

Improving Adherence to Growth Hormone (GH) Therapy via Easypod™ May Help Maximize the Treatment Outcome

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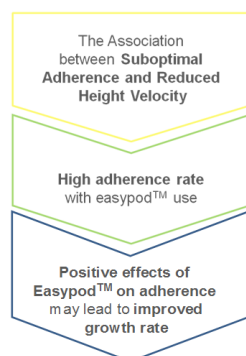
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In Growth Hormone (GH) therapy, suboptimal adherence is a common problem, reaching up to 82%, and there is a need for interventions to improve adherence and to maximize patients' growth potential eventually. Current studies have demonstrated the association between the rate of non-adherence and reduced height velocity. In order to maximize patients' potential to grow, an auto-injecting/recording device, such as easypod™, may help improve adherence and optimize the treatment effects of GH therapy. The use of easypod™ has contributed to high adherence rates: 87.5% and 93% in Bozzola et al.'s study and the Easypod™ Connect Observational study (ECOS), respectively. Improvement of adherence by easypod™ may lead to higher growth rates of patients receiving GH therapy. Additionally, patients' positive acceptability of easypod™ suggests easypod™ is a preferred device by patients for better adherence.

Keywords: Automatic injector device, GH therapy, Adherence, Easypod™

Abstract Graphics

Improving adherence to Growth Hormone(GH) therapy via Easypod™ may help maximizing the treatment outcome



- Suboptimal adherence is a common problem, reaching up to 82%¹: Current studies including Cutfield et al. and Kappor et al. had demonstrated the association between the rate of non-adherence and reduced height velocity.^{2,3}
- The use of easypod™ had contributed to high adherence rates: 87.5%, 93% in Bozzola et al. and ECOS study, respectively.^{4,5}
- Improvement of adherence by easypod™ may lead to higher growth rates of patients on GH therapy.
- Also, patients' positive acceptability of easypod™ suggests easypod™ as a preferred device by patients for better adherence.³

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Introduction

Suboptimal adherence is a common burden for patients with chronic diseases, and the importance of adherence has been emphasized throughout recent studies. The World Health Organization states, "Increasing the effectiveness of adherence interventions may have a far greater impact on the health of the population than any improvement in specific medical treatments"¹. Growth hormone (GH) therapy also faces the challenge

of suboptimal adherence, reaching up to 82%, and adherence interventions are required that may help patients with a suboptimal response of GH therapy reach their growth potential¹⁻³.

Somatotropin, a recent form of recombinant human growth hormone (rhGH), is indicated in children and adolescents with growth disorders⁴. Because the majority of patients receiving GH therapy are children or adolescents, GH treatment often involves a third party (parent/guardian), and patients themselves are not motivated to take the medication^{2,5}. In addition, the daily chal-

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length of needle injection becomes a big barrier for medication adherence in young patients^{2,5}). Therefore, growth hormone often comes with devices like easypod™ to help overcome the barriers to adherence.

Easypod™ is an electronic auto-injector device that features preset dosing, a skin sensor, and one-step administration to improve the convenience of patients^{6,7}). Additionally, it automatically tracks the injection schedule so patients can follow an appropriate dose/schedule and clinicians can stay informed with data on patients' adherence to GH therapy⁷). In this review article, we will

assess the general trend of adherence in GH therapy, the association between non-adherence and height velocity, and the effects of easypod™ on adherence, which may lead to worse treatment outcomes eventually.

Suboptimal Adherence to GH Therapy²⁾

Several studies have measured non-adherence to GH therapy using various methods and definitions (Table 1). The methods for measuring adherence include issued, renewed, or encashed

Table 1. Previous studies about measured non-adherence to GH therapy using various methods and definitions

Study	Patient population	Method of assessing adherence	Definition of non-adherence	Proportion of patients, %
Smith et al.	188 patients attending the Middlesex Hospital Endocrinology Clinic	Questionnaire completed by person responsible for Administering rhGH	Injections missed: >5 since last clinic visit	51
			Injections missed: >10 since last clinic visit	19
Stanhope et al.	107 patients attending Great Ormond Street Hospital Endocrinology Clinic and associated peripatetic clinics	Interview in the presence of a growth research nurse	Injections missed: ≥3 per month	10
Smith et al.	177 patients attending the Middlesex Hospital Endocrinology Clinic	Questionnaire completed by person responsible for administering rhGH	Failure to comply with all aspects of treatment	16–42
Rees	29 patients with renal disease in a multicentre UK study	Questionnaire completed by patient and/or parents	Injections missed: ≥1 per month	62
			Injections missed: ≥6 per month	7
Oyarzabal et al.	473 patients attending 17 paediatric endocrinology clinics in Spain	Questionnaire administered by nurse to patient and/or parents	Injections missed: ≥5% since last clinic visit	6
Postlethwaite et al.	17 patients with renal disease from 4 UK centres	Interview of parents	Injections missed: <1 per week	35–82
			Injections missed: ≥1 per week	6–9
Hunter et al.	Patients in Scotland	Encashed rhGH prescriptions	Injections missed: >20%	33
Desrosiers et al.	631 patients in North America	Unknown	Injections missed: ≥3 per month	15–24
			Injections missed: ≥15 per month	6–13
Wickramasuriya et al.	50 patients commencing GH through the Children's Hospital in Birmingham	Ampoule counts	Not specifically defined median adherence rate was 88–95%	
Haverkamp et al.	6,487 patients in Germany	Renewed rhGH prescriptions	Failure to renew prescription during first year of therapy	5–10
Kapoor et al.	75 patients attending Addenbrooke's Hospital Endocrinology Clinic	Issued rhGH prescriptions	Injections missed: >1 per week	39
			Injections missed: >2 per week	23
Resenfeld and Bakker	882 patients in California	Questionnaire completed by patient and/or parents	Occasionally noncompliant or noncompliant and sceptical	64–77
Cutfield et al.	175 patients in New Zealand	Number of rhGH vials required each month	Injections missed: >1 per week	34
		Number of used rhGH vials returned	Injections missed: >1 per week	66

