W34: Evaluation and management of neurogenic bladder and bowel in children and young adults .

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21 October 2014 14:00 - 18:00

Start	End	Topic	Speakers
14:00	14:05	Introduction	• Giovanni Mosiello
14:05	14:25	Causes of Neurogenic Bladder and Bowel Dysfunctions (NBBD) in childhood	• Giovanni Mosiello
14:25	14:45	Initial evaluation and follow-up of NBBD in childhood	• Eliane Fonseca
14:45	15:10	Conservative Management	• Stuart Bauer
15:10	15:30	Discussion	All
15:30	16:00	Break	None
16:00	16:20	Botulinum Toxin and Neuromodulation in children and young adults with NBBD	• Enrico Finazzi-Agrò
16:20	16:35	Surgical Treatment of NBBD	• Giovanni Mosiello
16:35	16:55	Upper Urinary tract and renal function follow-up	• Rejane Bernardes
16:55	17:10	NBBD and adolescents	• Kwang Myung Kim
17:10	17:25	Fertility and sexuality	• Enrico Finazzi-Agrò
17:25	17:40	Questions	All
17:40	17:55	Cases presentation	All
17:55	18:00	Conclusion and Take Home messages	• Giovanni Mosiello

Aims of course/workshop

Children with neurogenic bladder and bowel dysfunctions (NBBD) related to a congenital or acquired condition require lifelong evaluation and treatment, especially for continence and preservation of upper urinary tract. Different treatment options can be considered: rehabilitation, pharmacotherapy, endoscopic procedures and surgery reconstructions. A correct choice must be in one hand patient related always preserving the upper urinary tract and increasing quality of life (urinary and faecal continence). This workshop would like to offer a critical discussion on the diagnosis, treatment and follow-up of NBBD from childhood to adults, considering different worldwide scenarios and EBM results in order to increase knowledge of the participants.

INTRODUCTION

Neuropathic bladder dysfunction (NBD) in children is an ever-evolving condition. This condition contributes to various forms of lower urinary tract dysfunction which may lead to incontinence, urinary tract infections (UTIs), vesicoureteral reflux (VUR), and renal scarring. Conservative treatment is nowadays preferred but surgery may be required. Neurogenic Detrusor Sphincter Dysfunction (NDSD), if not managed properly, can cause renal failure, requiring dialysis or transplantation.

Management of NDSD in children has undergone major changes over the years. In the mid 1950's, there were few insights and minimal alternatives to being in diapers or wearing an appliance over an abdominal wall stoma. Initially long term renal preservation was the only aim of therapy and early diversion had the best long term results for preserving renal function.

During time we have learned a great deal about the pathophysiology, pathogenesis and treatment of these disorders and an evidenced based ways to manage.

First of all, the introduction of clean (self) intermittent catheterization revolutionized themanagement of children with NBD. It, not only made conservative management a very successful treatment option, but also made surgical creation of continent reservoirs a very effective alternative with a good quality of life.

Myelodysplasia, the most common cause of NBD in children, is the best example to explain how the recognition of 'at risk' patterns and CIC had dramatically changed the outcome. About 15 % of neonates with myelodysplasia have no signs of lower urinary tract dysfunction (LUTD) when initially studied. Nearly 60 % of them may develop upper tract deterioration due to increased detrusor filling pressures and infections, with or without reflux . Children do not develop upper tract deterioration when managed early with CIC and antimuscarinic medication .For Neurogenic

Bladder Dysfunction, urodynamic studies allow to understand the nature and severity of the problems and administer management in a rational manner accordingto the functional characteristics of the bladder. The main goals of treatment remain the prevention of urinary tract deterioration and the achievement of continence.

Children with neurogenic bladder and bowel dysfunctions (NBBD) require lifelong evaluation and treatment, especially for continence. Different treatment options in order to ameliorate continence can be considered lifelong including rehabilitation , pharmacotherapy, endoscopic procedures and surgery reconstructions. For this reason is very important for all health care professionals involved in the treatment of these patients to know about the effects in adult life of the procedure performed in childhood, in order to define a correct timing of management, discussing how the concerns for a correct choice in the management of the single patient are related to individual condition of the single person. Actually with the improvement in care, children with spina bifida (SB), that is the most common cause of NBBD in pediatrics, survive into adulthood, and a correct treatment choice permits to increase quality of life (QOL), preserve renal function and to avoid procedure that can impair in adult life aspects as fertility and pregnancy.

DEFINITION OF NEUROGENIC BLADDER

Neurogenic detrusor sphincter dysfunction (NDSD) can develop as a result of a lesion at any level in the nervous system, including the cerebral cortex, spinal cord or the peripheral nervous system.

CAUSES

The most common cause of NBD in children, and the most detrimental is **Neurospinal Dysraphism.** This condition presents with various patterns of detrusor-sphincter dysfunction within a wide range of severity. Traumatic and neoplastic spinal lesions of the cord are less frequent in children.

Spinal Dysraphism

The failure of mesodermal in-growth over the developing spinal canal results in an open lesion most commonly seen in the lumbosacral area. The degree of this closure deficiency contributes to a variable presentation of neural injury with varying degrees of LUTD and lower extremity problems.

