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Intrathecal Delivery of Baclofen As Functional Treatment of Severe Spasticity

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Summary

In some patients severe spasticity of cerebral or spinal origin cannot be treated successfully with conventional oral medication or physical modalities. Intrathecal baclofen therapy with implanted pump has represented effective treatment from mid-80's. Baclofen (Lioresal) is a muscle relaxant and a potent GABA agonist that acts via GABAb receptors at the posterior columns of spinal cord level, to inhibit the release of excitatory neurotransmitters by inhibiting calcium ions influx into presynaptic terminals. This direct binding on spinal cord receptors leads to higher efficiency compared to peroral therapy in which baclofen does not pass the brain-blood barrier. The article overviews indications and contraindications for intrathecal baclofen therapy, selection and preparation of patients for surgery, the surgical procedure of pump implantation, long term follow-up with pump refill procedure and possible complications of intratecal baclofen therapy. The experiences of the Center for spasticity treatment at the University Rehabilitation Institute in Ljubljana are described.

Key words: spasticity, intrathecal baclofen therapy

Intratekalna primjena baklofena kao funkcijsko liječenje teške spastičnosti

Sažetak

U nekih bolesnika teška spastičnost, moždanog ili spinalnog porijekla, ne može se uspješno liječiti konvencionalnim, oralnim lijekovima ili fizikalnom terapijom. Intratekalna terapija baklofenom s implantiranom pumpom predstavlja učinkovit tretman još od sredine 80-ih godina prošlog stoljeća. Baklofen (Lioresal) mišićni je relaksant i moćan agonist GABA receptora koji djeluje preko GABAb receptora u stražnjim rogovima leđne moždine, inhibirajući oslobađanje ekscitatornih neurotransmitera inhibicijom dotoka kalcijevih iona u presinaptički terminal. Ovo izravno vezivanje na receptore leđne moždine dovodi do veće učinkovitosti u odnosu na peroralnu terapiju, u kojoj baklofen ne prolazi krvno-moždanu barijeru. Članak govori o indikacijama i kontraindikacijama za intratekalnu terapiju baklofenom, odabiru i pripremi bolesnika za operaciju, kirurškom postupku implantacije pumpe, dugoročnom praćenju s postupkom punjenja pumpe te o mogućim komplikacijama intratekalne baklofenske terapije. Opisana su iskustva Jedinice za liječenje spasticiteta na Sveučilišnom Rehabilitacijskom Institutu Soča u Ljubljani.

Ključne riječi: spastičnost, intratekalna baklofenska terapija.

Introduction

Spasticity as a clinical sign was excellently described by the editorial article in British Medical Journal in 1973: Spasticity is a condition in which the stretch reflexes that are normally latent become obvious. The tendon reflexes have a lower threshold to tap, the response of the tapped muscle is increased and usually the muscles beside tapped also respond. Tonic stretch reflexes are affected the same way (1).

The formal definition of Lance et al. was in use from 1980 (2): A motor disorder characterized by a velocity dependent increase in tonic stretch reflex (muscle tone) with exaggerated (phasic) tendon jerks resulting from hyper excitability of the stretch reflex as one component of an upper motor neuron syndrome.

In 2004, an "EU-SPASM (Support Programme for Assembly of database for Spasticity Measurement 2002-2004)" group published the latest definition of spasticity (3): "Disordered sensori-motor control, resulting from an upper motor neuron lesion, presenting as intermittent or sustained involuntary activation of muscles".

Nevertheless, "spasticity" as a clinical sign should be distinguished from "spasticity" as one factor only among many that contributes to motor dysfunction in the presence of the upper motor neuron syndrome (4).

