ORIGINAL ARTICLE ASIAN JOURNAL OF MEDICAL SCIENCES

Outcome of delayed versus immediate casting on spasticity of lower limb muscles in cerebral palsy post-botulinum toxin injection

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Submission: 05-08-2023 Revision: 02-12-2023 Publication: 01-01-2024

ABSTRACT

Background: Botulinum toxin type A (BTX-A) is widely used to treat spasticity in children. The optimal strategy for the combined treatment of casting and BTX-A injections is not known. This prospective study is conducted to know the functional outcome of immediate versus delayed casting post-BTX-A injection in children with cerebral palsy (CP). **Aims and Objectives:** The aim of this study is to compare delayed versus immediate casting as an adjunct to botulinum toxin therapy for spasticity of lower limb muscles in CP. The objectives of the study are to test the hypothesis that delayed casting is superior to immediate casting post-botulinum toxin injection and to know the feasibility of using the Edinburgh visual gait score (EVGS) as a single qualitative and quantitative outcome measure. **Materials and Methods:** A prospective study is conducted to compare immediate casting with delayed casting post-botulinum toxin injection to spastic lower limb muscles in patients with CP from July 2018 to February 2019. **Inclusion criteria**: A diagnosis of CP with associated spastic monoplegia, diplegia, or hemiplegia with aided or unaided ambulation. **Exclusion criteria**: History of orthopedic surgery in the preceding 12 months; selective dorsal rhizotomy; mixed CP; ataxia; athetosis; non-ambulatory subjects. **Results:** The botulinum toxin injection + delayed POP casting group fared better in terms of clinical and functional outcome (as shown by improved EVGS scores) in our study. **Conclusion:** There is a clear benefit in delaying casting after the injection of Botulinum toxin in the recurrence of spasticity.

Key words: Cerebral palsy; Botulinum toxin; Delayed versus immediate casting; EVGS

Access this article online

Website: http://nepjol.info/index.php/AJMS

DOI: 10.3126/ajms.v15i1.57403

E-ISSN: 2091-0576

P-ISSN: 2467-9100

INTRODUCTION

Cerebral palsy (CP) refers to a group of non-progressive movement and posture disorders resulting from injuries to the developing fetal or infant brain. The worldwide incidence of CP is 2–3/1000 live births, making it the most common cause of physical disability in childhood.[1] Spasticity is not only the most common motor disorder but also the main cause of slowly developing secondary problems such as contractures and bony deformities in children with CP.[2] Muscle in CP is characterized by increased resting tone resulting from the primary brain lesion. Stretch, an important stimulus for normal muscle growth, is vigorously opposed by an exaggerated stretch reflex response, and both spasm and spasticity tend to maintain the muscle in a shortened position. In children, physiotherapy, augmented by serial casting and orthoses, has been the mainstay of treatment to reduce tone, prevent secondary deformities, and improve function. Conservative management is favored in younger children to avoid potential risks such as overlengthening, infection, scarring, and anesthetic problems, whereas in older children, orthopedic surgery has a significant role.[3]

Typically, conservative management is indicated during the high-growth phase of a child's development, starting at between 1 and 4 years of age, up until 7 years (on average). There are only two conservative treatment options for children with CP that has been shown to be effective in the clinical trial setting: Serial casting and

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botulinum toxin type A (BTX-A).[4] BTX-A is widely used to treat spasticity in children by acting on acetylcholine receptors in the neuromuscular junction. When injected intramuscularly in therapeutic doses, BTX-A produces partial chemical denervation of the muscle. 2–3 days following the BTX-A injection, spasticity is reduced; maximum effects occur in the 2nd week, and the effect continues for 3–6 months.[5] Published casting procedures differ in terms of the duration of casting, from a single cast for 3 weeks to changing casts after 2 weeks to serial casting until attainment of a target range of motion (ROM).[6] The immobilization associated with precocious casting may inhibit the effect of BTX-A. Electrical stimulation studies in both human and animal models have demonstrated that increased muscle activity enhances the clinical effect of BTX-A. Nerve stimulation accelerates the internalization of BTX-A into the motor nerve terminal, thus facilitating its inhibitory effect on acetylcholine release.[7] Therefore, it seems likely that immobilization by casting immediately after the injection decreases the uptake of the substance and, as a consequence, its clinical effect. Another potential advantage of delaying casting is the opportunity that is present during the 1st month after injection to improve joint ROM both during physical therapy and by habitual walking with a lesser degree of spasticity. Although there is evidence in the literature suggesting that combined treatment of casting and BTX-A injections might have additional benefits in short- and long-term outcomes to either treatment alone and might provide better patient compliance in children with CP, the optimal strategy for this combined treatment is still not known. Hence, to observe the functional outcome of immediate versus delayed casting post-botulinum toxin A injections in children with CP, this prospective hospital-based study is selected.

