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ORIGINAL ARTICLE

# Occurrence of Adverse Events in Long-Term Intrathecal Baclofen Infusion: A 1-Year Follow-Up Study of 158 Adults

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**Abstract**

**Objective:** To assess the frequency and types of adverse events (AEs) related to intrathecal baclofen (ITB) therapy in adults, and associated risk factors.

**Design:** A prospective, observational cohort study of adults followed up from January 1 to December 31, 2010.

**Setting:** A neurologic rehabilitation department in a university hospital.

**Participants:** All consecutive adult subjects (N = 158) receiving ITB via a pump, either implanted or followed up during the study period.

**Intervention:** Not applicable.

**Main Outcome Measures:** Frequency and type of AEs.

**Results:** In 2010, 158 subjects were followed up for ITB therapy, of whom 128 were implanted before 2010 (nonsurgical subjects), and 30 underwent implantation in 2010 (surgical subjects). Of these 30 subjects, 20 were "newly implanted" and 10 were "replacements." The most frequent pathologic disorders were spinal cord injury (42%) and multiple sclerosis (28%). Twenty-eight subjects (18%) experienced a total of 38 AEs. The rate of AEs was .023 per month of ITB treatment. AEs were related to the surgical procedure in 53% of cases, to the device in 29% (predominantly catheter dysfunctions), and to adverse effects of baclofen in 18%. AEs related to the surgical incision (scar complications and collections) were more frequent in replacement than newly implanted subjects ($P = .009$). No significant association between occurrence of an AE and subject characteristics (age, gait capacity, spinal vs cerebral spasticity, duration of ITB therapy follow-up) was found. Nearly half of the AEs were serious, extending admission time by a mean of 16 days. No AE induced long-term morbidity or death.

**Conclusions:** The AE rate was relatively low in this cohort. This has to be balanced against the clinical, functional, and quality-of-life improvements, which are expected from ITB therapy.

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Spasticity, a manifestation of central nervous system lesions, can have various negative consequences, including reduced movement capacity and gait perturbations, difficulty with transfers, and difficulty in the provision of nursing care, and it can also cause pain.[1] Since the first publication by Penn and Kroin,[2] the long-term administration of intrathecal baclofen (ITB) via an implanted pump has become an essential therapeutic resource for generalized refractory spasticity. Major indications for ITB therapy are spinal cord injury (SCI), cerebral palsy, and multiple sclerosis (MS); however, indications are becoming broader after successful trials in different neurologic conditions.[3,4] ITB therapy dramatically reduces spasticity and spasms, improving activities and quality of life.[5,6] It has also been used to reduce spasms, which are not

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spasticity related, in Friedreich's disease.[7] Moreover, cost-effectiveness studies support ITB therapy compared with conventional treatments for disabling spasticity.[8]

Adverse events (AEs) related to ITB therapy are mostly reported in retrospective studies or in small cohorts.[5,6,9-11] Some studies describe the total number of AEs in a cohort without any relation to follow-up duration. Other studies describe "device-related" AEs (caused by problems relating to the pump or catheter) or "surgical procedure—related" AEs (occurring during, or as a result of, pump or catheter implantation or revision); however, "drug-related" AEs (related to the baclofen itself) are not reported. It would therefore be useful to expand the knowledge base about ITB-related AEs in order to help evaluate the benefit-risk balance of ITB therapy, and to institute preventive measures to reduce the incidence of ITB-related AEs. An increased understanding of ITB-related AEs would also help to better inform subjects and their carergivers, and to direct treatment strategies. The aims of this study were to prospectively assess ITB-related AEs in a large cohort of adult subjects treated by ITB therapy and to determine their risk factors.