Spasticity as a clinical problem has nevertheless an important influence on patients' ability and quality of life, and therefore represents a major rehabilitation problem and should be a focus of therapy for P&R medicine specialists. Spasticity is an expensive, often undertreated condition, with heavy economic burden for the patients, caregivers and society and a cause of disability due to decreased mobility, weakness, and fatigue (5, 6). Spasticity results in increased dependence on family and institutional caregivers for activities of daily living. It consequently ends in costly complications such as joint contractures and pressure sores with decreased quality of life (7, 8). On the other hand, patients are often undertreated due to side effects of oral antispastic medication. Spasticity treatment should be initiated when: Spasticity interferes with functioning, positioning, comfort and care, it is not useful (e.g. during transfers) and when treatment is expected to provide meaningful improvement.

Intrathecal Drug Delivery of Baclofen with Programmable Pump

Baclofen is a first line drug in the treatment of spasticity. It is structurally similar to the neurotransmitter GABA and it is a muscle relaxant and a potent GABA agonist that acts via GABAb receptors at the posterior columns of spinal cord level, to inhibit the release of excitatory neurotransmitters by inhibiting Ca influx into presynaptic terminals (9). What is most important is that it does not pass the blood-brain barrier, therefore the majority of oral intake of baclofen remains in the serum and is present in the spinal fluid only in traces.

General indications for treatment with intrathecal baclofen pump

Spasticity of cerebral or spinal origin, which is a cause of restriction:
- ambulation/transfer/seating,
- daily activities & care,
- rehabilitation interventions & progress,
- daily rest or sleeping or
- causes pain / discomfort and
- is a potential factor for late complications (pressure ulcers, contractures…).

Typical conditions suitable for intrathecal baclofen therapy are: spinal cord injury, multiple sclerosis, traumatic and hypoxic brain injury, stroke, cerebral palsy and hereditary spastic paraparesis.

Pump implantation is contraindicated with severe internistic diseases, acute or chronic infections, severe psychiatric disturbances and resistant epilepsy. The pump cannot be implanted in asthenic children with body weight less than 10 kilograms. When tissue and tendon contractures are already developed, intrathecal baclofen would not improve tone nor range of joint motion or function. Implanted electronic devices (i.e. pacemaker) and frequent generalized epileptic seizures are relative contraindications (precautions) for implantation.

Prior to implantation a test of intrathecal baclofen is performed by repeated boluses via catheter or by temporary continuous infusion with an external pump. Lumbar puncture at the L3-L4 interspace is performed and then a bolus of baclofen is given every 24 hrs via epidural catheter in the range 25 – 100 μg in adults and 10 – 50 μg in children. Alternatively, an external pump can be attached to the catheter and this can simulate the real situation with an implanted pump, which is particularly useful in ambulatory and high-functioning patients. Positive test is confirmed, when a reduction of spasticity is observed for at least one grade on the Modified Ashwort scale in key muscles, without a decrease in functional status, preferably an increase. In the period of 2, 4 & 6 (or 8) hours after bolus, the following parameters are recommended to observe: muscle tone in target muscles with (Modified) Ashwort scale, adductor tone rating in hip adductors and spasm frequency, clonus rating, pain scale (VAS 0 – 100), Barry-Albright dystonia scale, active & passive ROM in target joints (degrees), muscle action – MRC scale.

After consideration of indications and after a positive baclofen test, the patient is scheduled for the surgical procedure. The procedure is performed under general anaesthesia and usually lasts 60 minutes. It consists of placing the catheter intrathecally, forming a subcutaneous pocket for the pump left suprainguinally and connecting the lumbar catheter via subcutaneous tunelling with the pump. The pump is filled with the baclofen solution just before implantation and the pump itself is programmed and starts just after the surgical procedure. After the surgery patient stays at the neurosurgery department for a short time and is then transferred to a rehabilitation department for baclofen dose adjustment and post-implantation management. If there is no external spinal fluid leakage and wound complications, gradual mobilization (72 hrs) is promoted to the

wheelchair use or walking. In the meantime, the oral spasmolytic drugs are reduced and the intrathecal baclofen daily dose is adapted with a telemetric programmer in case the pump is programmable. Post-implantation rehabilitation management consists of gradual mobilisation, stretching, relearning the physical activities after the altered situation, occupational therapy, functional re-training and adaptation of equipment such as wheelchair.

