Managing loss of intrathecal baclofen efficacy

Review of the literature and proposed troubleshooting algorithm

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Summary

Spasticity is a debilitating symptom associated with numerous neurologic conditions. While intrathecal baclofen therapy (ITB) is an established treatment for spasticity, complications can lead to loss of efficacy (LOE) and baclofen withdrawal. Untreated withdrawal syndrome can be fatal. Prompt diagnosis and management of LOE is essential. Numerous methods have been described in the literature for diagnosing the cause of LOE. Many of the methods require equipment not readily available in the outpatient setting. Furthermore, there is no established consensus on the sequencing of these diagnostic tests. Herein, we review ITB literature on troubleshooting LOE for applicability to the managing clinician. Using this information and our clinical experience, we propose an algorithm with management recommendations to simplify and expedite the troubleshooting process in the outpatient setting.

Spasticity is associated with numerous neurologic conditions. It is painful, functionally debilitating, and associated with complications including joint contractures and decubitus ulcers. Baclofen, the most common pharmacotherapy for spasticity, is a synthetic agonist of the GABA_B receptor, found predominantly in Rexed lamina II and III of the dorsal spinal cord.¹ The use of oral baclofen for spasticity has some drawbacks. Being

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lipophilic, orally ingested baclofen has poor penetration through the blood–brain barrier and the ratio of CSF-to-plasma concentration is very low and usually variable.² Titrating oral baclofen often results in side effects such as somnolence and confusion, which limits the total oral dose that can be tolerated.³

The strategy devised to overcome this limitation is direct delivery of baclofen into the subarachnoid space via intrathecal delivery. Since their inception in the 1980s, advances in drug delivery system technology have led to the development of sophisticated pumps. The latest generation of implantable programmable pump is the SynchroMed II.⁴ In the United States, about 80,000 intrathecal drug delivery pumps have been implanted, and the number is expected to grow as more indications for intrathecally delivered therapeutics are defined.⁵

While intrathecal baclofen (ITB) therapy is an established treatment for spasticity, complications with the therapy can lead to loss of efficacy (LOE) and subsequent baclofen withdrawal.⁶ Since untreated baclofen withdrawal syndrome can be fatal, efficient troubleshooting is essential. There is no established consensus on troubleshooting LOE, representing an unmet need in the field of spasticity management. Moreover, since LOE often presents to the managing clinician in an outpatient setting, specific consideration should be made for clinicians without access to fluoroscopy, CT catheter diagnostics, or in-clinic flat radiographs.

In this article, we review the ITB literature on troubleshooting LOE and managing its possible complications. Using this information and our clinical experience, we develop a simple and effective algorithm with management recommendations for the outpatient setting, including perioperative considerations, to simplify and expedite the troubleshooting process.

Review of the ITB troubleshooting literature

A literature search was performed via PubMed and Google Scholar. Searched terms included “intrathecal baclofen” combined with “troubleshooting,” “algorithms,” “exacerbated spasticity,” “complication,” or “enhanced spasticity.” The SynchroMed II Programmable Infusion System Clinical Reference Guide was also reviewed. This revealed 6 troubleshooting algorithms,^{4,7–11} summarized in the table. The authors employ a sequence of diagnostics designed to assess system integrity, identify specific causes of malfunction, and propose actions to restore therapy. There are a total of 12 diagnostics proposed. The following is a description of each troubleshooting method including commentary (in *italics*) on applicability for managing clinicians.

1. Triage history and physical examination: Assess for noxious stimulation, infection, concomitant medication effects, and underlying disease progression. *This is the first step in 4 algorithms and is a critical first step in evaluating LOE.*
2. Pump interrogation: Review logs for evidence of alarms or errors in recent programming. The SynchroMed II pump has alarms for low battery, low reservoir volume, memory error, elective replacement indicator, empty reservoir limit, end of service, motor stall, tube set interval, and stopped pump duration exceeding 48 hours.⁴ *This appears as the first or second step in all algorithms and takes minutes to perform in the clinic.*
3. Verify reservoir volume: Aspirate entire volume of baclofen from the reservoir and compare with the calculated volume provided by the programmer. Significant discrepancies (>25%) may indicate catheter occlusion, faulty catheter-pump connection, or motor stall.⁸ *This appears in 2 algorithms and takes less than 10 minutes to perform in the clinic.*
4. Plain radiographs: Obtain posterior-anterior and lateral views of the thoracic and lumbar spine to include the entire system from pump to catheter tip, which may reveal gross catheter fracture, dislodgment, migration, or kink.¹² *This appears in all algorithms without consensus on sequencing. Flat radiographs are unavailable in most clinics.*
5. Programmed ITB bolus: Program the pump to deliver a prescribed bolus, then observe the patient for several hours for decreased spasticity.⁴ *This appears in all algorithms without consensus on sequencing. Failure to respond suggests system malfunction.*
6. Rotor study: Obtain a radiograph of the pump to visualize the rotor. Then program a specific bolus that rotates the rotor a known amount and repeat radiographs. Failure to

