Electrical neurostimulation/neuro-modulation for treating neurogenic lower urinary tract dysfunction

A variety of methods to improve neurogenic lower urinary tract dysfunction (N-LUTD) has been developed, starting already at the end of the 19th century. Electrical neurostimulation is the direct stimulation of a neuron with an immediately activating effect on the end organ, e.g. sacral anterior root stimulation induces detrusor contraction, whereas electrical neuromodulation is the stimulation of a neuron which affects the function of subsequent neurons to inhibit or to activate the aimed organ, e.g. stimulation of the pudendal nerve inhibits detrusor activity although the pudendal nerve does not innervate the bladder.

Electrical neurostimulation for neurogenic LUT dysfunction

Two methods are currently used, one is anterior sacral root stimulation (SARS), the other is intravesical electrical stimulation (IVES), a third one, direct neuromuscular stimulation of the acontractile/underactive detrusor, has been used in the past.

Anterior Sacral Root Stimulation (SARS) has been developed by G. Brindley in the early 1980s to empty the unbalanced spinal reflex bladder.² However, to achieve both, balanced electro-micturition and continence in-between, SARS has to be combined with sacral deafferentation (SDAF). SDAF means that posterior roots from S2 to S5 have to be cut bilaterally, thus the spinal reflex arch is interrupted and the reflex activity of the detrusor abolished. SARS, together with SDAF, which can only be applied in complete spinal cord lesions, has excellent long-term results. According to a single center experience³ with 420 patients over 20 years electro-micturition with physiologic detrusor voiding pressure and minimal or no post-void residual urine was achieved in 92%, the continence rate was 83%. After SARS and SDAF the rate of urinary tract infections decreased dramatically and the upper urinary tract remained normal, improved or did not further deteriorate. SARS also enables electro-defecation in about 70% cutting down defecation time considerably.²

However, SDAF has also disadvantages. It abolishes any sensation from the lower urinary and bowel tract as well as reflex erections and may occasionally induce stress urinary incontinence. Nowadays patients are very reluctant against cutting nerves because they hope that one day the regeneration of the injured spinal cord may become possible and then all sublesional

KeyPoints

Which techniques of electrical neurostimulation/electrical neuromodulation should be used for which indication?

- For suppressing neurogenic detrusor overactivity non-invasive pudendal nerve stimulation should be tried before SNM or PNS are applied.
- For the hypocontractile and hyposensitive detrusor intravesical electrostimulation is the first-line treatment. If IVES is not successful, SNM and PNS should be considered.
- For the unbalanced spinal reflex bladder with uncontrollable reflex incontinence SDAF combined with SARS is an option with excellent results, but also relevant side effects.
- Methods used in the past and forgotten meanwhile, as direct bladder stimulation for the acontractile detrusor and direct electrostimulation of the flaccid pelvic floor to treat sphincter related fecal and urinary incontinence, should be reevaluated and further developed.
nerves would be needed. Moreover, in the era of botulinum toxin A injections the need for SDAF has somewhat decreased, though the failure rate of botulinum toxin A in these patients is around 20%.

Patients who benefit most from SARS and SDAF are paraplegic women with reflex urinary incontinence but also tetraplegic males who are not able to perform self-catherization but who may be able to manage the external device and void by electro-stimulation into a condom urine in order to avoid transfer out of the wheelchair.

Efforts have been undertaken to replace SDAF by sacral neuromodulation with some success, however, persisting detrusor-sphincter dyssynergia still remains a problem. Further investigations are needed.

**Intravesical electrical stimulation (IVES)**

*Intravesical electrical stimulation (IVES)* was already described in 1878 by the Danish surgeon Saxtorph for stimulating the „actonic bladder“. A few years later, in 1899, Frankl-Hochwart and Zuckerandl in Vienna reported better results with intravesical electrostimulation of the neurogenic bladder compared to Faradic stimulation. It was Katona in Budapest (Hungary), who improved the technique and popularized this method since 1975. The method involves an artificial activation of bladder mechanoreceptor afferents, responsible for the normal micturation reflex. This is achieved by filling the bladder with sodium chloride as the electrical current leading medium and by inserting a monopolar electrode into the bladder, which activates the mechanoreceptor afferents. From neurophysiology we know that repeated reflex pathway activation upgrades its performance. The prerequisites for successful IVES, often ignored by those having published disappointing results in the past, are incomplete nerve lesions, intact mechanoreceptors, a detrusor still able to contract, a cortex able for perception of afferent stimuli, and an experienced staff. Positive results with IVES have been reported in children and adults, only recently also in patients with incomplete spinal cord lesion. With IVES about 70% (re)gained bladder sensation, 50% showed improved detrusor contractility and about 30% achieved social continence. The potentials of IVES for bladder (re)habilitation are still underestimated.

