

Comparative Efficacy of Baclofen and Diazepam in Treating Spasticity Following Acquired Spinal Cord Injuries: A Randomized Controlled Trial

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ABSTRACT

Introduction: Spasticity is a pervasive and debilitating condition. Anti-spastic medications like Baclofen and Diazepam are most commonly used for spasticity management. **Objectives:** The study aimed to evaluate and compare the efficacy of Baclofen with that of Diazepam in the management of spasticity following acquired spinal cord injuries. **Methods:** In this randomised open-label study involving 60 patients, 30 patients received 5 mg of oral Baclofen thrice daily and 30 patients received 5 mg of oral Diazepam thrice daily for the management of spasticity. The extent of spasticity was measured by Modified Ashworth Scale (MAS). The efficacy of these drugs was measured with the mean improvement in the above parameters on days 7, 14, 28, 56 and 90 from the start of pharmacotherapy. **Results:** Baseline muscle spasticity scores were comparable. At the end-point, mean improvement in tone of right and left hip flexors (1.43 vs. 0.87), hip adductors (1.30 vs. 0.87), knee flexors (0.80 vs. 0.37), ankle plantar flexors (0.80 vs. 0.37) and ankle dorsiflexors (1.23 vs. 0.93) were significantly higher in Baclofen group ($p < 0.05$), while the tone of right and left hip abductors, hip and knee extensors showed no significant difference among the groups. **Conclusion:** Baclofen was found to be superior to Diazepam in terms of efficacy, especially for flexor spasticity of lower limbs in acquired spinal cord injuries.

KEYWORDS: Spinal Cord Injury, Muscle Disorder, Clinical Trial, Accidents, Muscle Relaxants

INTRODUCTION

Spinal cord injury (SCI) presenting with spasticity is recognized by the World Health Organisation (WHO) as a major musculoskeletal condition that presents a serious

disease burden.^[1] One Approximately 70% of individuals with spinal cord injuries experience spasticity following a period of spinal shock, which can negatively affect the quality of life and hence extremely debilitating.^[2]

The definition of spasticity that is most frequently cited was published in *Lancet* in 1980.^[3] It states that "Spasticity is a motor disorder characterized by a velocity-dependent increase in tonic stretch reflexes (muscle tone) with exaggerated tendon jerks, resulting from hyper excitability of the stretch reflex."

After a spinal cord injury (SCI), the spinal cord experiences a spinal shock with symptoms like the loss of tendon reflexes below the lesion, muscle paralysis, and reduced muscle tone in the initial days. Spasticity slowly emerges over the course of several months. Over time, spasticity sets in, leading to intense muscle spasms that can be triggered by stimuli like temperature changes and bladder fullness. While spasticity can help prevent venous thrombosis and improve reflexive bladder and bowel function, it can also cause problems with mobility, comfort, positioning, and hygiene that can lead to limb contracture and lower quality of life for the patient.^[4]

The goal of treatment is to overcome functional impairments related to spasticity.^[5] The most popular treatments are the non-invasive ones, such as oral drugs and physical therapy. Pharmacotherapies are believed to be the most efficacious for the treatment of spasticity failing which, surgical lines are followed. The most commonly used anti-spastic drugs are baclofen, diazepam, clonidine, and tizanidine. Among these drugs, numerous studies attest to the effectiveness of Baclofen and Diazepam as anti-spastic agents in Spinal cord injuries. Majority of the research studies demonstrate the efficacy of the study drugs when given alone or compared with drugs other than our study drugs.^[6] However only a very few studies, have compared the efficacy of

Baclofen and Diazepam in treating spasticity after Spinal cord injuries. [7] This study designed as a Randomised controlled trial aimed to explore the better therapeutic options of the two anti-spastic medications: Oral Baclofen versus the Oral Diazepam in terms of efficacy.

MATERIAL AND METHOD

The research study was planned as a single centre, parallel, open-label, comparative, randomised controlled study with balanced randomisation 1:1 in a tertiary care hospital. The study was approved by the Institutional Ethics Committee of the Government Medical College, Kozhikode. The Kozhikode Government Medical College's Department of Pharmacology and Department of Physical Medicine and Rehabilitation both hosted research sessions for the study. The study was carried out from January 2013 to January 2014, spanning a full year.

The purpose of the study was to evaluate and investigate the efficacy of two medications in terms of managing spasticity: oral Diazepam (5 mg three times a day) and oral Baclofen (5 mg three times a day). In light of this, the Modified Ashworth Scale (MAS), which gauges resistance during passive soft-tissue stretching, was used to evaluate the patients' muscle tone. [8] The MAS rating system has six points: 0, 1, 1+, 2, 3, and 4. It is a quick and simple way to gauge how well a treatment is working. The average improvement in muscle tone at scheduled follow-ups was evaluated.

