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Successful management for baclofen tolerance using pulsatile bolus infusion during intrathecal baclofen therapy: a case report

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Case Report

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Abstract

Background

Intrathecal baclofen (ITB) therapy is an established treatment for severe spasticity associated with spinal cord injury, multiple sclerosis, cerebral palsy, and other neurological disorders. Although ITB therapy generally provides durable symptom control, baclofen tolerance occasionally develops during long-term treatment. Pulsatile bolus infusion has been proposed as a therapeutic strategy; however, detailed reports describing optimization of infusion timing remain limited.

Case presentation

A 66-year-old Japanese man with spinal myoclonus underwent ITB therapy after oral antispastic medications failed to control severe spasticity. Approximately 15 years after initiation of ITB therapy, progressive worsening of spasticity occurred despite escalation of the intrathecal baclofen dose to >250 μg/day. Mechanical complications of the ITB system were excluded radiologically, and baclofen tolerance was clinically suspected.

The infusion mode was changed from continuous infusion to pulsatile bolus infusion. Four daily bolus infusions failed to improve symptoms, whereas eight daily bolus infusions reduced spasticity but exacerbated arrhythmia. Subsequently, six daily bolus infusions timed before anticipated symptom exacerbation successfully improved spasticity without increasing the total daily baclofen dose. Sleep quality and activities of daily living also improved, and arrhythmia resolved.

Conclusions

This report describes the detailed clinical course of baclofen tolerance successfully managed using individualized pulsatile bolus infusion during long-term ITB therapy. Optimization of bolus timing according to symptom patterns and concomitant medications may improve therapeutic efficacy while minimizing adverse effects. Pulsatile bolus infusion should be considered before further dose escalation in patients with suspected baclofen tolerance.

Background

Spasticity is a motor disorder characterized by increased muscle tone, exaggerated tendon reflexes, and increased resistance to passive movement. Severe spasticity may markedly impair mobility, sleep, and activities of daily living. Intrathecal baclofen (ITB) therapy is widely recognized as a safe and effective treatment for medically refractory spasticity associated with spinal cord injury, multiple sclerosis, cerebral palsy, and other neurological disorders [1–4].

Baclofen acts as a gamma-aminobutyric acid B (GABA_B) receptor agonist at the spinal cord level. Because oral baclofen penetrates the blood–brain barrier poorly, high systemic doses are often required to achieve sufficient therapeutic concentrations within the central nervous system, resulting in adverse

effects such as drowsiness and muscle weakness [5, 6]. ITB therapy enables direct drug delivery into the cerebrospinal fluid, allowing effective spasticity control at substantially lower doses.

Although ITB therapy generally provides durable symptom control, baclofen tolerance has occasionally been reported during long-term treatment [7–9]. Management strategies for baclofen tolerance include dose escalation, drug holidays, and modification of infusion patterns. Previous studies have suggested that pulsatile bolus infusion may reverse baclofen tolerance [10, 11]; however, detailed descriptions of the stepwise clinical course and optimization of infusion timing remain limited.

We report the detailed clinical course of a patient with baclofen tolerance that developed approximately 15 years after initiation of ITB therapy and was successfully managed using individualized pulsatile bolus infusion.

Case presentation

A 66-year-old Japanese man underwent cervical laminoplasty from C4 to C7 for cervical myelopathy 18 years previously. Although neurological symptoms initially improved after surgery, he subsequently developed progressive spasticity involving both the upper and lower extremities and was diagnosed with spinal myoclonus 16 years previously. Because oral medications failed to adequately control his symptoms, he was referred to our department for consideration of ITB therapy.

The patient had no relevant family history and no history of smoking or alcohol consumption. A programmable intrathecal baclofen pump (SynchroMed II; Medtronic, Minneapolis, MN, USA) was implanted in the left lower abdomen 15 years previously. Following ITB pump implantation, the patient experienced marked improvement in spasticity, and the spinal myoclonus disappeared.

During long-term follow-up, the patient underwent two pump replacement procedures. Fifteen months before presentation, a new catheter was inserted because of catheter rupture, which was described in our previous case report [12]. Seven months before presentation, the ruptured catheter was removed and partial lumbar laminectomy was performed. Thereafter, spasticity in both the upper and lower extremities gradually worsened.

After partial lumbar laminectomy, the total daily baclofen dose was 150 μg/day; however, spasticity progressively worsened. Despite increasing the dose to more than 250 μg/day, symptom control remained inadequate, and baclofen tolerance was clinically suspected (Fig. 1).