Developmental anomalies that result from defects in neural tube closure are generically termed as **Myelodysplasia.** This term includes a group of lesions like spina bifida occulta, meningocele, lipomyelomeningocele, or myelomeningocele, which is the by far the most common defect. The neurologic lesions produced by myelodysplasia are variable contingent on the neural elements that protrude within the meningocele sac. The bony vertebral level correlates poorly with the neurologic lesions produced.

The deterioration is an acquired phenomenon secondary to the development or progression of various LUT hostility factors such as neurogenic DO, poor bladder compliance, detrusor-sphincter dyssynergia and/or high LPP from denervation fibrosis**.** Urodynamic studies corroborated their reliability by reporting that the prediction of upper urinary tract deterioration on the basis of urodynamic testing is possible with 90% accuracy.

In **Closed Myelodysplasia** the lesions are not overt and often with no obvious signs of neurologic lesion (**Occult Dysraphysm**). The diagnosis of this condition has increased since the advent of spinal ultrasonography and magnetic resonance imaging. In nearly 90% of patients, a cutaneous abnormality overlies the lower spine and this condition can easily be suspected by simple inspection of the lower back. These cutaneous lesions can vary from a dimple or a skin tag to a tuft of hair, a dermal vascular malformation, or an obvious subdermal lipoma. Back pain and an absence of perineal sensation are common symptoms in older children. Incidence of abnormal lower urinary tract function in patients with spina bifida occulta is as high as 40%.

Sacral agenesis

It is a rare congenital anomaly that involves absence of part or all of one or more sacral vertebrae. Perineal sensation is usually intact and lower extremity function is usually normal and the diagnosis is made when a flattened buttock and a short gluteal cleft is seen on physical examination. This lesion may produce variable degrees and patterns of LUTD.

The lesion that can be missed in infancy because of its subtle clinical manifestations, with generally no loss of lower extremity motor and sensory function, and the non-progressive nature of its pathophysiology. Urinary and/or foecal incontinence usually manifest themselves at an older age when the child fails to toilet train on time. A careful physical examination noting flattened buttocks and a short gluteal crease is pathognomonic for the diagnosis: 30 and 40% of these patients have an upper motor neuron type lesion with DO and an intact but dyssynergic sphincter, while 25 to 50% have signs of a lower motor neuron deficit with acontractile detrusor and denervation in the sphincter, and 15 to 20% have normal LUT function.

Imperforate anus

This rare anomaly with a closed rectum may present with accompanying spinal cord pathology.

The timing of investigational studies is critical. Spinal ultrasound in the newborn period are needed due to the likelihood of an intraspinal abnormality, respectively. The incidence of NBD approaches 40% but varies from 10% to 50% depending on the height of the rectal lesion (positive correlation) and how thorough the investigation. If a suspected neuropathic bladder is confirmed by UDS then spinal MRI is indicated. UDS determines the presence of DO, the degree of denervation in the external urethral and rectal sphincters and DSD in the first few months of life, after an initial colostomy or definitive pull-through surgery is performed, serving as a baseline for patients with an occult dysraphism .

Persistent urinary and bowel incontinence suggest unrecognized NBD from an occult spinal dyraphism. Some infants with normal lower urinary and bowel function in the first year of life suffer from tethering of the spinal cord with increasing age. This leads to permanent damage if not detected early. Thus, baseline and surveillance UDS help determine the current or changing neurologic lesion that warrants MRI imaging and possibly spinal cord untethering, if an operable lesion is found. It is

extremely rare for these children to exhibit lower extremity neurologic impairment or a cutaneous manifestation of this associated condition.

Spinal Cord Injury

SCL in pediatrics are not only related to congenital lesions, because we have to consider spinal cord injury (SCI) can be related to car accident, sports trauma, surgery and medical treatment. SCI in pediatric received scant attention due to its rarity. In Europe the incidence is documented in Portugal and Sweden (27 children/million children/year and 4.6 children/million children/year respectively). For the other countries, the estimated incidence of pedSCI varied from 0.9-21.2 children/ million children/year in the ages 0-14 years. The management differs between the countries depending on the age of the child and the local organization of health care. Knowledge of incidence and etiology of pedSCI is important in Ped SCI is unique with a high percentage of highcervical spinal cord injuries , very often associated to head trauma or politrauma: . Particularly unique to children is the lap belt injury. Theoretically the neuro-urological approach is the same in children with spinal cord injury (SCI) and congenital lesions as spina bifida (SB), because urological goals are the same: to establish a satisfactory bladder emptying, to maintaining a safe bladder storage pressure, avoiding infections, in order to prevent upper urinary tract deterioration, with the final goal to reach continence. The importance of neurogenic bladder dysfunction (NBD) has been well described, renal damage remains a real risk and children require a careful evaluation and follow-up because NBD change during time. T

According to the nature of the neurological deficit, the bladder and sphincter may be in either an overactive or inactive state: the bladder may be overactive with increased contractions, and low capacity and compliance, or inactive with no

effective contractions; the outlet (urethra and sphincter) may be overactive causing l obstruction, or paralysed with no resistance to urinary flow; these conditions may present in different combinations t.

