



## Early Is Better, Then, How Early and How to Apply: Practical Approach of Botulinum Toxin Injection

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Early rehabilitation after stroke has been one of key principles for successful rehabilitation [1]. It helps prevent secondary complications such as contractures or deep vein thrombosis and facilitates neuroplasticity. However, the AVERT (A Very Early Rehabilitation Trial) trial presented some cautionary findings. However, results of AVERT study reminded us that there are things to be careful about early rehabilitation and there is no one-size-fits-all approach to stroke patients. Moreover, it emphasizes the need for a personalized approach in stroke rehabilitation [2,3].

Similarly to early rehabilitation, early management of post-stroke spasticity (PSS) has been recommended, as it improves function and quality of life [4]. As for botulinum toxin injection (BoNT) which is a first-line treatment for PSS, early injection of BoNT is also advocated [5,6]. Still, there is no consensus regarding the “early” in early BoNT injection, such that variety of criteria have been used from 3 weeks after stroke to 6 months after stroke [7,8]. This heterogeneity is one of obstacles to widespread of early BoNT injection in clinics. Review on the post-stroke spastic movement disorder and botulinum toxin A therapy: early detection and early injection published in the previous issue of the *Annals of Rehabilitation Medicine* recommended injection within 3 months following stroke (until early subacute phase of stroke) based on several reasons including prevalence, pathophysiology, and neural plasticity of PSS [9]. Therefore, 3 months after stroke, that is until early subacute phase of stroke seems correct to define “early” in early BoNT injection.

Despite of this general recommendation on early BoNT injection, concern about optimal timing and dose remains. It is difficult to estimate optimal dose at the time of injection because it is difficult to predict spasticity in the future based on the present status, especially at the early injection time. If the current spasticity is on the plateau at the peak and there is no significant change in the future, there will be no difficulty in determining the injection dose. Problems can occur when spasticity changes at the time of early injection. When it is expected that the spasticity will become more severe than at the current time, the BoNT dose will be adjusted higher than the currently needed dose. However, if the spasticity does not get more severe than expected in the future after the injection, over-weakness secondary to BoNT will occur. On the contrary, if the spasticity becomes more severe than expected, the effect of the BoNT injection will be insufficient secondary to insufficient amount of BoNT. This lack of BoNT dose is also problematic because even if additional injections are needed, the patient must wait three months to

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prevent BoNT antibody production. At this point, it would be right to evaluate the state of spasticity through continuous follow-up and determine the optimal BoNT-A injection time and dose accordingly, rather than determining the BoNT-A dose through a single evaluation of spasticity.

Of note, over-weakness might not be a major consideration in early BoNT injection. Well-known concept “deforming spastic paresis,” which emphasized muscle extensibility as well as neural disorder of motor command, recommended prevention or minimization of emergence of spastic myopathy [10]. Furthermore, the concept of “therapeutic weakness” emphasized the BoNT-induced weakness of spastic antagonist, which is followed by less resistance to voluntary activation of agonist leading to improved voluntary control of both agonist and antagonists [11]. These conceptual approaches were confirmed to be effective among patients with chronic stroke and the beneficial effects is expected to be profound with early BoNT injection considering the chance to regain muscle strength, less developed deforming spastic paresis, and neuroplasticity [12].

Early BoNT injection, specifically within early subacute phase of stroke is strongly recommended as a standard care in stroke rehabilitation. Furthermore, decisions of optimal time and dose should be made on a case-by-case basis taking into account the individual's goal, strength as well as spasticity, keeping in mind that early BoNT-injection is not a one-size-fits-all solution.

## CONFLICTS OF INTEREST

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