On physical examination, severe spasms were observed in both the upper and lower extremities. The patient was unable to sleep in the supine position and usually slept in a lateral position with flexed hips. Involuntary lower-extremity movements occurred while washing his hair, driving, or when startled.

Spasticity severity was assessed using the Modified Ashworth Scale (MAS) (Table 1) [13]. Initial MAS scores were as follows: hip abduction, 2/1+; hip flexion, 2/1+; knee flexion, 2/1+; ankle dorsiflexion, 2/1+; wrist flexion, 2/1+; wrist extension, 2/1+; elbow flexion, 2/1+; and elbow extension, 2/1+.

Catheter angiography was performed through the catheter access port under fluoroscopic guidance. Spinal myelography demonstrated no leakage of contrast medium. Computed tomography revealed that the catheter tip remained positioned at the ninth thoracic vertebral level, unchanged from the original insertion site, and no contrast leakage was identified (Fig. 2). Mechanical failure, catheter obstruction, and cerebrospinal fluid leakage were therefore excluded.

At presentation, baclofen was administered via continuous infusion at a total daily baclofen dose of 280 μg/day, with a basal infusion rate of 11.7 μg/h. Further dose escalation was avoided because appetite loss worsened during dose escalation.

The infusion mode was therefore changed from continuous infusion to pulsatile bolus infusion. Initially, baclofen was administered as four daily bolus infusions (15 μg administered over 1 minute at 06:00, 10:00, 14:00, and 22:00). The total daily bolus dose was 60 μg, and the total daily baclofen dose remained unchanged at 280 μg/day (Fig. 3). However, spasticity did not improve.

Subsequently, eight daily baclofen bolus infusions were attempted (10 μg administered over 1 minute at 00:00, 03:00, 06:00, 09:00, 12:00, 15:00, 18:00, and 21:00). Although spasticity improved, arrhythmia worsened (Fig. 4). The patient was taking pirsicainide hydrochloride hydrate after meals, and arrhythmia appeared temporally associated with baclofen bolus administration when baclofen boluses were administered during periods of declining pirsicainide concentration.

To avoid bolus administration during periods of decreasing pirsicainide concentration, the infusion schedule was modified to six daily bolus infusions (10 μg administered over 1 minute at 03:00, 07:00, 11:00, 15:00, 19:00, and 23:00). The total daily bolus dose remained 60 μg, and the total daily baclofen dose remained unchanged at 280 μg/day. The basal infusion rate was reduced from 11.7 μg/h to 9.2 μg/h (Fig. 5).

Following this adjustment, spasticity in both the upper and lower extremities improved markedly. Sleep disturbance, appetite loss, and impairment of activities of daily living also improved. Furthermore, the arrhythmia resolved.

Follow-up MAS scores improved as follows: hip abduction, 1/1; hip flexion, 1/1; knee flexion, 1/1; ankle dorsiflexion, 1/1; wrist flexion, 1/1; wrist extension, 1/1; elbow flexion, 1/1; and elbow extension, 1/1.

During the subsequent 1-year and 4-month follow-up period, spasticity remained well controlled with six daily bolus infusions without increasing the total baclofen dose.

Discussion

ITB therapy is an established treatment for severe spasticity that is refractory to oral medication. Continuous intrathecal administration permits effective symptom control using substantially lower baclofen doses than oral therapy, thereby minimizing systemic adverse effects [5, 6]. However, baclofen tolerance occasionally develops during long-term treatment and may complicate clinical management.

Although standardized diagnostic criteria for baclofen tolerance have not been established, tolerance was clinically suspected in the present case because spasticity progressively worsened despite substantial dose escalation after mechanical complications had been excluded.

An important feature of the present case is the unusually delayed onset of baclofen tolerance, which developed approximately 15 years after initiation of ITB therapy. Previous reports have generally described tolerance occurring within months to several years after implantation [7–9]. This case therefore demonstrates that baclofen tolerance should remain an important diagnostic consideration even during very long-term stable ITB treatment.

Another clinically important aspect of this case was the need to distinguish baclofen tolerance from mechanical complications of the ITB system. The patient had previously undergone catheter replacement and partial lumbar laminectomy because of catheter rupture [12]. Worsening spasticity after catheter-related procedures may suggest catheter obstruction, disconnection, cerebrospinal fluid leakage, or altered drug delivery. In the present case, however, catheter angiography and computed tomography confirmed appropriate catheter positioning without evidence of leakage or obstruction.

