

Intrathecal Baclofen Therapy Effectiveness and Side Effects: A Retrospective Study

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ABSTRACT:

BACKGROUND:

Spasticity is a motor disorder characterized by a velocity-dependent increase in muscle tone with exaggerated tendon jerks, resulting from hyperexcitability of the stretch reflex, as a component of the upper motor neuron syndrome.

OBJECTIVE:

To evaluate the effect of intrathecal baclofen therapy after one to five years of treatment.

PATIENTS AND METHODS:

A retrospective questionnaire-based study was done including 20 patients operated for intrathecal baclofen pump insertion at neurosciences hospital from 1/1/2013 to 1/1/2018,

RESULTS:

According to GMFCS in C.P, only those who were grade 4 or 3 had benefit, while grade 5 patients only improved easier diapering and transfer. From 8 spinal cord injury cases, 7 had improvement, while both M.S. cases were improved, but one of them started to have tolerance four years after implantation. Eighteen out of 20 patients were satisfied from ITB therapy

One patient suffered from side effects (nausea, drowsiness) only after the test dose, and no side effects were mentioned during continuous therapy.

Two patients had drug tolerance were required to increase the dose.

CONCLUSION:

Intrathecal baclofen is a good treatment for spasticity, it can be considered safe as it caused no serious side effects, intrathecal baclofen is safer than oral baclofen because it uses a smaller dose, and it regarding tolerance, it occurs but not in every patient.

KEYWORDS: Baclofen, Infusion pump, Intrathecal baclofen, Spasticity.

INTRODUCTION:

Spasticity: is a motor disorder characterized by a velocity-dependent increase in muscle tone with exaggerated tendon jerks, resulting from stretch reflex hyperexcitability, as a component of upper motor neuron syndrome. It is related to loss of inhibitory effects from descending supraspinal nuclei.

Intrathecal baclofen:

Baclofen that's injected intrathecally acts on receptors in the grey matter of dorsal column of spinal cord, and by direct infusion into cerebrospinal fluid the drug is concentrated where it is needed for its therapeutic effect².

Physiologic action of baclofen:

Baclofen has an effect only on the B type (GABA_B) which is a transmembrane protein that affects calcium and potassium channels. Baclofen produces great reduction in monosynaptic and polysynaptic spinal reflexes, This effect is bought by activation of the

GABA_B receptors, which decreases Calcium entrance into the presynaptic ends of the afferent fibers; thus, it reduces the release of excitatory transmitters. Baclofen can also increase Potassium influx on the postsynaptic membrane, thereby stabilizing or increasing the membrane potential and inhibiting neuronal firing².

Instrumentation:

The Medtronic Synchromed Infusion II ® system is used to treat spasticity with continuous intrathecal Baclofen in children with cerebral palsy. The components of this system are a surgically implanted, battery-powered pump that's connected to a flexible, radiopaque intrathecal Silicone catheter. The drug dose and mode of delivery (bolus or continuous) are adjusted to every patient's needs with an external programming device using radiofrequency telemetry (Figure 1-1). The pump is available in two sizes that are both about the diameter of a hockey puck; still, there is difference in volume of the drug reservoir (either 20 or 40 mL) (Figure 1-2). The drug reservoir is accessed percutaneously in the outpatient clinic

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INTRATHECAL BACLOFEN PUMP

setting to refill the pump. The 20-mL reservoir pump is slimmer and has less volume occupancy compared to the 40-mL pump, making it more

suitable for smaller, thinner patients⁵. Catheters are available in 1- or 2-piece models that are supplied with, guide wires, spinal needles, and suitable anchoring devices.

Table (1-1): Gross Motor Function Classification System³.