Aims and objectives

The aim of this study is to compare delayed versus immediate casting as an adjunct to botulinum toxin therapy for spasticity of lower limb muscles in cerebral palsy. The objectives of the study are to test the hypothesis that delayed casting is superior to immediate casting post botulinum toxin injection and to know the feasibility of using Edinburgh visual gait score- EVGS as a single qualitative and quantitative outcome measure.

MATERIALS AND METHODS

The approval of the institutional ethical board was obtained from Sri Padmavathi Medical College for Women-SVIMS.

Study design

A prospective study is to compare immediate casting with delayed casting post-botulinum toxin injection to spastic (dynamic) lower limb muscles in patients with CP with gait problems.

Study area

BIRRD (T) Hospital, Tirupati

Study duration

July 1st, 2018–February 28th, 2019.

Study sample

All CP patients walking into the outpatient department must meet the inclusion criteria for the study and be willing to participate in it.

Inclusion criteria

(1) A diagnosis of CP with associated spastic monoplegia, diplegia, or hemiplegia. (2) Aided or unaided ambulation.

Exclusion criteria

(1) History of orthopedic surgery in the preceding 12 months; (2) history of selective dorsal rhizotomy; (3) children with so-called mixed CP, ataxia, and athetosis; (4) non-ambulatory subjects.

Method of randomization

Group allocation was done by block randomization. All the patients were randomized into two treatment groups: Group A and Group B. In our study, we compared the functional outcomes of patients who had undergone immediate POP casting post-botulinum toxin injection (Group A) with those of patients who had undergone delayed POP casting post-botulinum toxin injection (Group B). Before the study started, the total number of patients was randomized using the blocked randomization technique, and Groups A and B were mentioned on a 3×3 cm piece of paper according to the serial order and sealed in envelope covers. Just before the administration of botulinum toxin, the envelope covers were opened, and the respective group allocation was done according to the serial number allotted on the envelope covers.

Intervention

Injection of botulinum toxin A to target muscles is followed by cast immobilization either immediately after injection or 3 weeks (delayed) after injection. Above-knee POP cast with good padding over bony prominences was applied with knee extension for children who received Botox to the hamstring and gastrosoleus muscle groups. An above-knee POP cast with an abduction bar was applied to children who received botox to the adductor group of muscles. In each group, a fixed cast was continued for 3 weeks once applied. After 3 weeks of casting, cast removal was done, and the child was put through rehabilitation for a period of 3 weeks before the final outcome was assessed. The outcome was assessed using the Edinburgh visual gait score (EVGS) (observational gait

score). A video was recorded using the high-quality mobile camera in both the coronal and sagittal planes, both before and after the intervention. We used Kinovea 0.8.15 software for analysis of the gait recorded on video.

Injection technique

A vial of BOTOX, BTX-A, contains 200 units of freeze-dried toxin.

