infect Dis J 2000;19:37–41.
19. Mohler JL, Cowen DL, Flanigan RC. Suppression and treatment of urinary tract infection in patients with an intermittently catheterized neurogenic bladder. J Urol 1987;138:336–40.
20. Schlager TA, Anderson S, Trudell J, et al. Nitrofurantoin prophylaxis for bacteriuria and urinary tract infection in children with neurogenic bladder on intermittent catheterization. J Pediatr 1998;132:704–8.
21. Carapetis JR, Jaquiery AL, Buttery JP, et al. Randomized, controlled trial comparing once daily and three times daily gentamicin in children with urinary tract infections. Pediatr Infect Dis J 2001;20:240–6.
22. Defoor W, Ferguson D, Mashni S, et al. Safety of gentamicin bladder irrigations in complex urological cases. J Urol 2006;175:1861–4.
23. Wan J, Kozminski M, Wang SC, et al. Intravesical instillation of gentamicin sulfate: In vitro, rat, canine, and human studies. Urology 1994;43:531–6.
24. Stensballe J, Looms D, Nielsen PN, et al. Hydrophilic-coated catheters for intermittent catheterisation reduce urethral micro trauma: A prospective, randomised, participant-blinded, crossover study of three different types of catheters. Eur Urol 2005;48:978–83.
25. Vapnek JM, Maynard FM, Kim J. A prospective randomized trial of the LoFric hydrophilic coated catheter versus conventional plastic catheter for clean intermittent catheterization. J Urol 2003;169:994.
26. Moore KN, Fader M, Getliffe K. Long-term bladder management by intermittent catheterisation in adults and children. Cochrane Database Syst Rev 2007;2:CD006008.
27. Hagerty JA, Richards I, Kaplan WE. Intravesical electrotherapy for neurogenic bladder dysfunction: A 22-year experience. J Urol 2007;178:1680–3.
28. Cheng EY, Richards I, Balcom A, et al. Bladder stimulation therapy improves bladder compliance: Results from a multi-institutional trial. J Urol 1996;156: 761–4.
29. Boone TB, Roehrborn CG, Hurt G. Transurethral intravesical electrotherapy for neurogenic bladder dysfunction in children with myelodysplasia: A prospective, randomized clinical trial. J Urol 1992;148:550–4.
30. Guys JM, Haddad M, Planche D, et al. Sacral neuromodulation for neurogenic bladder dysfunction in children. J Urol 2004;172:1673–6.
31. Capitanucci ML, Camanni D, Demelas F, et al. Long-term efficacy of percutaneous tibial nerve stimulation for different types of lower urinary tract dysfunction in children. J Urol 2009;182:2056–61.
32. Johnston JH, Kathel BL. The obstructed neurogenic bladder in the newborn. Br J Urol 1971;43:206.
33. Park JM, McGuire EJ, Koo HP, et al. External urethral sphincter dilation for the management of high risk myelomeningocele: 15-year experience. J Urol 2001;165:2383–8.
34. Miller DC, Bloom DA, McGuire EJ, et al. Temporary perineal urethrostomy for external sphincter dilation in a male patient with high risk myelomeningocele. J Urol 2003;170:1606.
35. Kiddoo DA, Canning DA, Snyder HM III, et al. Urethral dilation as treatment for neurogenic bladder. J Urol 2006;176:1831–34.
36. Wang SC, McGuire EJ, Bloom DA. Urethral dilation in the management of urological complications of myelodysplasia. J Urol 1989;142:1054–55.
37. Lee MW, Greenfield SP. Intractable high-pressure bladder in female infants with spina bifida: Clinical characteristics and use of vesicostomy. Urology 2005;65:568–71.
38. Morrisroe SN, O'Connor RC, Nanigian DK, et al. Vesicostomy revisited: The best treatment for the hostile bladder in myelodysplastic children? BJU Int 2005;96:397–400.
39. Hutcheson JC, Cooper CS, Canning DA, et al. The use of vesicostomy as permanent urinary diversion in the child with myelomeningocele. J Urol 2001;166:2351–3.
40. Nomura S, Ishido T, Tanaka K, et al. Augmentation ileocystoplasty in patients with neurogenic bladder due to spinal cord injury or spina bifida. Spinal Cord 2002;40:30–3.