The sample size used in the study was calculated using the formula [9]

$$N = \frac{2 \sigma^2 (Z_{crit} + Z_{pwr})^2}{D^2}$$

Where, N — Sample size in each group, σ — Assumed SD of each group, Z_{crit} — desired significance criterion, Z_{pwr} — desired statistical power and D — Minimum expected difference between the two means.

Using the formula above, it was possible to calculate the minimum number of patients required in each group (assuming a 10% dropout rate) to be 30. In order to prevent bias, a computer-generated table consisting of 10 blocks, each with 6 patients, was used to randomly divide the enrolled patients into two study groups. Patients who met the following requirements were eligible for inclusion: they had to be over the age of eighteen and under seventy-five, have written informed consent, be at least eighteen months post-spinal cord injury, have established spasticity of any grade that is not in spinal shock, and have spasticity that impairs their ability to function and sleep. The following conditions were not included in the study: patients scheduled for surgery, pregnant, glaucoma patients, patients with respiratory disorders such as chronic obstructive lung disease, sleep apnoea, chronic liver disease, renal disease, urinary tract infection, psychiatric illness of any kind, broken skin, and any infections that trigger spasticity.

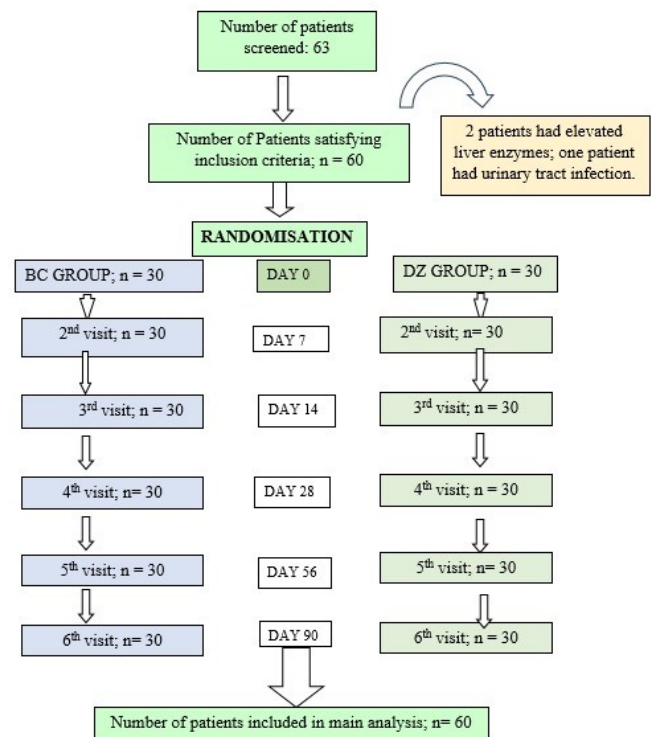


Figure 1: Flowchart showing the entire study process

Baseline demographics and blood investigations of both groups were comparable. The patients received detailed information about the study and all of its steps. After meeting the inclusion criteria, 63 patients in total were screened for the study, and 60 patients were eventually enrolled. These patients were randomly assigned to one of the two treatment groups, that is, the Baclofen treatment group (30 patients) assigned as the BC group and the Diazepam treatment group (30 patients) assigned as the DZ group. Baclofen was administered as 5 mg oral tablets three times daily and diazepam was administered as 5mg oral tablets three times daily after food. Figure 1

The study was registered with the Clinical Trials Registry of India (CTRI): **CTRI/2014/10/005150**. The study process was updated regularly under the CTRI platform.

RESULT

The two groups were assessed for the mean improvement in the muscle tone as measured on days 7, 14, 28, 56 and 90. The patients were regularly given reminders for their follow-up appointments and followed up regularly. The mean tone of right and left Hip Flexors (HFT), Hip extensors (HET), Hip adductors (THAD), Hip abductors (THAB), Knee flexors (TKF), Knee extensors (TKE), Ankle plantar flexors (APF) and Ankle dorsiflexors (ADF) were evaluated in their follow-up visits.