Toxin is reconstituted with 4 mL of 0.9% normal saline so that each 1 mL contains 50 units of botulinum toxin. A 1-cc tuberculin syringe and four 27 gauge, 1.5-inch needles will be used for injection purposes. Ketamine-based procedural sedation and analgesia (PSA) is given.[8] Parts are prepared using 0.9% normal saline and draped. Needles are placed into the targeted muscle bellies 4–5 cm apart after clinical palpation, and the position of the needles is confirmed by passively stretching and relaxing the muscle and checking for the movement of the needles.[9] If the needle moves, the toxin is injected after initial withdrawal to rule out intravascular positioning of the needle. If the needle does not move or if there was aspiration of blood into the syringe, the needle is removed and repositioned. Children in Group A were casted immediately, whereas Group B children received a sterile dressing on the injected part, which was removed after a while. All children were allowed orally after a period of 2 h. No antibiotics were advised after receiving the botox injection. Syrup paracetamol was advised for pain relief following the injection.

RESULTS

The total number of male children was 27 (67.5%) and female children were 13 (32.5%). Group A had 14 (70%) male children and 6 (30%) female children. Group B had 13 (65%) female children and 7 (35%) male children. In this study, 25 children (62.5%) were under the age of 5 years, and 37 children (92.5%) were under the age of 10 years. Only 3 children (7.5%) were aged above 10 years. The mean age in Group A was 5.65±2.852 (mean± standard deviation [SD]) and in Group B was 5.45±3.052 (mean±SD). In this study, 30 children (75%) were under 15 kg of weight. A total of 5 children (12.5%) weighed between 16 and 20 kg, and another 5 children (12.5%) weighed over 21 kg. The mean weight was 15.37±7.788 (mean±SD) in Group A and 16.15±6.360 (mean±SD). The mean dose of Botox given in Group A was 77.00±39.149 (mean±SD) and in Group B was 76.75±26.817 (mean±SD). Table 1 gives us the information regarding muscle groups injected in Group A and Group B.

Interpretation

Table 2 shows the mean EVGS score pre-botulinum toxin in Groups A (28.00±9.74) (mean ± SD) and Group B (28.30±11.18) (mean±SD), which were analyzed with the mean EVGS score post-botulinum toxin in Groups A (21.45±8.55) and Group B (17.45±7.37) using a t-test. Statistically significant differences were obtained in both groups and on comparison between Group A and Group B, Group B post-botulinum toxin EVGS scores fared better.

DISCUSSION

Young age at administration of botulinum toxin was found to be one of the factors that mark out patients

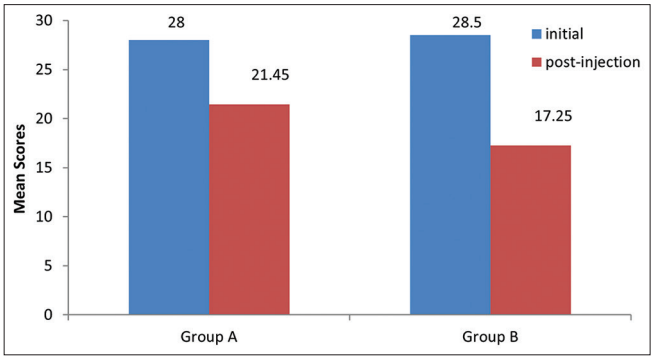
Table 1: Distribution on the basis of muscle groups injected

Muscle group injection	Group A		Group B	
	No. of patients	Percentage	No. of patients	Percentage
Adductors				
Bilateral	2	10.0	2	10.0
Hamstrings				
Bilateral	8	40.0	8	40.0
Right	1	5.0	0	0.0
Left	3	15.0	1	5.0
Gastrosoleus				
Bilateral	10	50.0	11	55.0
Right	1	5.0	2	10.0
Left	2	10.0	3	15.0

Table 2: Pre- and post-botulinum toxin EVGS scores

Group A-immediate casting Group B-delayed casting Pre-botulinum toxin versus post-botulinum toxin EVGS scores				
Study group	**n**	**Mean±SD**	**t-value**	**Sig.**
Group A				
Initial	20	28.00±9.74	3.939**	**P<0.01
Post-injection	20	21.45±8.55		
Group B				
Initial	20	28.30±11.18	5.924**	**P<0.01
Post-injection	20	17.45±7.37		
Overall				
Initial	40	28.25±10.37	7.221**	**P<0.01
Post-injection	40	19.35±8.00		