Level I	Children walk indoors and outdoors and in the community. They can climb stairs without the need for assisting devices. Children can perform gross motor skills such as running and jumping, but speed, balance and coordination are limited.
Level II	Children ambulate in most conditions and climb stairs holding onto a railing. They may have difficulty walking long distances and balancing on uneven terrain, inclines, in crowded areas or confined spaces. Physical assistance may be needed to help children walk, they may use a handheld mobility device or wheeled mobility over long distances. Children have only little ability to perform gross motor skills such as running and jumping.
Level III	Children walk using a hand-held mobility device in most indoor places. They can climb stairs holding onto a railing with supervision or assistance. Children need wheelchairs for traveling long distances and may be able to move by themselves in short distance.
Level IV	Children physical assistance or powered mobility for mobility in most settings. They may walk for short distances at home with physical assistance or use powered mobility or a body support walker when positioned. At school, outdoors and in the community, they need a manual wheelchair or use powered mobility.
Level V	Children use a manual wheelchair to ambulate in all settings. Ch Their ability to maintain antigravity head and trunk postures and control leg and arm movements is limited



Figure 1-1: The 8840 N'Vision programmer .

INTRATHECAL BACLOFEN PUMP



Figure 1-2: SynchroMed II pump showing the catheter access port and the reservoir fill port

PATIENTS AND METHODS:

A retrospective questionnaire based study was done including 20 patients operated for intrathecal baclofen pump insertion at neurosciences hospital from 1/1/2013 to 1/1/2018, 16 males and 4 females, (3 C.P and 1 S.C.I), ages are between 9 to 60 years old, the diagnosis was cerebral palsy in 10 patients, spinal cord injury in 8 patients, and multiple sclerosis in 2 patients.

Some of the patients interviewed during their hospital visit for refilling, and others by phone call.

6. .

All responded to an initial test dose of baclofen before surgery.

Data assessed:

1. Effect of intrathecal baclofen on motor function depending on GMFCS in CP patients
2. Effect of intrathecal baclofen on daily activity, in terms of diaper change, patient transfer and changing clothes.
3. Drug side effects
4. Drug tolerance
5. Overall patient and care giver satisfaction

RESULTS:

Table (3-1) : Showing the distribution of spasticity causes on gender

	CP	SCI	MS
Male	7	7	2
Female	3	1	-
age	9- 22	17- 60	40, 45

The cases of patients in the study were: 10 cerebral palsy cases, 8 spinal cord injury cases, and 2 multiple sclerosis cases.

According to G.M.F.C.S. in C.P, patients, 4 of them were grade 5, 3 of these did not improve in terms of GMFCS but had improvement in diaper

change, and using wheelchair and one of them did not show any improvement at all. The rest of C.P. patients were 3 grade 4, and 3 grade 3, patients, one of them improved by two scales and the rest improved by one scale, as shown in the following table:

Table (3-2) : Cerebral palsy patient response according to gross motor function classification system.

GMFCS grade	Number of patients	Average improvement according to GMFCS
Grade 5	4 of 10	No improvement
Grade 4	3 of 10	1.3 scale
Grade 3	3 of 10	One scale

8 spinal cord injury cases, 7 had subjective improvement in performing daily activities like diaper change, wheelchair use, and clothes change, one had temporary improvement and was back to pre-treatment state. And both M.S. cases were improved in terms of muscle tone and patient care, but one of them started taking oral medications along with intrathecal baclofen about four years after implantation because he started to develop tolerance, but a lower dose than oral treatment alone. Talking about patient satisfaction with treatment: 18 patients were satisfied and two of them (one CP, and one SCI) were not satisfied with their results. One patient suffered from side effects (nausea, drowsiness) only after the test dose, and no side effects were mentioned during continuous therapy. Two patients had drug tolerance and required to increase the dose.

DISCUSSION:

Penn and Kroin first reported the usage of ITB pump therapy in 1984 for the management of spinal spasticity^{5,6}.

Afterward, intrathecal baclofen therapy has been shown to improve spasticity, muscle function, and patient care by several studies involving patients with, stroke, spinal cord injury, cerebral palsy, and familial spasticity syndromes^{5,7,8,9}.

In this study which was done at neuroscience hospital in Baghdad, 20 patients suffering from spasticity were investigated after they had intrathecal baclofen pump implantation surgery.