Table Published ITB troubleshooting algorithms

Order	Reference 7	Reference 8	Reference 9	Reference 10	Reference 11	Reference 4
Step 1	Interrogate pump	Triage history	Triage history	Triage history	Interrogate pump	Triage history
Step 2	AP and lateral abdominal radiographs	Interrogate pump	Interrogate pump	Interrogate pump, workup rotor stall, consider program ITB bolus	Program ITB bolus	Interrogate pump
Step 3	Rotor test	Rotor test	Program ITB bolus	AP and lateral radiographs of TLS spine and abdomen	Plain radiographs	If motor stall alarm then rotor test
Step 4	If withdrawal syndrome then program ITB bolus	AP, lumbar, abdominal, and thoracic radiographs	Verify reservoir volume	Program ITB bolus (if not previously done)	Fluoroscopic dye study	Verify reservoir volume (calculate flow rate error)
Step 5	ITB bolus via LP	CAP aspiration	Thoracic and lumbar radiographs	CAP aspiration then fluoroscopic dye study and CCBCT	CT dye study	If flow rate normal then program ITB bolus
Step 6	CAP aspiration and fluoroscopic dye study	Program ITB bolus	Rotor study	Reprogram pump		If flow rate >25% error then radiographs
Step 7	DTPA study	Spiral CT dye study	CAP aspiration			CAP aspiration
Step 8		ITB bolus via LP or empirically replace catheter	Fluoroscopic dye study			If CAP aspiration unsuccessful then DTPA study
Step 9		CT dye study	DTPA study			If CAP aspiration successful then fluoroscopic dye study

Abbreviations: AP = anterior-posterior intrathecal baclofen; CAP = catheter aspiration port; CCBCT = C-arm cone beam CT; ITB = intrathecal baclofen; LP = lumbar puncture; TLS = thoracic, lumbar, and sacral.

rotate the expected amount indicates pump failure.¹² *This appears in 5 algorithms. We do not find a rotor study early in troubleshooting to be of high diagnostic yield. Rotor stall accounts for <1% of all systems malfunctions¹³ and should not occur without an audible alarm. This test is difficult to perform within a standard clinic visit.*

7. Catheter aspiration port (CAP) aspiration: Aspirate 3–4 mL of fluid from the CAP. Occlusion or difficulty aspirating (e.g., bubbles, poor return) is abnormal.¹² *This appears in 5 algorithms without consensus on sequencing. CAP aspiration is a key diagnostic troubleshooting step because a higher percentage of system malfunctions is attributable to catheter problems as compared to pump failure.^{13,14} It can be performed in 10 minutes in the clinic.*
8. Fluoroscopic catheter dye study: Aspirate CAP to clear baclofen from the catheter. If aspiration is unsuccessful, injecting dye is contraindicated because it could unplug an obstruction and overdose the patient with an ITB bolus. Intrathecally approved contrast material is injected through the CAP to identify catheter fractures and microfractures.¹² *This appears in 2 algorithms. Because the high pressure and volume of injected contrast can bypass fractures and overwhelm small loculations, dye studies have a high false-negative rate.⁸ Fluoroscopy is unavailable in most outpatient clinics.*
9. Spiral CT dye study: Conduct a fluoroscopic dye study while the patient is supine on the CT scanner gantry, immediately followed by spiral CT of the entire catheter length. The patient should not be injected in a different room then transferred to the CT suite because this results in mixing contrast and CSF, thereby diminishing sensitivity.^{8,15} *This*

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appears in 2 algorithms, intended to improve sensitivity over a traditional dye study. This is not available in most clinics and requires the clinician to be present at the study to inject dye.