The scarcity and variability of spinal cord injuries in children makes it difficult to propose any one treatment program unless the specific type of LUT function is known on the basis of urodynamic testing. Even if the individual regains the ability to void spontaneously and empty his/her bladder, it is imperative to know the detrusor filling and emptying (detrusor) pressures, in order to determine the potential risk for VUR and hydroureteronephrosis. Effective voiding with pressures below 40 cm H_2O in the absence of detrusor-sphincter dyssynergia ensures a stable upper urinary tract. A cauda equina injury usually leads to a lower motor neuron type of deficit of the striated sphincter that may not require any treatment to prevent upper tract damage because the bladder empties readily at low pressure, but it probably necessitates medical and/or surgical therapy to achieve continence. Urodynamic monitoring has demonstrated to be relevant in the follow up and prevention of upper tract deterioration in a retrospective cohort study. Further urodynamic follow up is 'standard' alike in adult patients.

Cerebral palsy

Patients may also present with varying degrees of LUTD usually in the form of overactive detrusor and wetting. The vast majority of the children with cerebral palsy tend to toilet train completely, but often at an age that is later than expected for normal individuals.It has been suggested on the basis of expert opinion that cystometry and sphincter EMG are to be considered only when frequent toileting or anticholinergic therapy fails to control incontinent episodes, the child develops urinary infection from ineffective voiding, or when ultrasonography reveals hydronephrosis. A conservative approach is the choice in most of the cases.

Tumors (either primary or metastatic)

Tumors of the central nervous system in children are rare and the symptom complexes; they produce quite varied; the workup should be individualized and tailored to the specific location of the disease. LUT dysfunction occurs after sacro-coccygeal teratoma resection, and urodynamic evaluation is necessary during follow-up of those children. A recent study showed that children with central nervous tumors can have urodynamic abnormalities, whether the tumor is in the

spinal cord or not. A child with a CNS tumor regardless of location needs urological and urodynamic testing.

CLASSIFICATION OF NEUROGENIC BLADDER

There are various systems of classification of the neurogenic bladder. Most systems are based on the localization of the neurologic lesion and findings of the neuro-urologic examination and have been of more value in adults with spinal cord injury. In children the spinal level and extent of congenital lesion is poorly correlated with the clinical outcome.

PATHOPHYSIOLOGY

The detrusor and sphincter are two units working in harmony to make a single functional unit. Determined by the nature of the neurologic deficit, they may be either in an overactive or in an inactive state. The detrusor may be overactive with increased contractions, with a diminished bladder capacity and compliance or be inactive with no effective contractions; the bladder outlet (urethra and sphincter) may be independently overactive causing functional obstruction or paralyzed with no resistance to urinary flow leading stress incontinence.These conditions may exist in any combination. Four major types are usually used to describe the detrusor-sphincter dysfunction:

1. Detrusor overactivity with sphincter overactivity (dyssynergia),
2. Detrusor overactivity with normal or underactive sphincter,
3. Detrusor underactivity with sphincter overactivity
4. Detrusor underactivity with sphincter underactivity

PATIENT EVALUATION

The first evaluation is based on several factors depending on: when the child presents and/or is diagnosed.

In the first years of life, being kidneys are highly susceptible to backpressure and infection, documentation on UDS pattern is required · Ultrasound studies and a VCUG or video-urodynamics to exclude reflux have to be performed soon after

birth. These studies provide a baseline for the appearance of the upper and lower urinary tracts. A urodynamic evaluation needs to be repeated at regular intervals, in combination with evaluation of the upper tracts

Approximately 90% of children born with meningomyelocele will have a normal upper urinary tract at birth. Over time, many children who have not received proactive urological care develop upper and/or LUT deterioration: it was calculated a urodynamic risk score including a DLPP of >40 cmH2O. The grades of renal dilatation are compatible with increases in relative unsafe cystometric capacity and the calculated urodynamic risk score[28]. Prevention of high bladder filling pressure (before upper tract dilatation is observed) is necessary and feasible even before any urodynamic diagnosis.

When incontinence develops in spite of strict adherence to bladder and bowel continence programs, or when changes occur in leg function or sensation, or when the child experiences back pain or increasing scoliosis, a change in neurological impairment might be expected. A number of myelodysplastic children have progressive neurological deficits as they grow up and reach puberty.

Regarding **Occult Spinal Dysraphism**, the preoperative urodynamic evaluation have documented abnormalities in striated urethral sphincter function (denervation and/or detrusor-sphincter dyssynergia) in 20 - 35% of babies under 2 years of age with normal neurologicalexaminations; thus emphasising the need for urodynamic testing in these children[31]. A closed urological follow-up is essential in children with OSD, because of possible upper urinary tract and renal function deterioration, in those with urodynamic at-risk conditions. An efficacious response in EMG activity, with stabilisation or improvement in up to 60% was shown on postoperative urodynamic assessment when the dysraphic state was corrected before 2 years of age. It was observed that children with meningomyelocele, as compared to closed dysraphism, tended to have more bladder dysfunction as exemplified on clinical history and urodynamic assessment. Evaluation after operation tended to show better outcome in children with closed dysraphism.

