

URODYNAMIC EVALUATION BEFORE AND AFTER CONTINUOUS INTRATHECAL BACLOFEN INFUSION (CIBI) IN PATIENTS ON VEGETATIVE/MINIMALLY CONSCIOUS STATE

Hypothesis / aims of study

Spasticity of either spinal or supraspinal origin may compromise patients severely and is associated with the development of pain, limb contractures and immobility. Baclofen is a structural GABA analogue substance acting on the GABA-B receptor subtype. It is assumed to act at the spinal level attenuating mono and polysynaptic conduction, primarily by inhibiting the release of excitatory transmitters. Baclofen hardly penetrates the blood-brain barrier; therefore, penetration into the cerebrospinal fluid is poor with oral administration. Penn and Kroin were the first to report good results with continuous intrathecal baclofen infusion (CIBI) in patients with severe spinal spasticity. A dramatic clinical improvement was reported. Spasticity of supraspinal origin is much more common than spinal spasticity, but treatment with CIBI has been evaluated far less frequently in this condition. Reports of successful treatment of patients with supraspinal spasticity are limited. Especially patients with severe traumatic and/or hypoxic brain injury often suffer from severe tetraspasticity that is unresponsive to oral medication, physiotherapy or other antispastic therapies. More limited are the reports on CIBI use in patients in vegetative or minimally conscious state.

Moreover CIBI has been demonstrated to be effective to improve bladder capacity or to decrease sphincter dyssynergia in patients affected by spinal cord spasticity. Only a few reports have been published on Traumatic Brain Injury (TBI), especially on the correlation of urodynamic findings, because injured patients commonly have behavioral, cognitive, or communication problems. The injury to the brain itself, impairment of cognitive and behavioral function, may induce voiding problems, such as incontinence. The most commonly expected urodynamic abnormality after TBI is involuntary detrusor contraction, which can be induced by the loss of cortical inhibition caused by suprapontine lesions. Coordinated relaxation of the distal sphincter during detrusor contraction is usually maintained. The incidence of urinary retention after TBI is lower than that after cerebrovascular accident (CVA). Very little is known about changes in urodynamic pattern in patients in Vegetative (VS) or Minimally Conscious State (MCS) after TBI or CVA treated with CIBI. The aim of this study is to urodynamically assess bladder function in patients on VC or MCS before and after CIBI.

Study design, materials and methods

We enrolled for this study 16 patients (13 males and 3 females), all patients were in VS or MCS for CVA (9 extensive brain hemorrhage) or TBI (7 patients). All patients were urodynamically evaluated before and one month after Baclofen pump implantation. During urodynamic study were evaluated Bladder Compliance (BC), presence and amplitude of Detrusor Overactivity (DO), Maximum Cystometric Capacity (MCC), detrusor pressure at opening bladder neck (detrusor leak point pressure, DLPP) that coincide to detrusor pressure required to void. In all patients were applied the Ashworth scale, separately for upper and lower limbs, and the spasm score, before and after implant, to evaluate changes in spasticity. In all patients were evaluated Post Void Residual (PVR) pre and post CIBI.

In 12 patients we performed a second urodynamic evaluation 6 months after implant, evaluating the same urodynamic findings (BC, DO, MCC, DLPP). Statistical analysis were performed using paired t-test and/or paired Wilcoxon test when appropriated to evaluate the difference in Ashworth and spasm scale, and to evaluate the urodynamic results at baseline and 1 and 6 months after CIBI. We used Fisher's exact test to evaluate the number of patients in Clean Intermittent Catheterization (CIC), and the conscious state at baseline and after CIBI. We considered statistical significant when $p < 0.05$.

Results

Mean age of patients included in the study was 41.3 ± 13.5 years, coma days were 17.4 ± 5.9 , elapsed time between cerebral injury and our centre's admission was 149.5 ± 41.5 days. At admission 3 patients were in MCS and 13 in a VS. Time of catheterization was 117.9 ± 98.4 days. At baseline all patients were in spontaneous micturition (reflex urinary incontinence), in 4 out of 16 patients CIC was necessary because high PVR. In all patients we observed an improvement of spasticity, especially of lower limbs after CIBI. The mean Ashworth scale pre-implantation was 2.8 ± 0.4 for upper limbs and 3.5 ± 0.5 for lower limbs, spasm score was 1.8 ± 0.7 . After CIBI Ashworth scale was reduced, 2.4 ± 0.5 for upper limbs and 2.2 ± 0.4 for lower limbs with a statistical significant difference ($p < 0.01$). Also spasm score was improved, after CIBI measuring 1.5 ± 0.5 with a significant statistical difference respect baseline ($p < 0.03$).