Among the two groups, at the end of the study, Table 1, the Baclofen group showed a statistically significant improvement in the tone of the mean of right and left Hip Flexors (HFT) ($p < 0.001$), Hip Adductors (THAD) ($p = 0.001$),

Efficacy (Muscle Tone)	Group	Mean improvement	SD	p-value [§]
Hip Flexors (HFT)	BC*	1.43	0.57	< 0.001
	DZ^	0.87	0.35	
Hip Adductors (THAD)	BC	1.30	0.54	0.001
	DZ	0.87	0.35	
Knee Extensors (TKE)	BC	1.10	0.48	0.73
	DZ	1.07	0.37	
Ankle Dorsi Flexors (ADF)	BC	1.23	0.50	0.005
	DZ	0.93	0.25	
Hip Extensors (HET)	BC	0.60	0.56	0.11
	DZ	0.37	0.49	
Hip Abductors (THAB)	BC	0.63	0.62	0.22
	DZ	0.43	0.50	
Knee Flexors (TKF)	BC	0.80	0.61	0.005
	DZ	0.37	0.49	
Ankle Plantar Flexors (APF)	BC	0.80	0.61	0.005
	DZ	0.37	0.49	

*BC: Baclofen, ^DZ: Diazepam, §: Mann-Whitney test

Table 1: Comparison of mean improvement in the tone of Spastic muscles of Baclofen and Diazepam groups

Knee Flexors (TKF) ($p=0.005$), Ankle Dorsiflexors (ADF) ($p=0.005$), and Ankle Plantar Flexors (APF) ($p=0.005$) and the mean improvement in the above-mentioned tones was statistically significant ($p < 0.05$). The mean improvement tone of right and left knee extensors (TKE) ($p=0.733$), Hip abductors (THAB) ($p=0.220$), and Hip extensors (HET) ($p=0.105$) of the Baclofen (BC) group compared to the Diazepam (DZ) group showed no significant difference ($p > 0.05$).

DISCUSSION

After a period of spinal shock, patients with spinal cord injuries (SCI) are at high risk for developing spasticity. Since spasticity has a significant impact on quality of life, best practices in its management are imperative. Spasticity can be managed in a number of ways, such as with tone-inhibiting casts, oral medications, targeted injections, exercise therapy, and surgery. The most popular kind of treatment is the use of oral medications, particularly when the spasticity interferes with daily functioning and causes pain or sleep disturbances. A medication plan should be developed with the goal of balancing improved function, patient satisfaction, and possible side effects.

Currently approved medications for use in spasticity patients are Dantrolene, Baclofen, Diazepam, and Tizanidine. The two most common and conventional drugs prescribed for individuals with spasticity are baclofen and diazepam. [7, 10]

Baclofen, a gamma aminobutyric acid derivative, is believed to reduce spasticity by increasing presynaptic inhibition, which in turn amplifies the effects of inhibition on the spinal stretch reflex. Fatigue, sedation, and seizures are common side effects. Diazepam, a benzodiazepine, inhibits central nervous system activity by acting postsynaptically on GABA_A receptors. Sedation, ataxia, discoordination, exhaustion, hypotension, memory impairment, and an increased risk of addiction are typical benzodiazepine side effects. [7]

Research that used these medications in comparison often presented their findings in a variety of ways. (for example: the number of patients improved or the improvement in muscle tones per patient etc.). Because of all of these factors, comparing trials can be difficult at times. In this study, the effectiveness of two anti-spastic drugs namely baclofen and diazepam, was compared.

The patients in the study were enrolled after being screened for eligibility in the baclofen and diazepam groups. The baseline comparisons between the study groups done on day 0 revealed that they were comparable ($p > 0.05$). The modified Ashworth scale was used to measure the mean improvement in tone of the spasticity-affected muscles, which served as the study's efficacy parameter. Tone of Ankle DorsiFlexors (ADF), Tone of Hip Extensors (THE), Tone of Hip Abductors (THAB), Tone of Knee Flexors (TKF), Tone of Ankle Dorsiflexors (TKF), Tone of Ankle Dorsiflexors (ADF), Tone of Hip Adductors (THAD), Tone of Knee Extensors (TKE), and Tone of Ankle Dorsiflexors (ADF) are among them. During routine follow-up visits on days 7, 14, 28, 56, and 90, the mean values of these parameters in the two study groups were compared. The Mann-Whitney test was used to analyze the data.

An interesting finding of this study was that the Baclofen group showed a significant improvement in tone, especially for the Flexor group of muscles, that is, for the tone of the hip flexors, hip adductors, ankle dorsiflexors knee flexors and ankle plantar flexors ($p < 0.05$). However, the mean improvement in the tone of right and left hip extensors, hip abductors, and knee extensors was not statistically significant for both groups indicating that both the study drugs were equally effective in reducing spasticity in these groups of muscles.