The mechanism underlying baclofen tolerance remains incompletely understood. One proposed mechanism involves downregulation or desensitization of spinal GABA_B receptors caused by prolonged continuous exposure to baclofen. Pulsatile bolus infusion may intermittently restore receptor sensitivity by introducing fluctuations in baclofen concentration around the catheter tip, thereby preventing sustained receptor desensitization [11]. Another possible explanation is that intermittent bolus administration improves cerebrospinal fluid distribution and enhances drug delivery to the spinal cord.

Previous studies have suggested that changing from simple continuous infusion to complex continuous infusion may not effectively reverse baclofen tolerance [10]. In contrast, pulsatile bolus infusion has been reported to improve therapeutic responsiveness [11]. Nevertheless, detailed descriptions regarding optimization of bolus timing and frequency have been limited.

The present case provides a detailed stepwise clinical course demonstrating that simply increasing bolus frequency may not necessarily improve clinical outcomes. Four daily bolus infusions failed to improve symptoms, whereas eight daily bolus infusions improved spasticity but aggravated arrhythmia. Ultimately, six daily bolus infusions timed before anticipated symptom exacerbation achieved both satisfactory symptom control and acceptable tolerability.

These findings suggest that individualized optimization of infusion timing may be more important than maximizing bolus frequency alone. In the present case, the timing of baclofen administration relative to concomitant antiarrhythmic medication may have been clinically relevant. Arrhythmia worsened when baclofen boluses were administered during periods of declining pirsicainide concentration, highlighting the importance of considering pharmacokinetic interactions during ITB management.

Another notable finding is that symptom control was achieved without increasing the total daily baclofen dose. This observation suggests that infusion patterns themselves may significantly influence therapeutic responsiveness independently of absolute drug dose.

Improved spasticity control also resulted in better sleep quality and improved activities of daily living, emphasizing the importance of individualized long-term ITB management during rehabilitation.

This report has several limitations. First, this was a single-case observation, limiting generalizability. Second, cerebrospinal fluid baclofen concentrations were not measured objectively. Third, the potential influence of concomitant medications and postoperative changes could not be completely excluded.

Conclusions

We report the detailed clinical course of baclofen tolerance successfully managed using individualized pulsatile bolus infusion during long-term intrathecal baclofen therapy. Baclofen tolerance may occur even after more than a decade of stable treatment. Switching to pulsatile bolus infusion should be considered before further dose escalation in patients with suspected baclofen tolerance.

Careful optimization of bolus timing according to symptom patterns and concomitant medications may improve therapeutic efficacy while minimizing adverse effects. Further studies are needed to clarify the optimal infusion interval, dosage, and timing, as well as the mechanisms underlying baclofen tolerance and its reversal.

Abbreviations

CT: Computed tomography

GABA_B: Gamma-aminobutyric acid B

ITB: Intrathecal baclofen

MAS: Modified Ashworth Scale

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Written informed consent was obtained from the patient for publication of this case report and the accompanying images. A copy of the written consent form is available for review by the Editor-in-Chief of this journal.

Availability of data and materials

The datasets generated and/or analyzed during the current study are not publicly available because complete anonymization of imaging data could not be guaranteed but are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

YT and HH performed all surgeries. YT, HY, HE, HH, TU, RA, MK, AN, KK, TY and SD designed the treatment plans. YT conducted the follow-up. YT wrote the draft of the manuscript, which was revised by SD. All the authors have read and approved the final version of the manuscript.

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Not applicable.

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Table

Table 1 is available in the Supplementary Files section.