41. Herschorn S, Hewitt RJ. Patient perspective of long-term outcome of augmentation cystoplasty for neurogenic bladder. Urology 1998;52:672–8.
42. Medel R, Ruarte AC, Herrera M, et al. Urinary continence outcome after augmentation ileocystoplasty as a single surgical procedure in patients with myelodysplasia. J Urol 2002;168:1849–52.
43. Singh G, Thomas DG. Enterocystoplasty in the neuropathic bladder. Neurourol Urodyn 1995;14:5–10.
44. Scales CD, Jr., Wiener JS. Evaluating outcomes of enterocystoplasty in patients with spina bifida: A review of the literature. J Urol 2008;180:2323.
45. Nguyen DH, Bain MA, Salmonson KL, et al. The syndrome of dysuria and hematuria in pediatric urinary reconstruction with stomach. J Urol 1993; 150:707–9.
46. Metcalfe PD, Cain MP, Kaefer M, et al. What is the need for additional bladder surgery after bladder augmentation in childhood? J Urol 2006;176:1801.
47. Metcalfe PD, Rink RC. Bladder augmentation: Complications in the pediatric population. Curr Urol Rep 2007;8:152–6.
48. Gros DA, Dodson JL, Lopatin UA, et al. Decreased linear growth associated with intestinal bladder augmentation in children with bladder exstrophy. J Urol 2000;164:917–20.
49. Hensle TW, Gilbert SM. A review of metabolic consequences and long-term complications of enterocystoplasty in children. Curr Urol Rep 2007;8:157–62.
50. Greenwell HR, Nethercliffe JM, Freeman A, et al. Routine surveillance cystoscopy for patients with augmentation and substitute cystoplasty for benign urological conditions: Is it necessary? BJU Int 2009;104:392–5.
51. Kokorowski PJ, Routh JR, Borer JG, et al. Screening for malignancy after augmentation cystoplasty in children with spina bifida: A decision analysis. J Urol 2011;186:37–43.
52. Cartwright PC, Snow BW. Bladder autoaugmentation: Early clinical experience. J Urol 1989;142:505–8.
53. Dik P, Tsachouridis GD, Klijn AJ, et al. Detrusorectomy for neuropathic bladder in patients with spinal dysraphism. J Urol 2003;170:1351–4.
54. Stothers L, Johnson H, Arnold W, et al. Bladder autoaugmentation by vesicomyotomy in the pediatric neurogenic bladder. Urology 1994;44:110–3.
55. Kryger JV, Gonzalez R, Barthold JS. Surgical management of urinary incontinence in children with neurogenic sphincteric incompetence. J Urol 2000; 163:256–63.
56. Scott FB, Bradley WE, Timm GW. Treatment of urinary incontinence by implantable prosthetic sphincter. Urology 1973;1:252–9.
57. Catti M, Lortat-Jacob S, Morineau M, et al. Artificial urinary sphincter in children—Voiding or emptying? An evaluation of functional results in 44 patients. J Urol 2008;180:690–3.
58. Gonzalez R, Merino FG, Vaughn M. Long-term results of the artificial urinary sphincter in male patients with neurogenic bladder. J Urol 1995; 154:769–70.
59. Kryger JV, Spencer BJ, Fleming P, et al. The outcome of artificial urinary sphincter placement after a mean 15-year follow-up in a paediatric population. BJU Int 1999;83:1026–31.
60. Mattsson S, Gladh G. Tap-water enema for children with myelomeningocele and neurogenic bowel dysfunction Acta Paediatr 2006;95:369–74.
61. Kokoska ER, Keller MS, Weber TR. Outcome of the antegrade colonic enema procedure in children with chronic constipation. Am J Surg 2001;182:625–9.
62. Siddiqui A, Fishman SJ, Bauer SB, et al. Long-term follow-up of patients after antegrade continence enema procedure. J Pediatr Gastroenterol Nutrit 2011;52:574–80.
63. Bond C, Youngson G, MacPherson I, et al. Anal plugs for the management of fecal incontinence in children and adults: A randomized control trial. J Clin Gastroenterol 2007;41:45–53.