URODYNAMIC TESTING

For the last 20 years initial urodynamic studies very early in the neonatal period have been recommended for children with myelodysplasia, to help identify children at risk for subsequent urinary tract deterioration or a changing neurological picture. In an exhaustive review of the efficacy and reliability of urodynamic studies in newborns with myelodysplasia. Of 24 studies analysed, 21 studies were at level of evidence 4, 2 were at level 3 and 1 was at level 1. The urodynamic patterns of normal detrusor function (66%), acontractile detrusor (33%), DO (57%), and detrusor compliance, as well as detrusor-sphincter synergia (21%), dyssynergia (37%) and sphincter denervation (60%) were similar, with little variability across comparable studies.

Technique, Reliability and reproducibility of tests. Differences in urodynamic parameters exist from one study to another. Chou et al provided reference ranges for "normal" variability in urodynamic parameters that can be considered as "no real change". A reduced rate of filling, e.g. 10% of the expected bladder volume per minute, has been recommended in children to accurately determine detrusor compliance and bladder volume. The temperature of the instillate (25^{o} versus 37.5^{o} C) no significantly affect detrusor pressures . For very young infants it may be better to insert a suprapubic catheter under anaesthesia the day before the test to be more accurate. Most children can undergo urodynamic studies without premedication, some requiring some sedation. In the 2012 ICI Consultation the recommendation was made that children should receive comprehensive urodynamic testing in a laboratory that is specialised in pediatrics, with appropriately trained personnel.

FOLLOW-UP of congenital neurogenic bladder in children

Newborn to Childhood. Once UDS has been performed a decision can be made as to whether the child is a candidate for continuing CIC or allowed to void freely. It is advisable to repeat UDS (cystometry) 2–3 months later to confirm that therapy is adequately reducing bladder pressures. Indications for repeating a VCUG or RNC include a change in upper urinary tract dilation, poor renal growth, loss of parenchyma, or symptomatic pyelonephritis. It would be wise to consider a baseline DMSA study if reflux is noted at the primary examination, for later comparison.

During this time a yearly or biannual ultrasound is recommended to follow the child, looking at residual urine or changes in the degree of hydronephrosis or bladder wall thickening. If any one of these is noted, UDS should be reconsidered.

Adolescents and Transitional Care to Adulthoods. It is during the rapid growth that tethering can occur, so careful monitoring of signs is mandatory. New onset wetting, or recurrent UTI are indicators of potential changes in lower urinary tract function: UDS or Upper tract evaluation are necessary. In general patients who have completed their growth are not likely to develop any further changes in the spinal cord that would precipitate tethering. It is imperative these young adults be followed closely to insure they are maintaining good CIC routines and are periodically being checked for unrecognized UTI or stone formation.

Sexuality becomes progressively more important as the patient gets older. This issue has historically been overlooked in individuals with myelodysplasia. Patients with myelodysplasia have sexual encounters, and studies indicate that at least 15-20% of males are capable of fathering children and 70% of females can conceive and carry a pregnancy to term. Therefore counseling patients CIC regarding sexual development is important in early adolescence.When reconstructing girls it is essential to have a future pregnancy in mind: the reservoir and pedicles should be fixed on one side to allow enlargement of the uterus on the other. Pregnancy may be complicated and requires the joint care of obstetrician and urologist: chronic urinary infection is almost inevitable and occasionally an indwelling catheter is needed in the third trimester

MANAGEMENT OF THE NEUROPATHIC BLADDER.

The main aim in management of NBD in children is to ensure and maintain a reservoir with normal age-matched capacity and good compliance that can be emptied completely at low pressures and at regular intervals. 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.

CONSERVATIVE TREATMENT

There are multiple conservative modalities of intervention for infants and children with NBD, which should be promoted before undertaking surgical interventions.

These treatment modalities include pharmacologic agents, medical devices and neuromodulation. Indications for these non-surgical treatments depend on issues related to intravesical pressures, upper urinary status, prevalence of UTI and degree of incontinence.

Clean Intermittent Catheterization

As mentioned in Introduction Intermittent Clean Catheterization 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.

The early initiation of intermittent catheterization in the newborn period, makes it easier for parents to master it and for children to accept it as they grow older **.** 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 . 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. 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. This review found a lack of evidence to state that the incidence of UTI is affected by using sterile or clean technique[46]. Thus, modification of catheters and catheter regimens should be made on an individual basis for children with NBD.

Pharmacotherapy

Anticholinergics/Antimuscarinics 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 **.**

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. The incidence of side effects of oral

oxybutynin ranges from 6% to 57% whereas side effects from intravesical oxybutynin are approximately 9%.7 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 than quaternary amines propantheline and trospium).