Figures

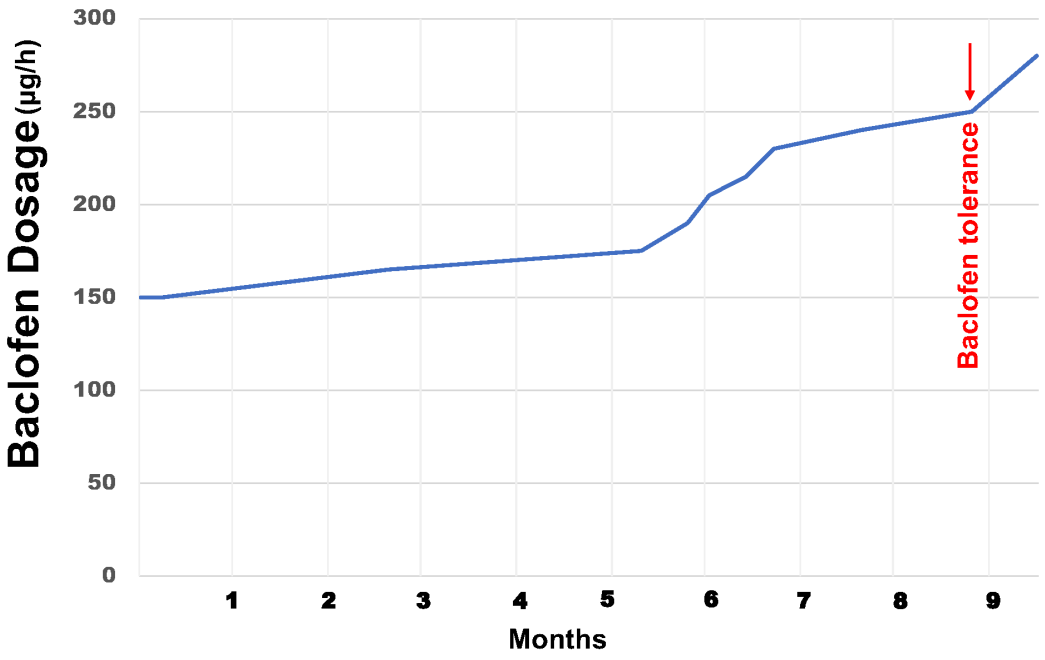


Figure 1

Progressive worsening of spasticity despite escalation of the intrathecal baclofen dose following partial lumbar laminectomy.

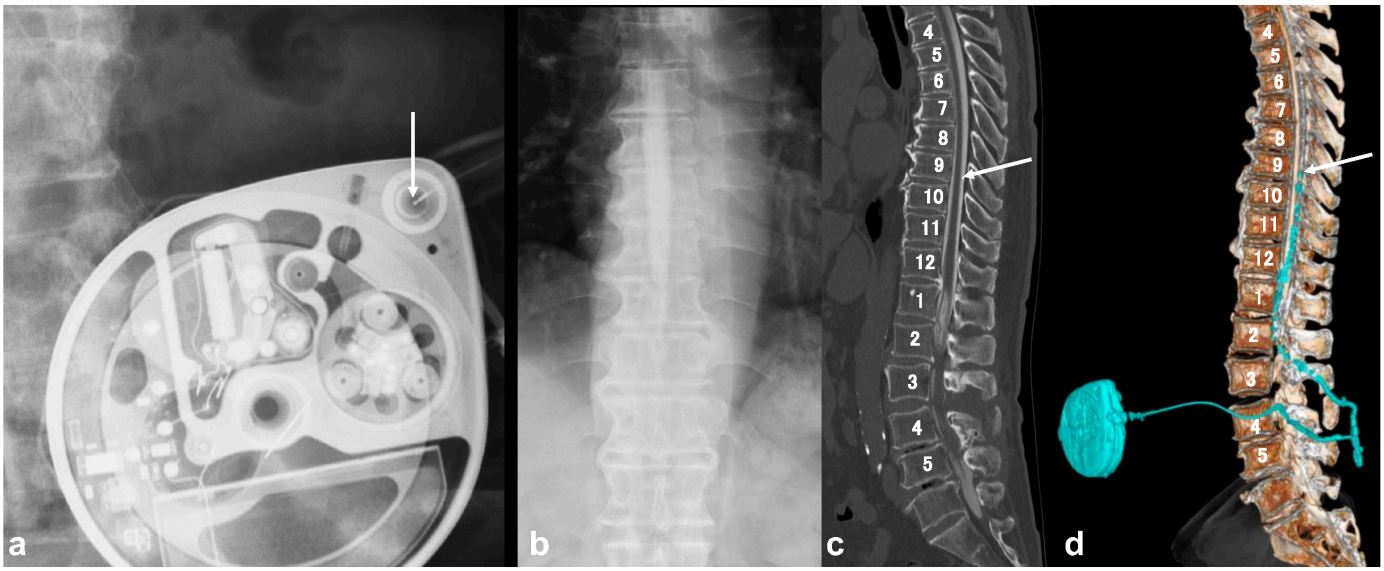


Figure 2

Catheter angiography performed through the catheter access port under fluoroscopic guidance demonstrated no contrast leakage. Computed tomography and three-dimensional computed tomography confirmed that the catheter tip remained positioned at the ninth thoracic vertebral level without evidence of leakage or displacement.