10. Combination C-arm fluoroscopy dye study and C-arm cone beam CT (CCBCT). Conduct fluoroscopic dye study then confirm findings with CCBCT.¹⁰ *This appears in 1 algorithm, intended to improve sensitivity over a traditional dye study. Interventional radiology suites with fluoroscopy and CCBCT are unavailable to most managing clinicians.*
11. DTPA nuclear scintigraphy: ¹¹¹In DTPA, a radioisotope with a long half-life is injected into the reservoir. Radioactivity is monitored as it travels through the catheter into the subarachnoid space over several days.¹⁶ *This appears in 1 algorithm. This test is costly, requires ≥ 2 days to perform, has low sensitivity, and requires precise flow rate calculations to predict the timing of final imaging acquisition.*¹⁶
12. Lumbar puncture ITB injection: As with an initial ITB screening test, this clarifies the patient's response to intrathecally delivered baclofen. *This appears in 2 algorithms.*

All 6 algorithms contain a host of useful troubleshooting measures. However, the protocols vary regarding which diagnostics to include and their sequencing. Several include steps that are time-consuming, have high false-negative rates, and require equipment unavailable to most managing clinicians. There remains a need for a troubleshooting algorithm including diagnostics with low false-negative rate, ordered to optimize speed and ease of diagnosis. We appropriated many of the tests provided by the aforementioned authors, combined with our own clinical experience, to create such an algorithm (figure). This diagnostic algorithm was developed with the following assumptions: managing clinician is not the implanting surgeon and does not have ready access to fluoroscopy, CT catheter diagnostics, or in-clinic flat radiographs.

When to consider ITB troubleshooting

LOE typically presents in 3 ways. The first scenario is return of pathologic tone following adequate spasticity control on stable ITB dosing. The second scenario is inability to optimize ITB therapy despite adequate dose escalation. The third scenario encompasses a group of uncommon syndromes involving fluctuations in ITB response.¹⁵ All scenarios can include signs and symptoms of baclofen withdrawal, including pruritus, return of pathologic tone, fever, confusion, somnolence, and seizures. The withdrawal syndrome manifests as a spectrum from mild to life-threatening and patients can experience LOE in the absence of symptoms. If baclofen withdrawal is suspected it must be treated as a potential medical emergency.⁶ As part of best practices, we recommend initiating the algorithm when a patient's total daily ITB dose exceeds an a priori clinical threshold (e.g., >800 mcg/day). We recommend performing the algorithm up to and including a diagnostic CAP aspiration as part of a scheduled annual diagnostic evaluation of the ITB system.

Proposed diagnostic troubleshooting algorithm

Step 1: Evaluate patient-related etiologies for LOE including noxious stimulation, infection, concomitant medication effects, and underlying disease progression Evaluating noxious stimulation includes visualizing dependent body parts for pressure ulcers, assessing ergonomics of seating and sleeping conditions, and screening for constipation and urinary retention. Screening for infection should include a complete physical examination and appropriate

Figure ITB troubleshooting algorithm

CAP = catheter aspiration port; ITB = intrathecal baclofen; PA = posterior-anterior.

ancillary tests. Review medication history for agents that can exacerbate spasticity, including selective serotonin reuptake inhibitors,¹⁷ interferon- β ,¹⁸ dextroamphetamine,¹⁹ and theophylline.²⁰ If a patient-related cause of LOE is identified, it is addressed and the patient is reevaluated. Otherwise, proceed to step 2.

Step 2: Interrogate pump, read logs and alarms Evidence of pump malfunction results in referral for replacement; otherwise, proceed to step 3.

Step 3: Verify reservoir volume This information will be used in conjunction with step 4. If abnormal, proceed to step 4A. If normal, proceed to step 4B.

Step 4A: Diagnostic aspiration of the CAP If reservoir volume (step 3) is abnormal and CSF aspiration is impossible or ambiguous (e.g., difficulty withdrawing CSF, bubbles), then refer for catheter replacement. If reservoir volume is abnormal and CAP aspiration is unobstructed, then refer for pump replacement or possibly consider rotor study. This is an example of an unlikely instance where rotor studies are useful in diagnosing a pump-related problem.

We recommend performing the algorithm up to and including a diagnostic CAP aspiration as part of a scheduled annual diagnostic evaluation of the ITB system.

Step 4B: Diagnostic aspiration of the CAP If unable to aspirate, then refer for catheter replacement. If aspiration appears abnormal or ambiguous, then proceed to step 5. If aspiration reveals unobstructed CSF flow, then proceed to step 6.