Botulinum-A toxin (BTX-A). BTX-A Anyway the most important urological advancement in NBD treatment in these years remains the use of onaBotulinum toxin A that has revolutionized the treatment of NBD . In the recent years onabotulinum toxin A has changed dramatically the treatment of NBD in adults and pediatrics in many centers the indications to bladder augmentation were dramatically reduced, and children have been treated with success and during time, avoiding bladder augmentation. In our experience onabotulinum toxin A confirmed its efficacy and safety as well as in the experiences of other colleagues We have treated 91 patients with NBD, aged 2-18 years old, with 281 procedures (1-9 treatments). No severe complications were observed maybe due to our pre-intra and postoperative protocol treatment and only in 3 cases we observed persistent hematuria 24 hours longer. Botulinum toxina A safety was confirmed regarding the effects on bladder wall after repeated injections While this treatment seems to be more effective in bladders with detrusor muscle overactivity, scant data are reported on low-compliant high pressure bladders The most commonly used dose of botulinum toxin is 10 U/kg with a maximum dose actually still of 300 units, that of course will be reduced as in adults to 200 UI. Of course it is is unclear how many times this treatment can be repeated, although repetitive treatment has been found to be safe in children and in adults Histological studies have not found ultrastructural changes after injection

In the guidelines of European Urological Association for Neurogenic Lower Urinary Tract Dysfunction the role of onabotulinumtoxin A is presented in a different way respect to ICCS document. Onabotulinum toxin could be a treatment alternativein other pathologies as PUV.. Regarding bladder outlet insufficiency treatment, this may be well managed by bulking agents. Of course this a temporary treatment with a short term efficacy useful in pediatric population in order to postpone major surgical procedureis an attractive treatment for NBD because it inhibits acetylcholine neurotransmitter release at the neuromuscular junction. Intravesical BTX-A is considered an alternative to improving continence and urodynamic parameters of NBD in children. 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**.** 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 dose of BTX-A is10 U/kg up to a maximal dose of 300 U involving 30 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.

Neuromodulation Treatments

Intravesical electrical stimulation

Intravesical electrical stimulation of the bladder has been introduced more than four decades ago and it has been tested in some open clinical trials in children since 1984. Its practice is limited to a few centres who have reported varying results. It is labor intensive time consuming and controversialin the only reported randomized, placebo-controlled trial, there was no efficacy demonstrated .

Sacral nerve stimulation

Sacral nerve stimulation has primarily been reported in the treatment of patients with a non-neuropathic bladder **.** 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, by intra-spinal implantation, conducted in children with NBD had mixed results and the study design was limited. At our institution we experienced sacral implantation in a number of children and adolescent with NB, with very good results on improvement of bladder sensation of fullness, number of catheterisms needed per day, and very satisfactory response from patients and families. Other modalities of nerve electrical stimulation have been considered in children, i.e percutaneous posterior tibial nerve stimulation, but with little experience in neurogenic bladders.

Another very promising treatment option is Sacral neuromodulation (SNM), that was used extensively in adults.It has been suggested that sacral root stimulation facilitates bladder recovery, we have experienced sacral neuromodulation (SNM) in children with incomplete injury and SNM seems to be a promising therapeutic modality for NBD in selected ones. A total of 14 patients with NBD with a mean age of 16.1 yr (range 10-21) were implanted between 2008-2014. There were 10 boys and 4 girls of which 6 had a congenital disorder and 8 had an acquired NBD.

The implant was in all time placed in the side which was identified being the best during preliminary testing. No post-operative complications were observed.

The average time of the intervention was 53 minutes for the first operation, and 40 minutes for the second one. All implants are in place and functioned well at last control.The evaluation is done by dividing patients in two groups: responders and non responders. Patients were considered responders if: they were satisfied and had one or more of the following criteria: <50% incontinence episodes, <50% post voiding residual, <50% of necessity for CIC, >50% voided volume.

In order to get a better understanding of the optimal indications for SNM, we systematically searched the PubMed, EMBASE and Cochrane databases Language restrictions were applied to other languages than English. No date restrictions were

applied. The last search was performed on … 2012. We hand-searched the reference list of all included studies and any relevant review articles.

Abstracts of all identified studies were independently reviewed by two authors and any study reporting on SNM for the treatment of neurogenic bladder in pediatrics was reviewed in full text. (Adult studies were reviewed if they reported on children as well if they were well described). We aimed to include any original SNM study that reported efficacy and/or safety data on tested and/or permanently implanted patients suffering from neurogenic bladder. Non original articles, studies not published as full-text articles, and those including adults were excluded.

The variables assessed included year of publication, level of evidence, study type, number of patients, gender, age, (duration of the underlying neurologic disease), success rate (total, according to the neurologic disease/injury causing neurogenic bladder, according to the type of LUTD) of test phase and permanent SNM, duration of test phase, length of follow-up, adverse event (total, type of adverse event), and surgical intervention (total, type of surgical intervention) of test phase and permanent SNM. (In accordance with the literature (see article), an improvement of >50% in bladder diary variables (number of leakages, pad use, number of voids, number of catherisations) was considered a success.

We compared the results of our own study group with the results of studies found in literature.

We evaluated the results using a subgroup analysis comparing acquired with congenital NBD. The results of our own series showed an overall success rate of 71.4%, versus 70.4% in the literature studies. Considering different pathologies, incomplete spinal cord injury (SCI) presented the highest success rate; 100% in the literature and 75% in our own experience. The lowest rate was reported in complete SCI and myelomeningocele (0%).