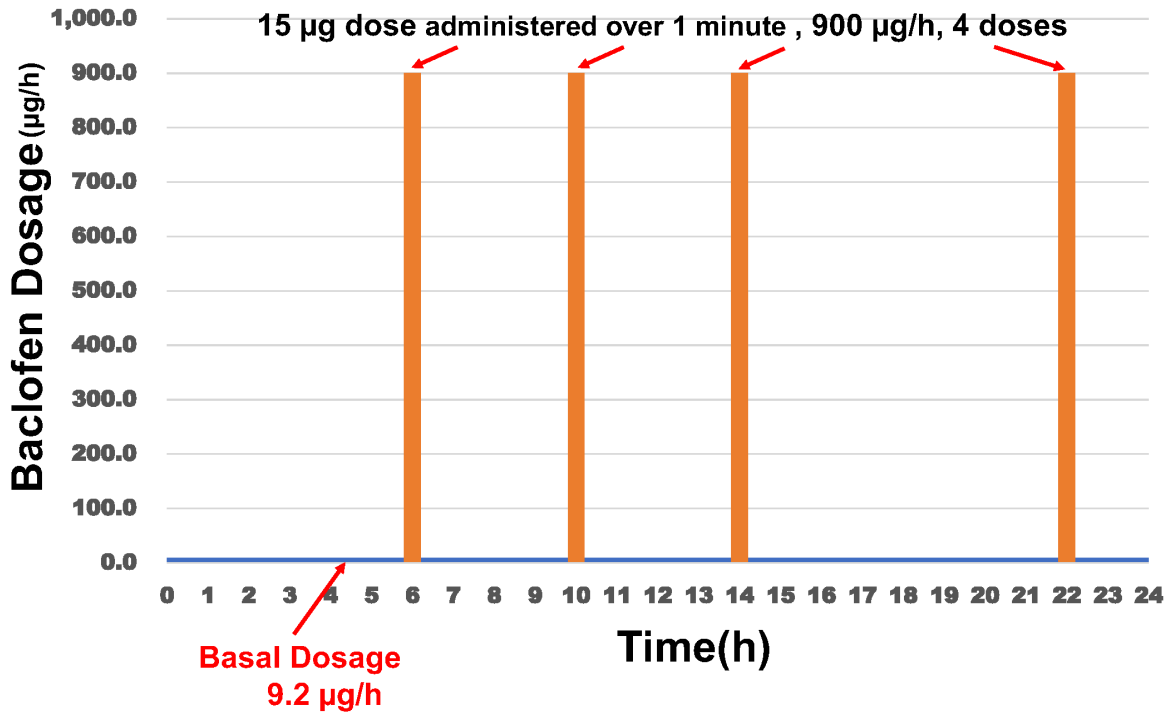


Figure 3

Four daily baclofen bolus infusions (15 µg administered over 1 minute at 06:00, 10:00, 14:00, and 22:00). The total daily bolus dose was 60 µg, while the total daily baclofen dose remained unchanged at 280 µg/day.