EVGS: Edinburgh visual gait score, **statistically significant



Graph 1: Pre- and post-botulinum toxin Edinburgh visual gait score scores

who are likely to achieve functional gains post botulinum toxin A treatment (Elisa Fazzi et al.).[10] We have had similar observations with younger children showing better functional outcome. Post-botulinum toxin A management protocols vary and include a wide variety of adjunct therapies such as stretching, taping, casting, physiotherapy, electrical stimulation, extracorporeal shock wave therapy, segmental muscle vibration, motorized arm ergometry, modified constraint-induced movement therapy, and dynamic splinting.[11,12] In our study, we have opted for casting as an adjunct therapy post-botulinum toxin, as it has been shown to be efficacious and feasible in our setup.

The timing of casting has a crucial effect on the improvement obtained after botulinum toxin A injections. Several studies have compared the effects of casting, botulinum toxin A injection, or combined treatments on spasticity in children with CP.[13-17] Only one of these studies examined issues surrounding the timing of casting post-botulinum toxin A injection, which was done by Newman et al. Our study had a higher sample size (40 children compared to 12 children) compared to Newman et al.[18]

In our study, we have randomized children with CP into two groups. Group A consisted of children who underwent immediate casting post-botulinum toxin A injection, and Group B consisted of children who underwent delayed (3 weeks later) casting post-botulinum toxin A injection. In both groups, casts were retained for 3 weeks. A post-therapeutic assessment was carried out using EVGS. This was after allowing sufficient time for rehabilitation.

In our study, children in Group B fared better compared to children in Group A in functional outcome (as shown in Graph 1) as measured in terms of the EVGS score (observational gait analysis). Similar results were reported by Newman et al. They have observed a clear benefit in delaying serial casting until 4 weeks after injection of botulinum toxin in recurrence of spasticity for the gastrosoleus.

In our study, both groups showed improvement in EVGS scores, except for 3 cases in Group A and 2 cases in Group B, which showed deterioration in EVGS scores. In Group A, one child who received botulinum toxin to the left hamstrings and gastrosoleus had an unassisted gait pre-botox and had an assisted gait post-botox despite a reduction in spasticity. As the child was used to walk on his forefoot before therapy, he was facing difficulty in gaining balance with his newly achieved plantigrade foot, resulting in a deterioration of his EVGS score. Two children, one from each group, developed hyperextension of knees with plantigrade feet as a result of persistent spasticity in gastrocnemius, leading to a deterioration in EVGS scores. Both were provided with appropriate orthosis in the follow-up period. One child in Group B, who received botox to the right gastrosoleus, had a shortening of 2 cm of the right lower limb, which led to marginal deterioration (by 2 points) of the EVGS score post-botox administration. The child was provided with shoe risers subsequently. One child in Group A had developed pressure sores as a result of casting; hence, the child did not cooperate with passive stretching exercises post-cast removal, and weight bearing was delayed. The assessment got delayed by a month, which might have led to a decrease in the EVGS score post-treatment.

For reconstitution of botulinum toxin, in our study, we have opted for a lower volume of saline (4 mL for 200 U) for drug delivery.[19] Our intention is to reduce of systemic adverse effects. An increased frequency of systemic adverse events with large volume group has been reported by Lee et al.[20] We did not encounter any adverse events following botulinum toxin injections with a low volume of saline as a reconstituent, which was comparable to Lee et al.[20]

We employed PSA using ketamine for the administration of botulinum toxin in target muscle groups. This allowed us to carry out multilevel botulinum toxin A injections

by placing needles at multiple sites in each target muscle without much discomfort for the children. We have employed EVGS as the functional outcome measure. In our opinion, it is a feasible, reliable, and valid means of outcome measure. Such observations were also made by Rathinam et al., Orozco et al., Tzikalagia, and Ramdharry.[21-23] Hence, our study compared the functional outcomes of delayed casting post-botulinum toxin injection and immediate POP casting post-botulinum toxin injection using EVGS as a functional outcome measure, and our study showed a better outcome in the delayed POP casting group with a significant improvement in EVGS scores.