A total of 71 children with NBD treated with SNM with a mean age of 14,3 years (range 5-21) were included: 14 children (mean age 16.1 yr, range 10-21) of our own experience and 57 patients (mean 13.9 yr, range 5-21) from 11 studies identified by an electronic search on PubMed (6 pediatric studies and 5 adult studies). The clinical response was evaluated on the basis of patient satisfaction and one or more of the following criteria: <50% incontinence episodes, <50% post voiding residual, <50% of necessity for CIC, >50% voided volume, defining responders from non-responders. All clinical data of 71 patients were independently extracted and evaluated by 2 reviewers, both not directly involved in the surgical procedure.

Our study together with the literature found a favorable outcome for acquired versus congenital NBD. Subgroup analysis shows that the predictive value of the positive response of SNM depends on the specific indications

SURGICAL TREATMENT

Intermittent catheterization and drug therapy are usually sufficient in the majority of cases for maintaining continence and preserving upper tracts. Surgical procedures should be considered if conservative measures fail to achieve continence between catheterizations

or preserve upper tracts. 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. Urologists should identify that limited group that may require surgery. Surgical procedures develop gradually and often are tested without rigorous statistics. efforts to promote bladder healing, and protecting and achieving normal bladder function should be supported. research may lead to earlier and more aggressive treatment of many of the complex anomalies now treated by the surgical procedures

TO MANAGE CONTINENCE

Gastrostomy button

A modified technique of vesicostomy is described using a gastrostomy button, which could be used as a continent urinary stoma in children with incomplete voiding. Button vesicostomy is a useful addition to the options available for a catheterizable continent urinary stoma in children in the short or medium term. We decide to include this procedure in the treatment of VUR and NBD using BoNTA and DxHA in 12 children, unabled to perform CIC, in a extended combined endoscopic approach. The surgical procedure was performed in general anaesthesia: first of all endoscopic suburetheral injection of DxHA (0.5-1 ml/side) and bladder BoNTA injections (10 IU/Kg, max 300 IU) were performed and then as cistostomy a Mic-Key gastrostomy, button (Kimberly-Clark/Ballard,USA) was inserted endoscopically according to original Subramaniam's techniqueThe mean overall operative time was 40 minutes, no surgical complications were reported., At the mean follow-up of 11,8 months urinary tract infections was solved in all, as well as VUR , but in one renal unit.. All the buttons are in situ, well working. No peristomal urine leakage , wound infection, erosion granuloma, were observed. Buttons were changed every 3 months and all relatives and patients are satisfied about urinary drainage , opening the button and connecting it the feeding tube.for intermittent bladder emptying that is regularly performed in all 4-5 times daily, as for CIC, with 1 patient performing nocturnal continuous emptying. This cumulative endoscopic treatment seems to be a valid alternative to derivation, augmentation and reimplantation in the short and medium term period, helping child maturation and family education and a correct definitive management choice , improving children status ,avoiding psychological pressure on relatives in patients with associated severe mental disability, where major surgical reconstruction could be considered an overtreatment.This treatment could be very useful to postpone major surgery in adult life

The Mitrofanoff principle

In the long term it is necessary to have a catheterizable channel. Mitrofanoff's name is given to the principle of burying a narrow tube within the wall of the bladder or urinary reservoir whose distal end is brought to the abdominal wall to form a catheterizable stoma suitable for intermittent catheterization. The technique is simple and familiar to all urologists who are accustomed to re-implanting ureters. Several narrow tubes are available for the Mitrofanoff conduit. In the original description, the appendix was used. The system achieves reliable continence (90-100%) which is maintained in long term follow-up, for a high proportion of patients.

TO AUGMENT BLADDER STORAGE

Enterocystoplasty

The indication for bladder augmentation, replacement of the bladder, or the creation of a continent urinary diversion, is either the morphological or functional loss of normal bladder function. The main goal of this surgery is to relieve high pressure and low capacity of the urinary bladder and create a new reservoir with low storage pressures that can be emptied periodically. It is particularly important that the patients understand that spontaneous voiding will not be possible after such surgery and life long intermittent catheterization will be required.

There are several important principles for bladder augmentation and replacement that should be respected:

• use the minimal amount of bowel,

• a low-pressure large capacity reservoir is essential (this requires detubularization of any intestinal segment used),

• a reliable continence mechanism (continent urinary outlet) must be assured,
• because of the only resorbable sutures and staples should be used (risk of stone formation)

The invasiveness of Enterocystoplasty, and its long-term severe complication rate, has greatly reduced its indication. Recently, it is gaining more attention, in relation of the availability of mini-invasive procedures, i.e. the robotic-assisted laparoscopy[51].

Autoaugmentation

The principle of auto-augmentation of the bladder is the excision of a great portion of the detrusor while leaving the urothelium intact, creating a large diverticulum for the storage of urine at lower pressures. This urine stored at a low pressure can be drained by intermittent catheterization. The theoretical advantages of this procedure are the low complication rates of the surgery, reduced operative morbidity with shorter stay in the hospital, absence of urine salt resorption, less mucous production in the urine and possibly absence of carcinogenic potential **.**

More recently, some authors have proposed the laparoscopic auto-augmentation as a minimally invasive procedure for the treatment of low capacity / low compliance bladder.