After setting the optimal daily dose of intrathecal baclofen, the patient is discharged home and scheduled for regular pump reservoir refill. Pump refill is done on an outpatient basis with the specially educated rehabilitation team. Refill is performed in clean environment through the needle inserted in the reservoir port of the upper surface of the pump. Average inter refill period is three (1 – 6) months and after seven or eight years most programmable pump models must be reimplanted due to battery end of life.

Nevertheless intrathecal baclofen therapy is connected with presumable costs, up-front costs of therapy can be expected to be reduced in: hospital bed days used in management of spasticity, number of orthopaedic procedures required, option of pressure sores/decubitus ulcers, oral treatment and orthoses and other aids (7, 10).

Complications After Baclofen Pump Implantation

Complications regarding treatment with intrathecal baclofen represents an overdose or withdrawal of the drug and peri/post-operative infections. Mistakes in programming or use of wrong solution concentration are major factors for overdose or withdrawal of the drug. Kinking or displacement of the catheter extradurally can be another reason for withdrawal of baclofen. Both conditions are potentially life threatening, so every patient must beside the symptomatic intervention undergo close observation, if needed, in the intensive care unit.

Signs of baclofen overdose:

- Sudden and unexplained hypotonus
- Narrow pupils (similar to opioid overdose)
- Hypersalivation, nausea, vomiting
- "Empty head" feeling, sleepiness, vertigo.
- Loss of consciousness
- Breathing depression, apnea, coma.

Signs of baclofen withdrawal:

- Sudden und unexplained raise of muscle tone
- Generalised pruritus
- Hyperthermia without inflammatory reason
- Tremor
- Headache
- Disorientation and hallucinations
- Vegetative autonomic dystonia in patients after spinal cord injury
- Rhabdomyolysis
- Acute renal failure, DIC, hypoxic brain injury, death

Infection of the pump system (pump or catheter) is a serious complication, because it represents an indirect threat of a central nervous system infection. Complications of an untreated pump infection are fulminant meningitis and ventriculitis. Therefore, the recommended decision after declaring presence of pathogenic bacteria on the material is immediate explantation of the pump and catheter with prolonged antibiotic treatment with an infection disease specialist follow up.

Presentation of Population

Altogether 97 patients with baclofen or morphine intrathecal delivery pump have been treated for intractable spasticity in Slovenia since 2001.

From the current population of 77 patients, there are 72 patients receiving baclofen only, two patients receiving an polyanalgetic mixture of morphine, clonidine and baclofen and three patients receiving morphine only with an intrathecal delivery pump.

The average age in the current population is 42.6 yrs (12-71). The leading pathology in the population is spinal cord injury / vertebral disease (26/77), followed by acquired brain injury (16/77), multiple sclerosis (16/77), cerebral palsy (13/77), cerebrovascular disease (2/77), moto-neuron disease (2/77) and one patient with Hereditary spastic paraparesis and with Stiff person syndrome. Eight patients died since the beginning of the programme and no death was connected with the ITB pump treatment. In five cases a definitive pump explantation was decided, due to sepsis (2/5), skin perforation (2/5) and discontinued need for therapy (1/5).

The average dose of the daily baclofen is 355 micrograms (55 – 1.750) and the average intrathecal dose of daily morphine in five pain patients is 9,8 mg.

The average pump inter-refill period in spastic and pain patients is 135 days, which on average means three refill sessions per patient per year.

Conclusion

Intrathecal baclofen therapy for spasticity is invasive, life-long, with possible life threatening complications. The selection procedure is therefore the most important part of the ITB treatment process. Benefits of therapy reveal the negative option. An informed and carefully selected patient at the right time and with reasonably defined treatment goals will match favourable results with satisfied patients and caregivers

Izjava o sukobu interesa

Autori izjavljuju da nemaju sukob interesa.

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