## Methods

### Study design

This was a prospective observational study of adult subjects undergoing ITB therapy in the neurorehabilitation department of a university hospital from January 1 to December 31, 2010. This department includes inpatients, outpatients, and ambulatory care for individuals with disabilities relating to various neurologic conditions. Trained practitioners routinely perform pretreatment evaluations, presurgical and postsurgical care, follow-up, management of complications, and refilling and adjustment of ITB therapy on site. All ITB-related surgery (implantation, replacement, surgical management of complications) is performed in a single neurosurgical department of another hospital. After implantation, subjects are transferred to our neurorehabilitation department for a stay of usually 15 days, to initiate management of their pumps.

### Implantation procedure

The patient undergoes general anesthesia and is placed in lateral decubitus. An incision is made in the lower lumbar spine. Then a Tuohy needle is used to enter the thecal sac, and the spinal catheter is advanced to the predetermined spinal level using a guidewire. The spinal catheter tip is usually placed in the lower thoracic region (T10-12). A suture loop can be made at the spinal canal exit to prevent cerebrospinal fluid (CSF) leak. The pump is placed in a subcutaneous abdominal pocket below the lower ribs and is connected to the abdominal catheter. Our neurosurgical team does not usually secure the pump in its pocket, since suture loops could fix the pump regardless of anatomic conditions. Furthermore, the neurosurgical team found that during pump revision, several complications of the scar occurred as a result of the Dacron pouch, so its use was discontinued. The abdominal catheter is tunneled from the abdominal incision to the spinal site and connected to the spinal catheter.

In case of pump replacement, the spinal catheter is not replaced unless a catheter dysfunction is suspected (if there is a large degree of spasticity or high daily doses of baclofen are required). When the catheter is not replaced and the baclofen concentration has not changed, the flow is checked and then the catheter is clamped before pump revision. When the catheter is not replaced and the baclofen concentration is changed, the catheter is emptied by aspiration before administering a baclofen bolus with the new pump.

*List of abbreviations:*

| | |
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| **AE** | **adverse event** |
| **CI** | **confidence interval** |
| **CSF** | **cerebrospinal fluid** |
| **ITB** | **intrathecal baclofen** |
| **MS** | **multiple sclerosis** |
| **OR** | **odds ratio** |
| **SCI** | **spinal cord injury** |

### Participants

All individuals undergoing ITB therapy who received any care in the study site were included, regardless of inpatient versus outpatient status. There was no exclusion criterion. Subjects who joined or left the cohort during the study period were also included. Their first or last consultation dates were used to calculate their duration (in months) of follow-up during 2010. Subjects were classified into 2 groups according to their clinical situation, as described in similar studies.[12] They were classified as "surgical" if they had either a primary pump placement (newly implanted subjects) or a pump revision (replacement subjects) in 2010. Subjects who had been implanted before 2010 were classified as "nonsurgical subjects."

### Data collection

AEs are routinely collected at several levels in the neurorehabilitation department. In addition to the usual medical records, individuals have a separate "pump record" that is completed at each refill or dose-adjustment consultation. Specific data relating to the ITB therapy are recorded in it (date, current and new dose or concentration, AEs, clinical examination, effectiveness on spasticity, printed pump settings). The pump is interrogated and the logs are checked at each refill appointment and after any incident occurring during follow-up. In the refill department, a consultation register is also used. This is for administrative purposes. The patients who attended each day, problems with appointment dates, and every incident (such as subjects missing an appointment or telephoning because of any problem) are recorded in it. Furthermore, during the study period, every department practitioner who received a telephone call or performed a clinical assessment because of an ITB therapy AE completed a specific file designed for the follow-up study. To further ensure that no AE was missed during the 12-month follow-up, the hospital database was searched for 2010 by using specific codes related to the presence, management, or implantation of an ITB device, and records of any individuals with these codes were reviewed.

Long-term adverse effects were defined as AEs that occurred over a long period and for which the initial onset was difficult to define. They were noted from spontaneous complaints of the individuals or their family. These long-term adverse effects are generally nonspecific, and it was necessary to ensure that they were related to ITB therapy. Imputability was defined as a change from the prepump clinical condition, associated with significant discomfort and confirmed by clinical and paraclinical investigations.