TO INCREASE OUTLET RESISTANCES

Bulking agents

The injection of bulking substances in the tissues around the urethra and bladder neck to increase outlet resistance in children dates back to at least 1985. The search for safer, biocompatible substances to create periurethral compression has first led to the use of cross-linked bovine collagen, with initially reported success in about 20-50% of children.

Usually the substance is injected endoscopically in the bladder neck area (finding the best spot is often the most difficult part of the procedure): more than one procedure may be necessary. On average 2.8 – 3.9 ml is injected.

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. Complication rates

are modest and include difficult catheterization and rectal injury, while in long-term erosions or persistent incontinence may occur

Bladder Neck Closure / Reconstruction

In 'desperate' cases the bladder neck may be closed, the indication being persistent leakage despite several attempts to enhance outlet resistance. Long-term results are usually disappointing: persistent urinary leakage, stomal stenosis and leakage or stone formation.

The optimal bladder neck procedure should increase bladder outlet resistance at minimal cost of decreasing bladder capacity, maintaining easy catheterization and still allowing 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.

Artificial Urinary Sphincters

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. However, with improved durability of newer models that have an average life span of about 8 years, revision rates have become less. The ideal patients for AUS implantation are post-pubertal males or females, who can void volitionally and empty the bladder completely. On the contrary, a common problem is the development of reduced bladder compliance with time. Overall, 40 to 50% of neurogenic patients require a bladder augmentation concomitantly or subsequently to the AUS implantation.

Evaluation of Outcome

Our prejudice is that reconstruction does, indeed, improve the lives of children, Quality of life does not mean absence of disease or a level of complications acceptable to the reviewing clinician. It is a difficult concept to measure because lack of validated instruments, difficulties in translating from one culture or language to another, of the difficulties in selecting control groups and variations in clinical situations.

The main justification for performing a bladder reconstruction or continent diversion is to improve the individual's Quality of Life (QoL). It would seem logical that continent urinary diversion would be better than a bag. This is not always the case, and in adults the only sure advantage is cosmetic. Validated QoL surveys in children have not been reported, primarily because of the lack of suitable instruments.

Treatment of constipation and fecal continence

.For the same reason children with bowel dysfunction are well managed using advanced trans anal irrigation, and Malone procedure indications were reduced during time. Some studies demonstrated the same effectiveness between surgical procedure (Malone) and rehabilitation (advanced trans anal irrigation), and for this reason this procedure must be attempted before any surgical procedure in a pyramid therapeutic approach.

ADULT LIFE :

Neurogenic bladder patients require lifelong care of continence , monitoring of renal function . Periodic investigation of upper tract changes, renal function and bladder status is mandatory . Patients operated on with reconstructive procedures using intestine should be regularly followed up for complications such as infection, stones, metabolic changes, and neoplasm, that has been found to occur in 0.6-2.8% of patients during median follow-up of 13-21 years . In a study including 153 patients with a median follow-up time of 28 years , malignancy was found in 4.5%. Who is involved in this lifelong care? The answer is the Neuro-Urologist, that is an the urologist with expertise in the diagnosis and management of congenital and acquired pathologies of the urinary tract related to a neurogenic damage . So the clinical interest of Neuro-Urologist will be very close and sometimes overlapped to the Adolescent Urologist to continue the management of continence in older children and young adults previously treated for major congenital anomalies of the

genitourinary system. Advances in paediatric medical care and surgical management resulted in improved survival and quality of life for children with Spina Bifida. All urologist can be considered as NeuroUrologist? The answer is no. NeuroUrologist involved in the life-long care of continence, fertility, sexuality from childhood through adolescence and into adulthood must be competent in reconstructive urology (ureter, bladder, urethra and genital); trained in paediatric and adult urology, competent in urodynamics, and finally to be a part of a specialized team with nephrologist, urotherapist nurse, uro-radiologist, endocrinologist, gynecologist , psychologist, etc.that meets on a regular basis to formulate patient treatment plans. In the past 25 years there has been an enormous development in the paediatric urology. Many surgical techniques have changed dramatically, and Paediatric urology has totally changed and where in the past the consideration was survival or not of a patient, today care has progressed such that continence is an expectation rather than rarity, with increased survival and better functional outcomes in term of quality of life (QoL)too, with the expectations of our patients , related to social life and sexuality too. If in the past it could be difficult to measure QoL, today we have more instruments as Qualiveen-30 that is a neurological urinary disorder -specific health-related quality of life (HRQL) instrument, recommended in the European Association of Urology guideline by 2008.