One month After CIBI in 8 out of 16 patients was necessary CIC for high PVR (Fisher's exact test $p = 0.27$). Six months after implantation CIC was necessary in 3 out of 12 patients (Fisher's exact test $p = 0.3$)

At urodynamic evaluation mean baseline MCC was 364.6 ± 150.1 ml, one month after CIBI was 391.9 ± 40.8 ml ($p < 0.03$). Mean MCC 6 months after implant (12 patients) was 368.1 ± 146.2 ml ($p = 0.11$)

DLPP was 98.3 ± 7.4 cmH₂O at baseline and 83.8 ± 11.5 cmH₂O 1 month after CIBI, with a significant statistical difference ($p = 0.04$). in the 12 patients evaluated 6 months after CIBI mean DLPP was 85.7 ± 12.8 cmH₂O ($p = 0.05$ respect baseline).

Mean PVR at baseline was 57.5 ± 21.7 ml, and 100.4 ± 50.9 ml one month after CIBI ($p = 0.01$), although 6 months after CIBI mean PVR was 56.8 ± 24.5 ($p = 0.58$ respect baseline). At baseline in 10 out of 16 patients a DO was identified, after CIBI DO was present in 3 out of 16 patients ($p = 0.02$), and in two patients 6 months after implant.

We observed an improvement in conscious state, at hospital admission 13 out of 16 patients were in VS and 3 out of 16 in MCS, at discharge 7 out 16 were in SV and 9 in MCS (Fisher's exact test $p = 0.14$).

Interpretation of results

The possibility to administer baclofen intrathecally, through a system of programmable infusion pump, has enabled the effective control of spasticity after severe brain injury with fewer side effects compared to oral treatment and with a significant improvement in overall function.

At the level of the urinary system, the γ -aminobutyric acid has an inhibitory action on the detrusor contractility, the origin of this mechanism is both in spinal cord and supraspinal. The GABA receptors are involved in the regulation of detrusor contractility through the action carried out on the pelvic ganglia, the sacral parasympathetic nucleus and supraspinal centers. Baclofen has therefore indications for use in the treatment of Lower Urinary Tract Dysfunctions (LUTD) with two main way of action: inhibition of hypertone involving the external urethral sphincter and the increase of detrusor compliance with the consequent increase in the filling capacity of the bladder. The use of intrathecal baclofen in the patients suffering from disorder of consciousness is spreading more and more, and not only for the treatment of spasticity and neurovegetative crisis but also for the possibility to induce a change in positive of the state of consciousness, many are today reporting in this sense. Another element to be reckoned with in clinical practice is the indication, suggested by some authors, to use early implant in order to prevent the impairment linked with spasticity before it is structured, thus making almost vain the only pharmacological or rehabilitative intervention. This study, even considering the modest numerosity of the sample, allowed to verify that after the implantation of CIBI a significant increase of MCC and a reduction of DLPP. Also the presence of DO is detected with a significantly reduced frequency respect baseline. Accordingly an increase in PVR in the first month was identified. While this data may seem a positive result of the therapy must be related to the type of patient treated, indeed the reduction of a detrusor contraction that it is not supported by supraspinal centers can create an increase of the PVR. However, this discrepancy was filled out 6 months after implantation, and the PVR returns comparable to the baseline. Instead, positive results on the reduction of DO were maintained in the long term. The data therefore indicate the need to monitor PVR closely, in the first weeks after implantation, to avoid the risk of bladder supra-distension in these patients with disturbance of consciousness.

Concluding message

This is a preliminary pilot study that needs further validation to determine which is the best management of the dynamics of micturition in patients in vegetative state/minimally conscious state after continuous intrathecal baclofen infusion.

References

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Disclosures

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