# A pilot study for Comparing efficacy and safety of the CinnaTropin® to the reference recombinant human growth hormone in children with isolated growth hormone deficiency and multiple pituitary hormone deficiency

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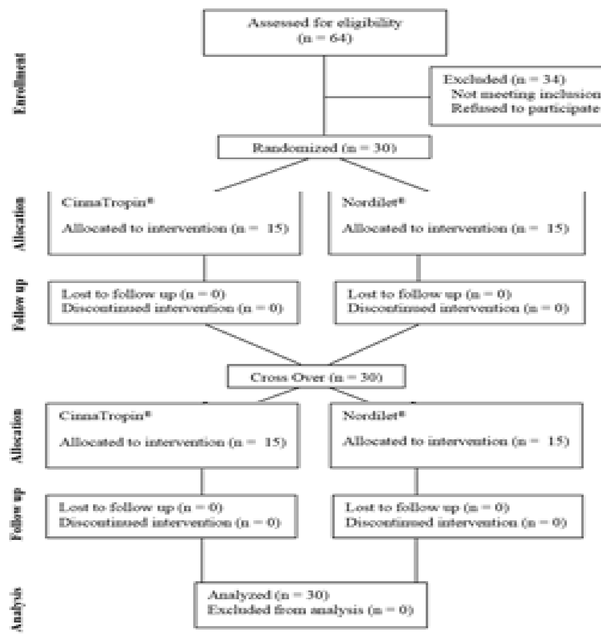
**Objectives:** Comparing efficacy and safety of CinnaTropin® to Norditropin ® Nordlet

**Study Design:** Randomized, active-controlled, two-arm, open-label, and cross-over

**Participants:** A total of 30 participants (4-16 years) with IGHD & PHP

**Intervention:** Daily subcutaneous injections of either CinnaTropin® or Nordilet® (0.03mg/kg/day) 0.7 IU/Kg/week, up to a maximum of 4 IU/day.

**Main outcome measures:** Efficacy of each treatment was evaluated in terms of changes in height velocity, height and changes in serum levels of IGF-1 and IGFBP-3 Safety was assessed by the incidence of adverse events and laboratory parameters.




Consort flowchart of the trial

Treatment intervention
- Daily subcutaneous injections of CinnaTropin® (0.03mg/kg/day)
- Daily subcutaneous injections of Nordilet® (0.03mg/kg/day)

## Inclusion criteria

- Pre-puberty or early-pubertal boys and girls between 4-16 years (Tanner stage 1 or 2)
- Height Standard Deviation Score (HSDS) ≤ -2 for chronological age at the time of diagnosis
- Ruling out of other causes of short stature
- Approved GH Deficiency following Clonidine stimulation test and low or low normal serum IGF-1 at the time of diagnosis
- **Six months to one year follow up before treatment**
- In case of the deficiency in other pituitary hormones, the patient can only be included, if the replacement of other pituitary hormones was done

## Exclusion Criteria

- Any Illness that prevent the proper conduct of the trial, such as seizure, acute or systemic infectious disease in the past 6 months, chronic pulmonary infection, AIDS, chronic liver disease (verified disease of the hepatic cells or 2-fold or more increase in liver enzymes). Any systemic disease in any organ.
- Any active malignancy (such as leukemia, etc.)
- Contraindications of the administration of growth hormone (sleep apnea syndrome)
- Turner syndrome
- Short stature due to chronic renal failure, other causes of GHD, such as craniopharngioma
- History of diabetes in patient or his/her first degree relatives
- Concomitant use of steroids other than replacement therapy in panhypopituitarism

## Baseline: Demographic information

✓No Significant difference was observed in demographic variables.

