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Long Acting Once Weekly Growth Hormone Replacement Therapy in Children and Adolescents with Growth Hormone Deficiency. Citing Evidence from Meta-Analysis Research

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Abstract

Children with growth hormone deficiency (GHD) demonstrate short stature due to blunted linear growth and diminished growth velocity. Daily injection with recombinant human growth hormone (rhGH) was developed to overcome this endocrine disorder. However, with daily injections there were compliance and adherence issues both for children and care providers with reduced efficacy. Hence, further research was initiated to synthesize recombinant analog growth hormone molecule with extended half-life. Thus, long acting once weekly injectable growth hormone were developed such as Sogroya® (somapacitan), Skytrofa® (lonapegsomatropin, TransCon hGH), NGENLA® (somatrogon) and Jintrolong®, a polyethylene glycol LAGH (PEG-LAGH). With these newer injectable once weekly growth hormone alternatives compliance and adherence issues were resolved with therapeutic flexibility. Current research paper was prepared to study the meta-analysis done in this regard to compare daily growth hormone (DGH) injections with once weekly long acting growth hormone (LAGH) therapy. Current review of meta-analysis has demonstrated that LAGH treatment was better than DGH in terms of achieving higher levels of IFG-1, height velocity and overall growth. We recommend LAGH as an alternative therapy for DGH for better growth, compliance and adherence.

Keywords: Bone age; Growth hormone; Growth hormone deficiency; Height velocity; Insulin like growth factor; Lonapegsomatropin; Long-acting growth hormones; Short stature; Somapacitin; Somatrogen

Introduction

Children with growth hormone defciency (GHD) are characterized by diminished growth and height velocity (HV) and slow or abnormal linear growth resulting in a short stature. The 'Growth Hormone Research Society' has developed consensus guidelines which recommends the use of recombinant human growth hormone (rhGH) for the management of GHD in paediatric age group and adolescence [1,2]. These injections are given once daily. However, it poses challenges in compliance with a daily growth hormone injection regimen, leading to low adherence and persistence rates. Phenomenon of the fear of needles, missing the daily dose, and poor compliance is associated with reduced efficacy of the drug [3]. Hence, long-

acting growth hormone (LAGH) are alternative for treating children with GHD and appears to address this issue by requiring fewer injections, providing increased acceptance, and therapeutic flexibility with better compliance for children, adolescents and adults. Several long-acting growth hormone products are currently available in the pharma industry, including Somapacitan (Sogroya®), Somatrogon (NGENLA®), and Lonapegsomatropin (Skytrofa®). Different recombinant technologies have been used to increase the time duration and half-life so these molecules remain active in the human body for a week [4,5]. Current research paper focuses on the meta-analysis research done for comparision between DGH and LAGH in term of efficacy, with growth and height velocity and studying the results for better understanding the difference between the patients groups either using DGH or LAGH. Furthermore, this research also highlighted the safety, patients' compliance and adherence to LAGH compared with DGH and studied different LAGH available in the medical field.

Methods

For comparing DGH versus LAGH, Clinical research, Systemic reviews and meta-Analysis were reviewed. We searched the PubMed, Embase, Google Scholar and other data bases including systemic reviews and meta-analysis from January 2020 to January 2025. Boolean operators ('OR'/'AND') were used in these databases with search MeSH terms "growth hormone deficiency" AND "somapacitan" OR "sogroya" OR "long-acting growth hormone. Several studies were retrieved, as mentioned in the references, and thereafter compared between daily growth hormone (DGH) and LAGH injections with meta-analysis reports including forest plots and other significant statistical tests.