At the endpoint, additional clinical and hematologic parameters were evaluated. These parameters were contrasted with the study's initial set. Both groups' parameters did not significantly differ from the baseline, indicating that neither treatment had an impact on them.

There are several research studies conducted on drugs for spasticity. In a systematic review on spasticity treatment

after spinal cord injury by Burchiel KJ et al, in which Baclofen was reported to be effective in spasticity management after spinal cord injury.^[11] In another study conducted by Elovic on the management of spastic hypertonia, among the antispastic medications, Baclofen is particularly effective in flexor spasms.^[12]

Mariko Kita and Donald E in their study on 'Drugs used to treat spasticity' reported that diazepam is effective in spasticity management but produces pronounced adverse effects.^[13] De souse et al in their study on baclofen and spinal cord injury found that baclofen to be most promising among the anti-spastic drugs.^[14]

Our study's findings concurred with those of the aforementioned investigations. In our study, we identified that Baclofen significantly improved the tone of the adductor and flexor muscles. The current study's findings indicate that when it comes to treating spasticity, particularly flexor spasms brought on by acquired Spinal Cord Injuries, oral Baclofen, 5 mg three times per day, is preferable to oral Diazepam, 5 mg three times per day.

CONCLUSION

Major conclusions were drawn from the study that identified oral Baclofen to be more efficacious in the management of spasticity, especially for flexor spasms due to acquired spinal cord injury when compared to oral Diazepam.

Despite limitations involved in the study like short study duration and study methods used, Baclofen is identified as the better therapeutic option when compared to diazepam in the management of spasticity in acquired spinal cord injuries. A greater amount of research is required to examine medical interventions aimed at mitigating the development and progression of spasticity, given the limitations of the study and the difficulties associated with these conditions.

LIMITATIONS OF THE STUDY:

The study was conducted in a single centre with a homogeneous group of patients, which was one of its many limitations. In comparison to other reports, this resulted in a smaller patient group and a shorter study duration. Additionally, because the study did not use a double-blind controlled methodology, bias cannot be completely ruled out.

REFERENCES

1. The Global economic and Health care burden of musculoskeletal disease. WHO Bulletin. 2003;81:646–56.
2. Johnson RL, Gerhart KA, Mccray J, Menconi JC, White-neck GG. Secondary conditions following spinal cord injury in a population-based sample. Spinal Cord. 1998;36:45–50.

3. Lance JW. The control of muscle tone, reflexes, and Movement. Neurology. 1980;30(12):1303–1303.
4. Elbasiouny SM, Moroz D, Bakr MM, Mushahwar VK. Management of spasticity after spinal cord injury: Current techniques and Future Directions. Neurorehabilitation and Neural Repair. Sept. 2010;1(1):23–33.
5. Dietz V. Spastic movement disorder. Spinal Cord. 2000;38:389–393.
6. Meythaler JM, Md C, Bs W, Davis LK. Journal of Head Trauma Rehabilitation. 2004;19(2):101–109.
7. Goyal V, Laisram N, Wadhwa RK, Kothari SY. Prospective randomized study of oral diazepam and baclofen on spasticity in cerebral palsy. Journal of Clinical and Diagnostic Research. 2016;10(6):1–5. doi:10.7860/JCDR/2016/17067.7975.
8. Blackburn M, Vilet PV, Mockett SP. Reliability of measurements obtained using the Modified Ashworth Scale in the lower extremities of people with stroke. Phys therapy. 2002;82:25–34.
9. Cartlidge N, Hudgson P, Weightman D. A comparison of baclofen and diazepam in the treatment of spasticity. J Neurol Sci. 1974;23:17–24.
10. Ertzgaard P, Campo C, Calabrese A. Efficacy and safety of oral baclofen in the management of Spasticity: A rationale for intrathecal baclofen. Journal of Rehabilitation Medicine. 2017;49(3):193–203.
11. Burchiel KJ, Hsu FP. Pain and spasticity after spinal cord injury: mechanisms and treatment. Spine. 2001;26:146–60.
12. Elovic E. Principles of pharmaceutical management of Spastic Hypertonia. Physical Medicine and Rehabilitation Clinics of North America. 2001;12(4):793–816. doi:10.1016/s1047-9651(18)30033-0.
13. Kita M, Goodkin DE. Drugs Used to Treat Spasticity. Drugs. 2000;59(3):487–95.
14. Sousa D, Santos N, Monteiro D, Silva S, Barreiro-Iglesias N, Salgado A et al. Role of baclofen in modulating spasticity and neuroprotection in Spinal Cord Injury. Journal of Neurotrauma. 2022;39(3-4):249–58.

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