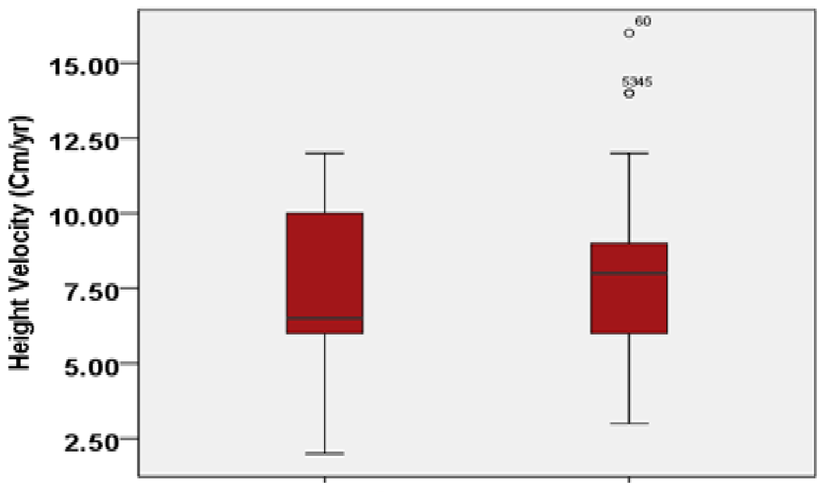
| | Cinnatropin (n=15) | Nordilet (n=15) | P-value |
|---|---|---|---|
| Age | 9.0±2.3 | 9.1±1.7 | 0.893 |
| Sex Female (%) | 62.5 | 50.0 | 0.491 |
| Height (cm) | 122.3±9.9 | 123.1±10.2 | 0.840 |
| Weight | 23.1±6.0 | 24.1±11.3 | 0.751 |
| BMI | 15.2±1.9 | 15.4±4.3 | 0.840 |
| Height-SDS | - 1.72±0.86 | - 1.75±0.68 | 0.898 |
| BMI-SDS | - 0.91±1.13 | - 1.14±1.31 | 0.606 |
| Pulse Rate | 101.3±15.3 | 99.3±9.6 | 0.705 |
| Systolic BP | 117.1±10.6 | 113.3±14.5 | 0.457 |
| Diastolic BP | 77.4±8.0 | 73.2±9.8 | 0.247 |

## Baseline: Laboratory tests

- ✓ There was no significant difference in values for hematologic, biochemistry, and hormonal laboratory tests at the end of the treatment.
- ✓ No adverse event (mild, moderate, serious) was observed during the study period.

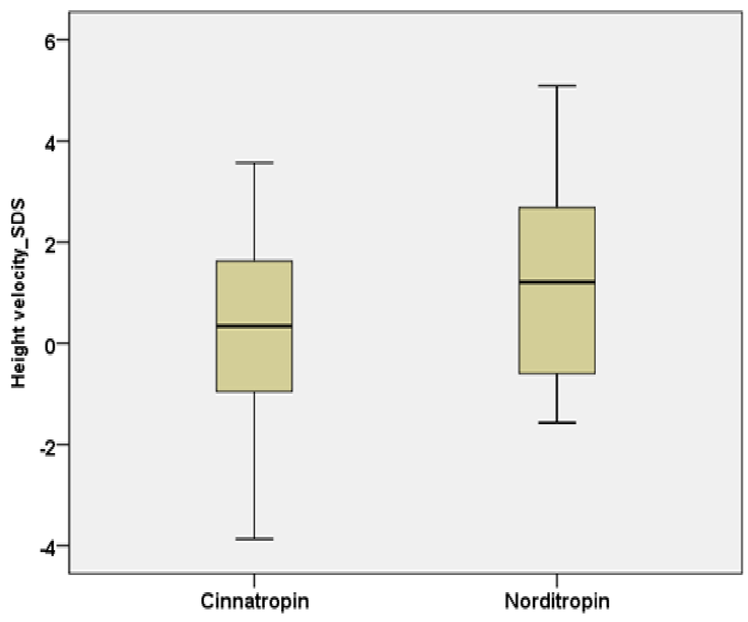
| | Cinnatropin (n=30) | Norditropin (n=30) | P-value |
|---|---|---|---|
| T4 | 8.2±1.2 | 8.2±1.8 | 0.905 |
| T3 | 30.3±3.0 | 31.5±1.9 | 0.063 |
| TSH | 2.5±1.4 | 2.8±1.7 | 0.411 |
| Fasting Insulin | 8.4±3.8 | 7.4±3.2 | 0.299 |
| Vitamin D | 35.3±20.8 | 31.2±21.1 | 0.455 |
| IGF-1 | 274.8±83.0 | 246.1±103.7 | 0.245 |
| IGFBP-3 | 6.1±2.0 | 6.4±2.3 | 0.586 |