Results

According to the retrieved meta-analysis studies, it was observed that long acting once weekly LAGH therapy provided better efficacy compared with daily growth hormone DGH injections with better safety profiles [6-16]. Several systemic reviews and meta-analysis results were studied for different available LAGH, mainly Sogroya® (somapacitan), Skytrofa® (lonapegsomatropin, TransCon hGH), NGENLA® (somatrogon) and Jintrolong®, a polyethylene glycol LAGH (PEG-LAGH) as an alternative, once weekly treatment, for the management of growth hormone deficiency in children. Hence, In one meta-analysis study (Tsurayya G et al.) six randomized controlled trials were included, with 289 pre-pubertal children diagnosed with GHD, with 206 males and 83 females, for maximum of 208 weeks (4.3 years). Somapacitan was administered at doses ranging from 0.02 to 0.16 mg/kg/week. The average age of the children was 6.58 ± 2.29 years (including five countries in Eurpe, North America, Asia and Middle East) [17]. During analysing data for meta-analysis, a daily growth hormone injection with a control dose of 0.034 mg/kg/day were utilized with the selected studies. Meta-analysis focuses specifically on the 0.16 mg/kg/week Somapacitan dosage, with the prediction of achieving higher insulin-like growth factor-I (IGF-I) levels compared to daily human growth hormones [18,19]. The results revealed similar outcomes in height velocity, height SDs, IGF-I SDs, and chronological age vs. bone age. Non-inferiority was observed in height velocity SDs (MD = −0.71 (95% CI: −1.53, 0.10); p = 0.09). Safety profiles were similar between the two groups, with an overall adverse event OR of 1.49 (95% CI: 0.85, 2.60; p = 0.16; I2 = 0%). Treatment adherence is three times higher in the Somapacitan group compared to Norditropin (OR = 3.02 (95% CI: 1.12, 8.13); p = 0.03). Similarly, in another meta-analysis (Zhu J et al.) has evaluated the relative efficacy and safety of long-acting growth hormone (LAGH) with total of 1,899 patients. It was concluded according to the forest plot that PEG-LAGH exhibited better efect on HV (MD: -0.031, 95% CrI: -0.278, 0.215) than somatrogon (MD: 0.105, 95% CrI: -0.419, 0.636), somapacitan (MD: 0.802, 95% CrI: -0.451, 2.068) and lonapegsomatropin (MD: 1.335, 95% CrI: -0.3, 2.989) when compared with DGH. PEG-LAGH ranked the highest in SUCRA (0.78), followed by DGH (0.72), somatrogon (0.61), somapacitan (0.26) and lonapegsomatropin (0.12) [20]. Furthermore, another research trial done by Mori J et al. has demonstrated the efficacy of somapacitan [21]. The main pharmacodynamic endpoint was IGF-ISDS, height velocity (HV; cm/year), HV SD score (SDS), height SDS, and bone age. Somapacitan was shown to be well-tolerated. During Weeks 0–52, mean adherence for the somapacitan group and the daily GH group was 98.2% and 94.8%, respectively. IGF-I SDS had a marginally higher mean baseline level. Observed mean (SD) HV during Weeks 0–52 was 10.3 (2.0) cm/year for the somapacitan group and 9.8 (2.6) cm/year for the daily GH group. IGF-I SDS from baseline to Week 52, and Weeks 52–104 was similar between treatment groups (2.0 (0.9) and 1.9 (1.5) and 1.4 (0.5) and 1.8 (0.9) for both somapacitan and daily GH respectively. The authors have recommended the utilization of LAGH for the management of growth hormone deficiency for beeter compliance and efficacy. Additionally, in another meta-analysis, it was demonstrated that all LAGH were well tolerated and were associated with an elevated IGF-I level compared to daily GH [22] similarly, several other clinical trials, systemic reviews and meta-analysis have demonstrated safety and efficacy of LAGH for achieving higher IGF-1 levels, growth and height velocity, as mentioned in the references section.

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Conclusion and Recommendations

Growth hormone deficiency (GHD) is a rare condition affecting approximately 1 in 3500–10,000 children, with blunted growth hormone production resulting in impaired growth, bone and muscle mass, and limited fat distribution [23,24]. Recombinant human growth hormone (rhGH) therapy has been used for decades for the treatment of this endocrine disorder [25,26]. Hence, this metabolic disorder of GHD can adversely impact quality of life and emotional well-being, leading to decreased functional capacity in the later life and adulthood [27]. Growth hormone therapy (rhGH) effectively restores normal growth in children with GHD, with no significant safety concerns [28,29]. Although daily rhGH therapy is effective to treating such endocrine hormonal disorder, however there were challenges and burdensome for both children and caregivers with compliance issues with these daily injections, leading to low adherence and reduced efficacy. Hence, there was an unmet need for an alternative therapy which can be injected once weekly to improve the patients' compliance and better adherence with flexibility [30-33]. This was achieved by manufacturing long acting once weekly growth hormone replacement therapy such as Somapacitan (Sogroya®), Somatrogon (NGENLA®), and Lonapegsomatropin (Skytrofa®). These injectable drugs were developed by using different recombinant technologies to extend growth hormone half-life. As discussed in this paper, systematic review and meta-analysis has demonstrated better patients' compliance with improved outcomes, safety and efficacy with LAGH therapy. Authors highly recommend use of LAGH instead of DGH to provide flexibility and better compliance and patients' adherence with improved efficacy. Global REAL4 trial had demonstrated that most caregivers who switched to once-weekly somapacitan after taking daily growth hormone injections usually preferred somapacitan because of reduced injection frequency [18]. once weekly recombinant long acting growth hormone molecule analogs which have been approved in the Europe, other parts of the world and United States Food and Drug Administration (US FDA) include Sogroya® (somapacitan), Skytrofa® (lonapegsomatropin, TransCon hGH), NGENLA® (somatrogon) and Jintrolong®, a polyethylene glycol LAGH (PEG-LAGH) [34]. We recommend using recombinant LAGH preparations instead of DGH for achieving better clinical outcomes.

Competing Interest

All authors declare no competing interest.

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