Another issue is *direct electrical stimulation of the neurogenic acontractile detrusor* due to second neuron damage. In the 1970s Merrill D.C. developed the „Mentor® bladder stimulator“. Over hundred of these devices have been implanted between 1971 and 1975 throughout the United States and in Europe. Also 11 patients with lower motor neuron lesion with chronic urinary tract infections received the implant: an extremely high PVR (1000-1800cc) was reduced in 82% to usually less than 60cc and the incidence of UTIs was reduced in 43%. It was concluded that lower motor neuron lesions, which fail more conservative treatment modalities, are suitable candidates for direct bladder stimulation. Jonas et al reported 8 patients, who had a benefit from such an implant. However, technical failures and implant infections as well as the fact that intermittent (self-)catheterization became more and more popular at this time, finished the era of direct neuro-myogenic bladder stimulation and the method was forgotten until recently. Improved bladder physiology knowledge and modern technology encouraged neuro-urologists to reevaluate the possibility for direct bladder stimulation but further studies are necessary.

Also during the 1970s Caldwell in Exeter (UK) implanted *a device for stimulating the underactive pelvic floor*, which was able to improve/to restore faecal and urinary continence due to neurogenic pelvic floor weakness successfully, in one of my patients for more than 20 years. With the technology of today this concept should be also reevaluated and further developed.

**Sacral neuromodulation (SNM) for neurogenic LUT dysfunction**

Neuromodulation of the sacral nerves has been introduced regularly from 1994 onwards and was used since then for several functional urological problems. The exact working mechanism of SNM remains unknown, but it is clear that electrical stimulation alters the afferent input into the central nervous system (CNS) and the processing of these signals, resulting in a better coordination between the different centers to balance abnormally excitatory or inhibitory reflexes.

SNM has been introduced by Schmidt and Tanagho in the 1990s. Since then, the introduction of tined leads, reducing lead migration, the buttock placement of the implantable pulse generator (IPG) reduce the occurrence of pain at the IPG site as well as new surgical implantation techniques with new device components have improved efficacy and decreased complications. In regards to neurogenic detrusor overactivity and neurogenic, non-obstructive urinary retention so far the available evidence regarding the general use of SNM for N-LUTD does not allow definite conclusions. The number of investigated patients is low and there is a high heterogeneity between studies. Moreover, there is a lack of RCT. So we need well designed and adequately powered studies taking into consideration heterogeneity of N-LUTD and specific questions are needed.

In regards to SNM (PNS) several issues need to be solved: uni- vs. bilateral sacral/pudendal nerve stimulation (different for detrusor overactivity and chronic retention?), automatic event driven electric stimulation for NDO, the development of an IPG with changeable battery to save costs and a device which inhibits the overactive detrusor and allows voiding without DSD.

Whether early sacral neuromodulation could prevent spinal detrusor overactivity after complete spinal cord
injury needs to be proven in controlled, multi-center medium and long term studies.\(^{14}\)

Already in 1986 Vodusek et al\(^{15}\) demonstrated in paraplegic patients detrusor inhibition by \textit{stimulation of pudendal nerve afferents}. Following this concept Spinelli et al\(^{16}\) presented their results with pudendal nerve stimulation to treat neurogenic bladder and bowel dysfunction: 12 patients with incomplete lesions with a follow-up of 6 months showed improvement of bladder and bowel function. In animal experiments bladder inhibition and/or voiding could be induced by pudendal nerve stimulation in chronic spinal injured cats\(^{17}\) considering a neural prosthesis device based on pudendal nerve stimulation to be suitable to restore micturition in SCI.

Clinical practice, placement and fixation of electrodes to the pudendal nerve by open surgery were difficult. In 2001 M. Possover\(^{18}\) developed a method for laparoscopic placement of electrodes to the pudendal nerve and claimed good results. However, with a closer look in 4 of his patients, using video-urodynamics, it became obvious that the improvement of incontinence, at least in these 4 patients, was not due to suppression of detrusor overactivity but due to increased PFM/sphincter activity. The exact reasons for failures are not clear.

Electrical neuromodulation of bladder can also be achieved by \textit{non-invasive methods}, e.g. stimulation of the post. tibial nerve or – a method we are using – by electrical stimulation of the dorsal penile/clitoral nerve, afferent branches of the pudendal nerve, with results regarding suppression of detrusor overactivity comparable to pharmacotherapy.

\section*{Literature:}
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