Efficacy, Safety and Tolerability of Gabapentin as Aduvant Therapy for Dystonic Cerebral Palsy: Randomised placebo-controlled trial

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INTRODUCTION

Oral medications prescribed for individuals with dystonia in CP can include baclofen, benzodiazepines, clonidine, gabapentin, levodopa, trihexyphenidyl, and tetrabenazine.

These patients usually receive multiple drugs for tone modification with little rationale.

OBJECTIVES

- To study the effectiveness of Gabapentin as adjuvant therapy in dystonic cerebral palsy compared to placebo
- To study the safety and tolerability of Gabapentin as adjuvant therapy

STUDY DESIGN

Randomised double-blind placebo-controlled trial

Inclusion criteria:

- Diagnosed case of dystonic or predominantly dystonic cerebral palsy
- Age 2-18 years of age
- Participants on (2 or less than 2) medications for tone management for 4 weeks (prior to onset of study)
- Participants on stable rehabilitation programme for atleast 6 weeks (prior to onset of study) and willing to continue the same therapy programme for study duration (with no new interventions)
- Parents/ caregivers are able to understand/comply with the study trial

Exclusion criteria:

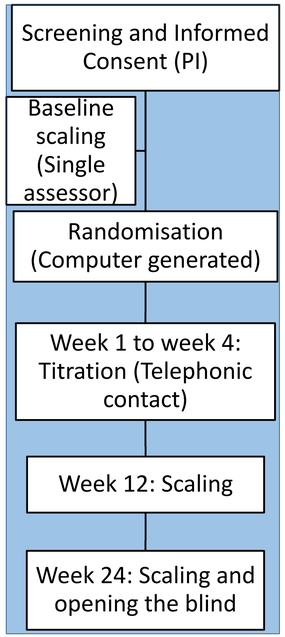
- Known allergy to study drug and its ingredients
- Any evidence of metabolic, degenerative, genetic or multisystem disorder

METHODOLOGY

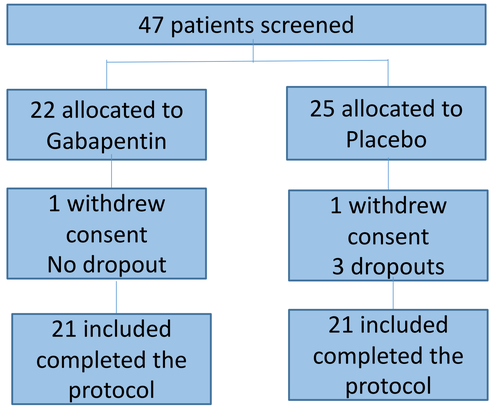
- Subjects enrolled from the Outpatient at study site.
- Validated written and audio-visual informed consent in native language
- All subjects were scaled by the same blinded assessor
- Randomisation done by computer generated block paradigms
- Study drug was initiated and dosage was titrated according to weight bands for the first 4 weeks. Dose reduction considered in case of side effects
- Thereafter they were continued on maximum tolerated dose till week 24.

Assessments:

- Motor classification of the patients was done by Gross Motor Functional Classification (GMFCS)
- Dystonia severity was measured by Barry Albright Dystonia Scale (BADS) and Movement Disorder Childhood Rating Scale (MD-CRS)
- Quality of life was assessed via PedsQL Cerebral Palsy module
- These assessments were done at baseline, 12 weeks and 24 weeks
- Side effects were assessed by patient and caregiver interview at each visit
- Scales were assessed in percentage due to variable denominators



RESULTS



Characteristic	Gabapentin (n=14)	Trihexiphenidyl (n=11)
Age (mean y)	4.64	5.2
Male	61.90%	71.42%
Female	38.10%	28.58%
Weight (mean)	16.47	19.65
GMFCS		
I	4.76% (1/21)	14.29% (3/21)
II	4.76% (1/21)	4.76% (1/21)
III	38.09%(8/21)	33.33%(7/21)
IV	28.57% (6/21)	38.09% (8/21)
V	19.04% (4/21)	9.52% (2/21)

Barry Albright Dystonia Scale (32)	Gabapentin	Placebo	p value
Mean Baseline score	55.96%	54.62%	0.41
Mean score 12 weeks	53.28%	51.34%	0.38
Mean score 24 weeks	51.49%	50.89%	0.46
Mean difference baseline-12 weeks	-2.38%	-4.02%	0.21
Mean difference baseline-24 weeks	-4.47%	-3.72%	0.41

RESULTS

MD CRS	Gabapentin	Placebo	p value
Mean Baseline Score	48.25%	50.39%	0.36
Mean score 12 weeks	46.03%	47.83%	0.29
Mean score 24 weeks	44.21%	45.98%	0.28
Mean difference baseline-12 weeks	-2.22%	-2.56%	0.403
Mean difference baseline-24 weeks	-3.89%	-4.41%	0.402

PedsQL	Gabapentin	Placebo	p value
Mean Baseline score	63.54%	60.77%	0.28
Mean score 12 weeks	60.55%	59.31%	0.41
Mean score 24 weeks	60.14%	58.80%	0.41
Mean difference baseline-12 weeks	-2.99%	-1.46%	0.103
Mean difference baseline-24 weeks	-3.27%	-1.96%	0.203

CONCLUSIONS

There are limited drugs available for medical management of dystonia in children with Cerebral Palsy

Efficacy: Gabapentin as adjuvant therapy is non-superior to placebo in patients with Dystonic CP.

Tolerability:

Incidence with **Gabapentin - 61.90%**, commonest **increased appetite** and **irritability.** With **Placebo** was **50%.**

Dose reduction was needed for **Gabapentin** in **19%** and for **Placebo** in **5%**

Gabapentin as adjunct to <= 2 drugs for dystonic CP was not well tolerated

Quality of life: Showed no significant difference between the two groups

Limitations: Small sample size (interruption due to COVID), single assessor, placebo group had mixed drug combination

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