Results that were obtained from patients with cerebral palsy were quantified using gross motor function classification system for children and young people, as all of them were either young adults or children. Intrathecal baclofen efficacy in patients with spinal cord injury, and multiple sclerosis was measured based on subjective improvement in terms of patient care, wheelchair use, changing diapers, and overall patient or next of kin satisfaction.

Among C.P. patients, the greater benefit was for those who were grade 4 according to GMFCS which were improved by an average 1.3 scales as compared to one scale in those who were grade 3 and grade 5 patients that had no improvement at all.

Ashworth scale was not used because this is a retrospective study and there is no available pre-implantation data about their Ashworth scale, so, results can not be compared.

Subjective overall satisfaction was 18 of 20 patients. 18 patients out of 20 patients had subjective improvement in their muscle tone manifested by easier limb flexion during patient

transfer and diaper change and it was easier for them to use wheelchairs, and these results are similar to another study done by Stempien, et al. from the Rehabilitation Center, The Children's Hospital, University of Colorado on 40 centers that done 936 pump placements, and showed Improved daily activities including easier diapering, dressing, transfers, orthotic wear and comfort, and sitting tolerance that reported in the majority (>90%) of patients¹⁰. and a study done by Peter Kan, et al. on Surgical treatment of spasticity in children: comparison of selective dorsal rhizotomy and intrathecal baclofen pump implantation that resulted in a high degree of patient satisfaction on both intrathecal baclofen therapy and selective dorsal rhizotomy¹¹ and care provider satisfaction as one study done by Judith L Gooch showed that Ninety-five percent of care providers agreed that they would have this procedure performed again⁸.

The neuroscience hospital contains a multiple sclerosis consultation clinic, and there is a lot of drainage of M.S. patients to this hospital from all over the country, hence the two M.S. patients that were included in the study who could get benefit from ITB, although one of them had drug tolerance and needed oral baclofen along with intrathecal baclofen.

There weren't any drug side effects except for one patient who had nausea and drowsiness after receiving the test dose as compared to 2.2% N/V and 2.6% sedation on the test dose in a study published by American Journal of Physical Medicine & Rehabilitation¹⁰ which is nearly close to our study.

Tolerance is experienced only in two patients, and both of patients that experienced tolerance were using the drug for four and five years, an article by S. Estrela Rego⁹ that included a patient who underwent intrathecal baclofen implantation in 2002 on a dose of 310 mcg/day, then in 2009 suffered resurgence of severe spasticity resistant to a fast increase on daily dose of baclofen up to 360 mcg/day, and after a drug holiday of 4 weeks, the patient condition was controlled again on 220 mcg/day, so drug holidays can be a solution for drug tolerance.

Another study¹² about the incidence and management of tolerance in intrathecal baclofen therapy published on October 2009 found that after initial dose stabilization, 22% of patients needed the dose to be increased to >100 microgram per year, and in that study, pulsatile bolus infusion and a drug holiday were both effective in reducing the daily baclofen dose.

CONCLUSION:

- Intrathecal baclofen therapy is a good solution for those who suffer disabling spasticity of different causes.
- baclofen is a safe treatment as it caused no serious side effects, except for the test doses, as most of patients in the study could get the wanted therapeutic effect.
- Intrathecal dose is so small that it even causes more tolerable side effects.
- Tolerance does occur sometimes after using the drug for a long time and the patients may need their dose to be increased to have the same therapeutic effect, but it does not occur to every patient.

Recommendations

- More studies need to be done on intrathecal baclofen therapy including larger numbers and longer follow up, and more investigations about drug tolerance and its solutions
- We need to spread awareness among general populations about such therapies to give chance to spasticity patients to reach medical care before they develop limb contractures that makes treatment less effective on patients' lives
- A spasticity clinic to be started, to make it easier for the patient to know where to go and what to do, and help them get better medical care.
- Making baclofen ampoules and infusion pump devices more readily available for spasticity patients as many of them suffer a low socioeconomic state and are unable to buy baclofen.

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