# Results




CinnaTropin® Nordilet®

Height Velocity comparison between treatment arms




Height velocity SDS, Cinnatropin: 0.36 ± 2, Norditropin: 1.3 ± 1.95,

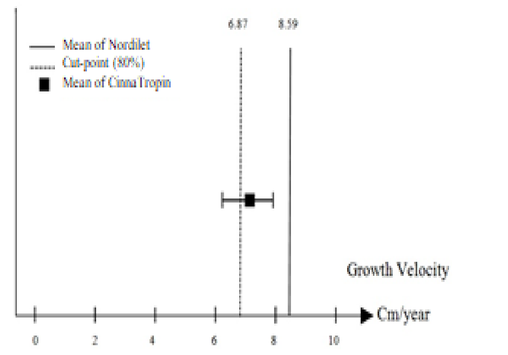
✓ Due to crossover design of the trial, the carry over effect was evaluated in this study.

- ❑ Mean (CI) of 3-month height change difference between groups was 0.52 (-0.01, 1.05) for the first three months and 0.33 (-0.14, 0.80) for the second three months.
- ❑ Therefore, the carry over effect in this study was not statistically significant; and the findings of two treatment periods were analyzed cumulatively.

Height and growth velocity changes in treatment arms

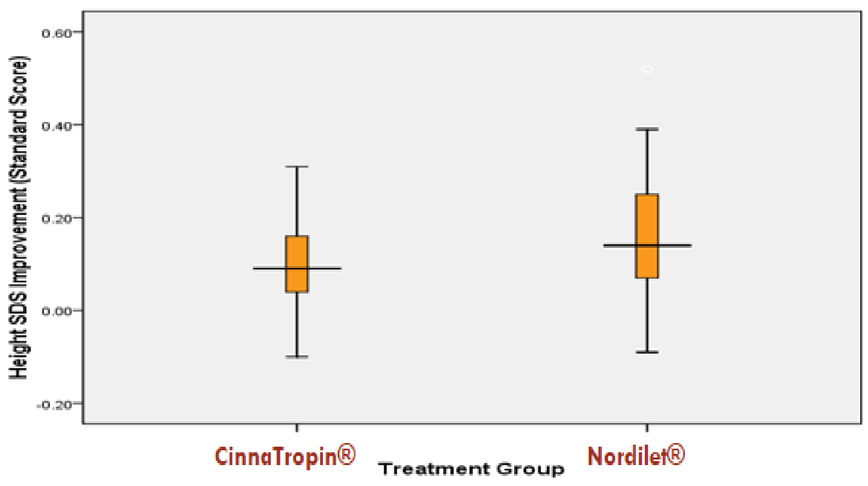
| | CinnaTropin® (n=30) | Norditropin® (n=30) | P-value |
|---|---|---|---|
| Height difference month 1 | 0.54±0.47 | 0.67±0.58 | 0.345 |
| Growth velocity month 1 | 6.52±5.59 | 8.08±7.02 | 0.345 |
| Height difference month 2 | 0.75±0.42 | 0.83±0.55 | 0.543 |
| Growth velocity month 2 | 9.00±5.06 | 9.93±6.56 | 0.543 |
| Height difference month 3 | 0.47±0.39 | 0.65±0.55 | 0.156 |
| Growth velocity month 3 | 5.60±4.71 | 7.74±6.59 | 0.156 |

Evaluation of growth velocity between CinnaTropin® and Nordilet®




BMI Standard Deviation Score in treatment arms

| | CinnaTropin (n=30) | Norditropin (n=30) | P-value |
|---|---|---|---|
| BMI SDS, month 1 | 0.09±0.45 | 0.01±0.45 | 0.538 |
| BMI SDS, month 2 | 0.01±0.45 | 0.03±0.25 | 0.788 |
| BMI SDS, month 3 | 0.01±0.27 | 0.02±0.56 | 0.925 |
| BMI SDS, baseline to month 3 | 0.10±0.38 | 0.05±0.63 | 0.698 |




Height Standard Deviation Score improvement in treatment arms

## Height Velocity

| Height Velocity Total | CinnaTropin (n=30) | Norditropin (n=30) |
|---|---|---|
| Height velocity (cm/yr) mean | 7.6 | 8.0 |
| Standard deviation | 2.7 | 2.9 |
| P-Value | 0.489 | |

## Conclusion

In our study safty and efficacy of Cinnatropin was similar to Norditropin (Novo Nordisk, Denmark)