Limitations of the study

A multicentric study with a larger sample and use of 3-Dimensional gait analysis as functional outcome measure would be required to detect significant effect between delayed versus immediate POP casting post Botulinum toxin.

CONCLUSION

The present study was undertaken to compare the clinical and functional outcomes of botulinum toxin injection plus immediate POP casting and botulinum toxin injection+delayed POP casting. The botulinum toxin injection+delayed POP casting group fared better in terms of clinical and functional outcome (as shown by improved EVGS scores) in our study. There is a better outcome in delayed casting groups in the recurrence of spasticity. None of the cases showed adverse events following botulinum toxin administration. Hence, botulinum toxin was found to be safe and effective in treating spasticity in children with CP. A multicentric study including a larger sample with the use of three-dimensional gait analysis as a functional outcome measure would be required to detect significant outcome between delayed versus immediate POP casting post-botulinum toxin.

ACKNOWLEDGMENT

The authors would like to thank the study participants in the study.

REFERENCES

1. Pin TW, Elmasry J and Lewis J. Efficacy of botulinum toxin A in children with cerebral palsy in Gross Motor Function Classification System levels IV and V: A systematic review. Dev Med Child Neurol. 2013;55(4):304-313.
https://doi.org/10.1111/j.1469-8749.2012.04438.x
2. Dursun N, Gokbel T, Akarsu M and Dursun E. Randomized controlled trial on effectiveness of intermittent serial casting on spastic equinus foot in children with cerebral palsy after botulinum toxin-A treatment. Am J Phys Med Rehabil. 2017;96(4):221-225.
https://doi.org/10.1097/PHM.0000000000000627
3. Jefferson RJ. Botulinum toxin in the management of cerebral palsy. Dev Med Child Neurol. 2004;46(7):491-499.
https://doi.org/10.1017/s0012162204000817
4. Houltram J, Noble I, Boyd RN, Corry I, Flett P and Graham HK. Botulinum toxin type A in the management of equinus in children with cerebral palsy: An evidence-based economic evaluation. Eur J Neurol. 2001;8 Suppl 5:194-202.
https://doi.org/10.1046/j.1468-1331.2001.00052.x
5. Dai AI and Demiryürek AT. Serial casting as an adjunct to botulinum toxin Type A treatment in children with cerebral palsy and spastic paraparesis with scissoring of the lower extremities. J Child Neurol. 2017;32(7):671-675.
https://doi.org/10.1177/0883073817701526
6. Kelly B, MacKay-Lyons MJ, Berryman S, Hyndman J and Wood E. Assessment protocol for serial casting after botulinum toxin a injections to treat equinus gait. Pediatr Phys Ther. 2008;20(3):233-241.
https://doi.org/10.1097/PEP.0b013e3181825c1b
7. Edgar TS. Clinical utility of botulinum toxin in the treatment of cerebral palsy: Comprehensive review. J Child Neurol. 2001;16(1):37-46.
https://doi.org/10.1177/088307380101600107
8. Chow C and Choong CT. Ketamine-based procedural sedation and analgesia for botulinum toxin A injections in children with cerebral palsy. Eur J Paediatr Neurol. 2016;20(2):319-322.
https://doi.org/10.1016/j.ejpn.2015.11.009
9. Chin TY, Nattrass GR, Selber P and Graham HK. Accuracy of intramuscular injection of botulinum toxin A in juvenile cerebral palsy: A comparison between manual needle placement and placement guided by electrical stimulation. J Pediatr Orthop. 2005;25(3):286-291.
https://doi.org/10.1097/01.bpo.0000150819.72608.86
10. Fazzi E, Maraucci I, Torrielli S, Motta F and Lanzi G. Factors predicting the efficacy of botulinum toxin-A treatment of the lower limb in children with cerebral palsy. J Child Neurol. 2005;20(8):661-666.
https://doi.org/10.1177/08830738050200080501
11. Scott AB. Botulinum toxin injection into extraocular muscles as an alternative to strabismus surgery. Ophthalmology. 1980;87(10):1044-1049.
https://doi.org/10.1016/s0161-6420(80)35127-0
12. Mills PB, Finlayson H, Sudol M and O'Connor R. Systematic review of adjunct therapies to improve outcomes following botulinum toxin injection for treatment of limb spasticity. Clin Rehabil. 2016;30(6):537-548.
https://doi.org/10.1177/0269215515593783
13. Koman L, Mooney JF 3rd, Smith B, Goodman A and Mulvaney T. Management of cerebral palsy with botulinum-a toxin: Preliminary investigation. J Pediatr Orthop. 1993;13(4):489-495.
https://doi.org/10.1097/01241398-199307000-00013
14. Corry IS, Cosgrove AP, Duffy CM, McNeill S, Taylor TC and Graham HK. Botulinum toxin A compared with stretching casts in the treatment of spastic equinus: A randomised prospective trial. J Pediatr Orthop. 1998;18(3):304-311.
15. Desloovere K, Molenaers G, Jonkers I, De Cat J, De Borre L, Nijs J, et al. A randomized study of combined botulinum toxin type A and casting in the ambulant child with cerebral palsy using objective outcome measures. Eur J Neurol. 2001;8 Suppl 5:75-87.
https://doi.org/10.1046/j.1468-1331.2001.00040.x
16. Glanzman AM, Kim H, Swaminathan K and Beck T. Efficacy of botulinum toxin A, serial casting, and combined treatment for spastic equinus: A retrospective analysis. Dev Med Child Neurol.

