Efficacy, Safety and Tolerability of Gabapentin for Dystonic Cerebral Palsy: Randomised active-controlled trial

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INTRODUCTION

- Dystonia can be a significant deterrent in motor function, activities of daily living and inclusion for children with cerebral palsy
- Medical management of dystonic cerebral palsy is complex and challenging due to the paucity and inconsistency of treatment options.

OBJECTIVES

- To study the effectiveness of Gabapentin as monotherapy in dystonic cerebral palsy compared to accepted conventional therapy (Trihexyphenidyl)
- To study the safety and tolerability of Gabapentin as monotherapy

STUDY DESIGN

Randomised double-blind active-controlled trial

Inclusion criteria:

- Diagnosed case of dystonic or predominantly dystonic cerebral palsy
- Age 2-18 years of age
- Participants not on any medications for tone management in 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 with same therapy programme for the period of the study (with no additional intervention)
- Parents/ caregivers are able to understand/comply with the study trial

Exclusion criteria:

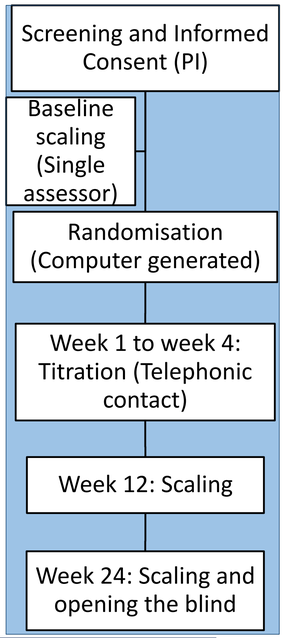
- Known allergy to study drug and its ingredients
- No evidence of any metabolic, degenerative, genetic or multisystem disorder

METHODOLOGY

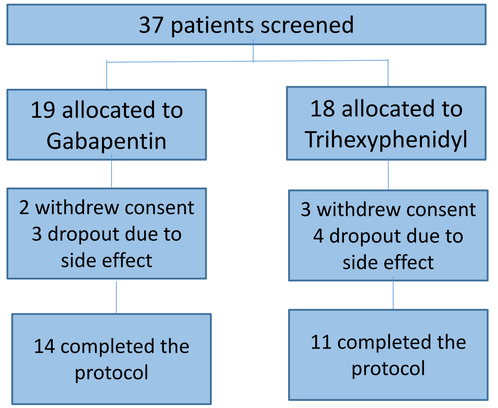
- Subjects enrolled from the Outpatient at study site.
- Validated written and audio-visual informed consent in native language
- All subjects were scaled by the same blinded assessor
- Randomisation done by computer generated block paradigms
- Study drug was initiated and dosage was titrated according 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.

Assessment:

- Motor classification was done by Gross Motor Functional Classification (GMFCS).
- Dystonia severity measured by Barry Albright Dystonia Scale (BADS) and Movement Disorder Childhood Rating Scale (MD-CRS).
- Quality of life assessed via PedsQL Cerebral Palsy module.
- Assessments done at baseline, 12 weeks and 24 weeks by the same blinded assessor.
- 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)	Trihexyphenidyl (n=11)
Age (mean y)	5.18	4.23
Male	78.50%	45.40%
Female	21.50%	54.60%
Weight (mean)	14.95	21.83
GMFCS		
I	21.42% (3/14)	36.36% (4/11)
II	28.58% (4/14)	18.19% (2/11)
III	-	-
IV	14.28% (2/14)	27.27% (3/11)
V	35.72% (5/14)	18.19% (2/11)

Barry Albright Dystonia Scale	Gabapentin	Trihexyphenidyl	p value
Mean Baseline score	50.45%	36.94%	0.70
Mean score 12 weeks	44.42%	32.96%	0.97
Mean score 24 weeks	43.57%	32.67%	0.11
Mean difference baseline-12 weeks	-6.03%	-3.98%	0.17
Mean difference baseline-24 weeks	-6.07%	-4.26%	0.18

RESULTS (contd)

MD CRS	Gabapentin	Trihexyphenidyl	p value
Mean Baseline Score	39.29%	33.11%	0.26
Mean score 12 weeks	35.36%	31.98%	0.35
Mean score 24 weeks	33.10%	30.76%	0.34
Mean difference baseline-12 weeks	-3.93%	-1.21%	0.05
Mean difference baseline-24 weeks	-5.24%	-2.35%	0.10

PedsQL	Gabapentin	Trihexyphenidyl	p value
Mean Baseline score	48.51%	42.94%	0.28
Mean score 12 weeks	44.23%	40.94%	0.36
Mean score 24 weeks	42.65%	41.04%	0.43
Mean difference baseline-12 weeks	-4.28%	-1.89%	0.11
Mean difference baseline-24 weeks	-4.63%	-2.00%	0.08

CONCLUSIONS

- Trihexyphenidyl is widely recognized in the management of dystonia in children with CP.
- **Efficacy**: Gabapentin is as efficacious in improving dystonia as Trihexyphenidyl.
- **Tolerability:**
- Incidence of side effects: **Gabapentin-41.18%**, commonest **increased drooling** and **constipation.** **Trihexiphenidyl-60%**, commonest **drowsiness** and **increased looseness**.
- Further, dose reduction was needed for **Gabapentin** in **10%** and for **Trihexphenidyl** in **37.5%.**
- Gabapentin was better tolerated as compared to Trihexiphenidyl in terms of dosage and side effects.
- **Quality of life**: Improvement was higher in Gabapentin group, however, not statistically significant.
- **Limitations:** Small sample size (interruption due to COVID), single observer.

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