Step 5: Obtain posterior-anterior and lateral radiographs of thoracic and lumbar spine Identification of gross kink, fracture, or dislodgment results in referral for catheter replacement.

Step 6: Program an ITB bolus⁶ If there is no subsequent reduction in spasticity, then refer for catheter replacement. If spasticity decreases, proceed to step 7.

Step 7: Switch programing from simple continuous to bolus dosing²¹ and consider increasing daily dose If the patient's spasticity improves, then follow per standard clinic practices. If not, discuss next steps with the implanting surgeon, such as replacing ITB system, catheter study, or ITB bolus via lumbar puncture.¹²

Preoperative management

Clarify surgical goals including catheter tip placement, pump size, postoperative rehabilitation plans, and preoperative and postoperative ITB dosing. This last point is particularly important because if a system malfunction accounts for LOE, then the patient's actual preoperative ITB dose is unknown. Therefore, there is a risk of unintentional overdosing or underdosing postoperatively. We recommend tapering the dose by 20%–30% weekly to a preoperative target (e.g., 100 mcg/day). Return of tone is managed with oral baclofen. As part of best practices, we recommend that catheter integrity be assessed whenever a pump replacement is scheduled. This allows replacement of the entire system if a concomitant catheter problem is detected.

Best surgical practices during ITB pump/catheter replacement

When a system malfunction has been identified, then the patient is referred to replace the dysfunctional components. The following section provides the managing clinician with an overview of surgical techniques employed to accomplish this and reduce risk of future system complications.

In situations of pump malfunction or end of battery life, the surgical objective is limited to pump replacement. When catheter malfunction is the source of LOE, we recommend changing the entire catheter system, even if a specific cause (e.g., fracture) has not been identified in the preoperative workup, as there may be multiple microfractures or intraluminal obstructions along the length of the catheter. During revision surgery, obvious catheter disruptions or fractures are visualized. We do not perform further studies intraoperatively as the preferred strategy is to change the entire catheter system. It should be noted that CSF might still flow in partially blocked catheters, which further supports our preference for changing the entire catheter. We are encouraged by our early experiences using the Ascenda catheter, which we hope will result in fewer catheter malfunctions.

Removing the entire catheter system will require reopening the incisional scar over the pump location to disconnect the catheter from the old pump. In this case, a mesothelial subcutaneous pocket will have usually formed over the old pump and there is no need to recreate another pocket. Importantly, a nonabsorbable suture is applied to the lumbar fascia at the entry point of the removed old catheter to prevent CSF leak.

The objective of new catheter implantation is to reduce risk of breakage by minimizing catheter stressors such as compression between spinous processes. Proper intrathecal catheter tip

placement is confirmed by visualizing CSF egress during each step of the procedure and prior to connecting catheter and pump. The new pump is placed within its subcutaneous pocket and any extra length of catheter is coiled below the pump to protect it from needle puncture during reservoir refilling. A strain relief loop of catheter is left in the lumbar wound. Successful CAP aspiration prior to system component connections provides a final visual confirmation of system integrity before anchoring and wound closure.

Postoperative considerations

The use of abdominal binders for the first postoperative month reduces risk of seroma formation and may reduce spinal headaches. We recommend restarting postoperative dosing ≤ 100 mcg/day to avoid unintentional overdose.

DISCUSSION

Loss of ITB efficacy does occur and should be identified early and dealt with efficiently. We reviewed ITB troubleshooting literature for applicability to outpatient practice. Based on this critical review and our clinical experience, we constructed an algorithm with management recommendations, including perioperative considerations, to simplify and expedite the troubleshooting process. Our proposed algorithm differs from previously published work in several ways. We omitted several commonly used diagnostic tests because, although they may help identify the exact cause of a system malfunction (e.g., microfracture), they do not change the need for system replacement. We recommend early CAP aspiration because of its high diagnostic yield for detecting catheter obstruction, a common cause of system malfunction. When abnormal, this allows for prompt referral for catheter revision and avoids additional time-consuming and complicated testing such as catheter dye studies. We also included tests that can be performed efficiently during a standard outpatient appointment, making our algorithm widely applicable to most managing clinicians. Whereas no single troubleshooting algorithm could diagnose every possible cause of LOE, we find our proposed algorithm to address most problems commonly seen in the outpatient setting.

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