2004;46(12):807-811.

https://doi.org/10.1017/s0012162204001410

17. Ackman JD, Russman BS, Thomas SS, Buckon CE, Sussman MD, Masso P, et al. Comparing botulinum toxin A with casting for treatment of dynamic equinus in children with cerebral palsy. Dev Med Child Neurol. 2005;47(9):620-627.
18. Newman CJ, Kennedy A, Walsh M, O'Brien T, Lynch B and Hensey O. A pilot study of delayed versus immediate serial casting after botulinum toxin injection for partially reducible spastic equinus. J Pediatr Orthop. 2007;27(8):882-885.

    https://doi.org/10.1097/BPO.0b013e31815b4d7d
19. Awaad Y, Tayem H, Munoz S, Thomas R, Soliman S, Michon A, et al. High dose of botulinum toxin type-A (BTX/A): Safety and efficacy in patients with cerebral palsy. J Pediatr Neurol. 2015;2(2):91-96.
20. Lee JH, Sung IY, Yoo JY, Park EH and Park SR. Effects of different dilutions of botulinum toxin type A treatment for children with cerebral palsy with spastic ankle plantarflexor: A randomized controlled trial. J Rehabil Med. 2009;41(9):740-745.

    https://doi.org/10.2340/16501977-0418
21. Rathinam C, Bateman A, Peirson J and Skinner J. Observational gait assessment tools in paediatrics -a systematic review. Gait Posture. 2014;40(2):279-285.

    https://doi.org/10.1016/j.gaitpost.2014.04.187
22. del Pilar Duque Orozco M, Abousamra O, Church C, Lennon N, Henley J, Rogers KJ, et al. Reliability and validity of Edinburgh visual gait score as an evaluation tool for children with cerebral palsy. Gait Posture. 2016;49:14-18.

    https://doi.org/10.1016/j.gaitpost.2016.06.017
23. Tzikalagia T and Ramdharry G. Using the Edinburgh Visual Gait Score to assess gait in children with cerebral palsy: A feasibility evaluation. Int J Ther Rehabil. 2017;24:419-426.

Author's Contributions:
SKCK- Definition of intellectual content, literature survey, prepared first draft of manuscript, implementation of study protocol, data collection, data analysis, manuscript preparation and submission of article; **NBT-** Clinical protocol, manuscript preparation, editing, and manuscript revision; **SK-** Statistical analysis and interpretation; **NKP-** Review manuscript, review manuscript, literature survey and preparation of figures, coordination and manuscript revision; **JG-** Concept and design of the study.

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Source of Funding: Nil, **Conflicts of Interest:** None declared.