Sexuality and spinal cord injury (SCI) :there are very scant data on analysis on the sexual impact of medical and psychological treatments related to SCI. Literature reports that some co-morbidities are more prevalent in women with SCI compared with able-bodied women but data on sexual functioning are missing.To improve sexual rehabilitation services, sexual issues and response require evaluation during periodical check-ups using validated questionnaires administered by a physician 'guide' who coordinates professional operators thus providing personalized programmable interventions. as we have done investigating a possible correlation between sexual hormonal status and the presence of female sexual dysfunction

(FSD) using the Female Sexual Function Index (FSFI) in females with spinal cord injuries (SCI), in selected 39 SCI fertile-aged women. Very interesting appear the results of SNM . Over the last few years, sacral neuromodulation (SNM) has become an established treatment option for lower urinary tract symptoms (LUTS). In our study we have evaluated if SNM improves sexual function in females, measuring the Improvement in sexuality by the Female Sexual Function Index (FSFI) and the Female Sexual Distress Score (FSDS). We included 31 women, 17 of whom were neurogenic with permanent SNM Both questionnaires indicated a clinically significant improvement in sexuality that was maintained up to the final visit for 4 out of 11 neurogenics with sexual dysfunctions:The positive effects regarding sexuality may be due either to enhancement of LUTS or to the direct stimulation of the sacral roots (S3). SNM may be beneficial in men too with selected incomplete SCI . 22 subjects (42.3%) showed erectile impairment (14 were neurogenic). In the first visit post-SNM, five retentionists of neurogenic origin and two with overactive bladder syndrome of idiopathic origin achieved noticeable erectile improvement and their median IIEF-5 score shifted from 14.6 to 22.2, and 15.5 to 22.5, respectively. Future research should test SNM in a larger sample of subjects, exclusively with sexual dysfunctions, in order to better understand the mechanism of action of SNM on erectile function. Another treatment option asi Literature suggests is oral PDE5 inhibitors that represent a safe and effective treatment option for ED caused by SCI. Further research is needed on head-to-head comparative trials and SCI patient preference for these drugs; their impact on ejaculation and orgasm function, their early use after SCI for increasing the recovery rate of a spontaneous erection, and their effectiveness and tolerability in the long-term are still to be investigated.Prostate volume and PSA levels are lower in SCI patients and are inversely related to the patient age at lesion onset. Whether this effect is mediated directly or indirectly by a impaired nerve supply to the prostate remains to be determined. Despite the present observation of reduced prostate disease, as during

the last twenty years life expectancy in SCI patients has improved significantly, the need to screen these patients for the occurrence of prostate disease should not be disregarded. Continence and Sexuality are inseparable because the same nerves that control urinary function also control sexual function. Therefore, if one has poor sensation, the other will also. It is very important to have an understanding partner and to communicate clearly about the possibility of urine or stool leakages during sex. The other issue might be low self esteem. Pregnancy is possible for almost all women with Spina Bifida so appropriate contraception is strongly recommended if pregnancy is not currently desired. Indications and cautions similar to general population. Pre-pregnancy counselling ideal to optimise health prior to conception is recommended Spina bifida is best prevented by taking 400 micrograms (mcg) of folic acid every day. Studies have shown that if all women who could become pregnant were to take a multivitamin with the B-vitamin folic acid, the risk of neural tube defects could be reduced by up to 70%. Women who have experienced a pregnancy affected by a NTD like Spina Bifida need a higher intake of folic acid i.e 4 milligrams (mg) and is available by prescription from a health care provider. Pregnant women with Spina Bifida should also see their urologist and neurosurgeon in addition to their gynecology team to make sure the pregnancy is not adversely affecting their shunt or kidneys.

The type of delivery depends on multiple physical factors, including sensation level, ability to push with pelvic muscles, size of the pelvis, and flexibility around the hips and knees. The more conducive these factors are to the birthing process, the more likely a vaginal delivery can be performed.

If it appears the baby will not be able to be pushed safely through the pelvic area and down the birth canal, a Cesarean section will be recommended. If a C-section is chosen, the urinary tract is evaluated for re-implantations, diversions, or conduits to make sure they are avoided during the delivery incision.

Women with SB have successfully and safely received epidural anesthesia for their delivery. Because the anatomy of the spine is different, the epidural may need to be placed using ultrasound guidance. There are reports of successful epidurals for most myelomeningocele lesion levels, with or without scoliosis.

As with all pregnancy issues in Spina Bifida, monitoring the effects of the epidural is trickier than in usual pregnancies. Therefore, it is best to deliver with an obstetrician and hospital experienced in high-risk pregnancies.

Conclusions

We have analyzed the most common neurological disorders, mainly myelodysplasia, which deal with neurogenic bladder dysfunction (NBD). The pathophysiology and the consequences on urinary continence and urological/renal function are described. Management of NBD in children has undergone major changes over the years. Reliable urodynamic investigation (UDS), the advent of clean intermittent catheterization (CIC), a plethora of drug therapies that modulate lower urinary tract function, a multitude of rehabilitative modalities and advancement in surgical techniques, had furnished the evidenced based ways and tools to manage Neurogenic Bladder in children.

The steps of a clinical work-up, both for those conditions starting at birth and the occult lesions detected later on, are underlined. The main goals of treatment remain the prevention of urinary tract deterioration and the achievement of continence.

The newborn must be protected by those “at-risk” bladder, which can significantly alter renal function. 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. Nowadays, the treatment of choice is initially conservative. Multiple conservativemodalities, i.e pharmacologic agents, medical devices and neuromodulation, should be promoted before undertaking surgical interventions. Intermittent catheterization and drug therapy are usually sufficient for maintaining continence and preserving upper tracts. Surgical procedures should be considered if conservative measures fail to achieve

continence between catheterizations or preserve upper tracts. However today the improvement of Quality of life is the final goal.

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