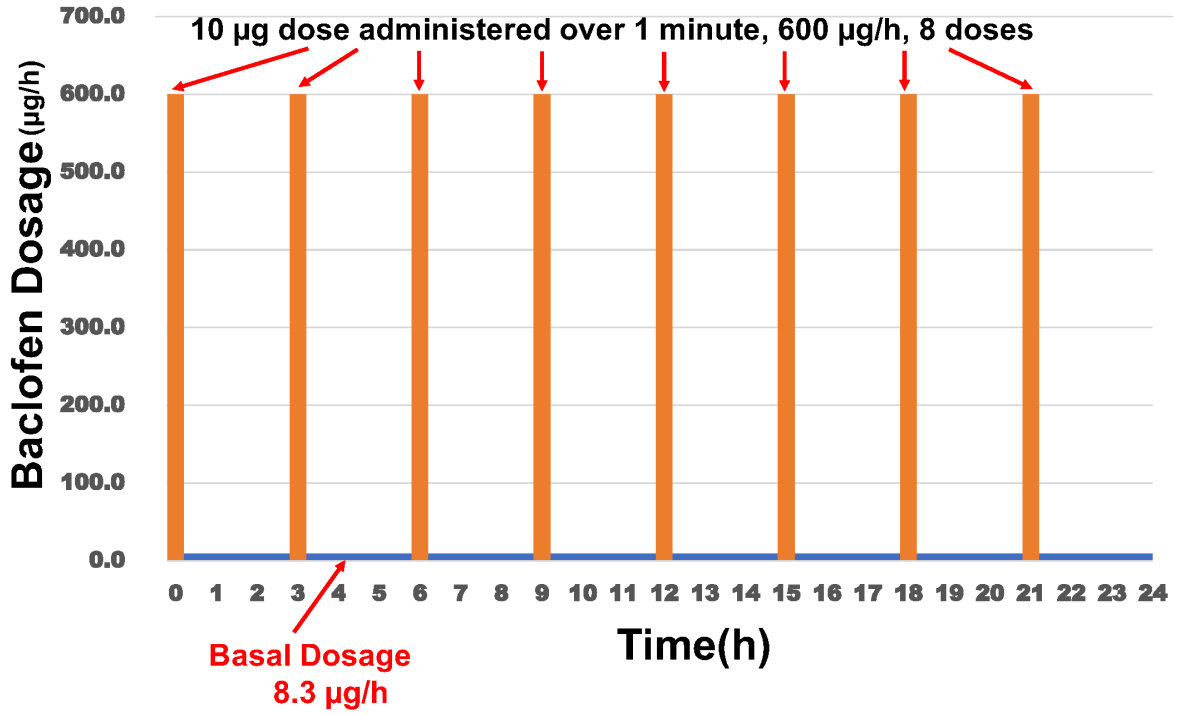


Figure 4

Eight daily baclofen bolus infusions (10 µg administered over 1 minute at 00:00, 03:00, 06:00, 09:00, 12:00, 15:00, 18:00, and 21:00). Spasticity improved; however, arrhythmia worsened.

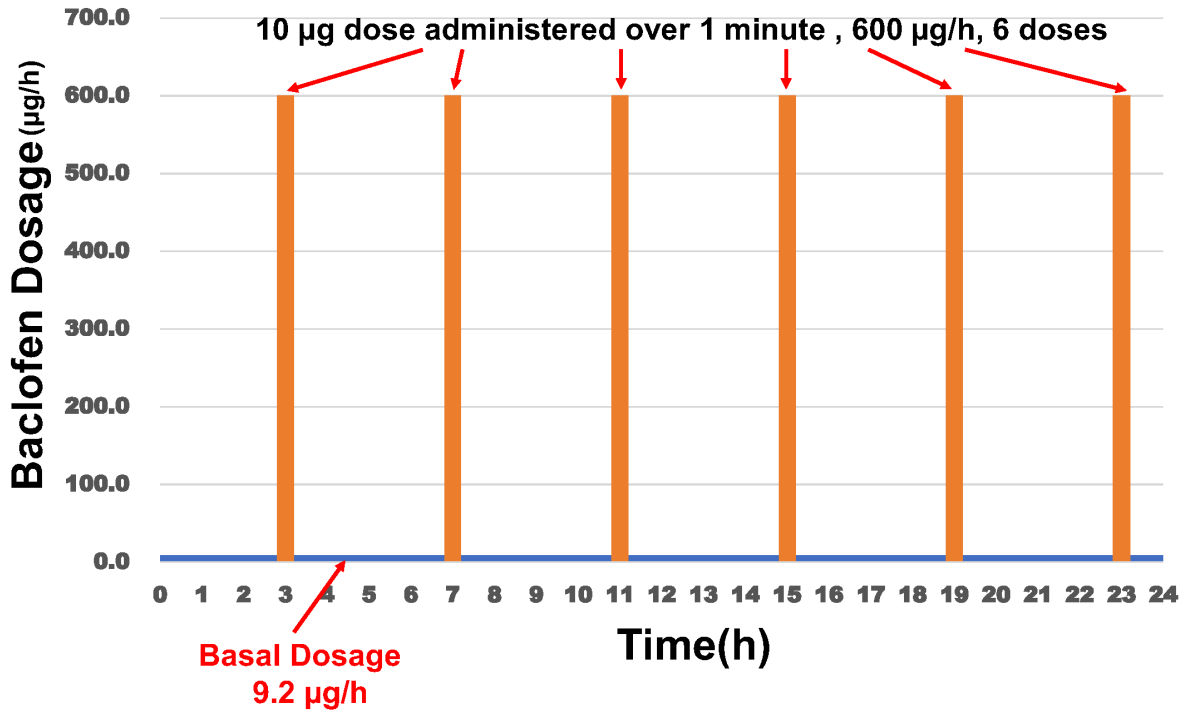


Figure 5

Six daily baclofen bolus infusions (10 μg administered over 1 minute at 03:00, 07:00, 11:00, 15:00, 19:00, and 23:00). Spasticity improved markedly without worsening arrhythmia.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- CAREchecklistEng2025TAKAGI.docx
- BaclofentoleranceTable.pdf