rhGH prescriptions, vials/ampoule count, and a questionnaire/interview completed by patients or parents. Postlethwaite et al. interviewed the parents of 17 patients with renal disease and defined non-adherence as missing some injection doses per week. The proportion of patients who are categorized as non-adherents reached up to 82 percent. A questionnaire or interview was the most commonly used method among the reviewed studies, but its low sensitivity to non-adherence and subjectivity does not reflect the true adherence rate to GH therapy.

Cutfield et al. measured adherence by counting the number of rhGH vials required each month and the number of used rhGH vials returned. The patients who missed more than one injection per week were considered non-adherents, and the proportion of non-adherent patients was 66 percent (out of 175 patients in New Zealand). The method Cutfield et al. used is more objective, and the definition of adherence used was more realistic than that of the previous study.

There is no gold standard for methods or definitions of non-adherence. Therefore, depending on the measure and definition of non-adherence, studies have shown a wide range of non-adherence rates, from 5 to 82%. Regardless of the various rates of non-adherence in different studies, the prevalence of suboptimal adherence is evident for patients who are undergoing GH therapy, and clinicians should confirm good adherence before making any changes to current therapy⁸⁾.

Association Between Non-adherence and Height Velocity

Cutfield et al. observed 175 patients receiving government-funded GH in New Zealand³⁾. Height velocity standard deviation score (HVSDS) over 6–8 months was controlled for sex and age differences; it was significantly lower in patients with low adherence (missed more than three doses/week) compared with patients with high adherence (missed less than or equal to one dose/week) ($P<0.001$). HVSDS positively correlated with adherence ($P<0.05$)³⁾. In a study in England, Kapoor et al. observed 75 patients using GP prescriptions data over 12 months⁹⁾. Low adherence was associated with reduced height velocity (HV) ($P<0.005$) and HVSDS. The association remained significant regardless of how long patients were receiving GH therapy⁹⁾. Ayidin et al.'s study of 217 GH-naïve patients in Turkey also demonstrated the association between impaired growth rates and low adherence⁸⁾. Patients with low adherence had significantly lower HV and HVSDS compared with patients with excellent (100%) or good adherence ($>=95%$) ($P=0.014$ and $P=0.015$, respectively)⁸⁾.

Current studies persistently demonstrate that non-adherence to GH therapy is associated with reduced height velocity. In order to overcome the barriers of non-adherence and to maximize the patient's potential to grow, an auto-injecting device, such as easypod™, may help improve adherence and identify non-adherence

Table 2. Patients using easypod™

	Total (N=824)	Treatment-naïve (n=601)	Treatment-experienced (n=223)
(A)			
<i>Recorded adherence - all children</i>			
Overall, n (%)*	649/772 (84.1)	484/561 (86.3)	165/211 (78.2)
<i>Recorded adherence - children who provided 3 months of data</i>			
Overall, n (%)	597/682 (87.5)	445/496 (89.7)	152/186 (81.7)
<i>Reported adherence - all children</i>			
Overall, n (%)*	677/790 (85.7)	497/573 (86.7)	180/217 (83.0)
<i>Reported adherence - children who provided 3 months of data</i>			
Overall, n (%)	607/673 (90.2)	447/489 (91.4)	160/184 (87.0)
(B)			
<i>Recorded adherence - children who provided 3 months of data</i>			
Month 1, n (%)	617/682 (90.5)	458/496 (92.3)	159/186 (85.5)
Month 2, n (%)	594/682 (87.1)	441/496 (88.9)	153/186 (82.3)
Month 3, n (%)	606/682 (88.9)	449/496 (90.5)	157/186 (84.4)

(A) Adherence as recorded and reported by children/parents overall over the 3-month survey. (B) Adherence as recorded by easypod™ over each month of the 3-month survey.

*Overall adherence calculated by imputation of missing period(s) using non-missing period(s).

in patients.

Positive Effects of Easypod™ on Adherence and Health Outcome

In the study of Bozzola et al., 682 patients were observed at 206 endocrinology centers across 15 countries⁶. Adherence was defined as injection taken with less than or equal to two missed doses per month. The majority of patients (87.5%) using easypod™ were adherents over 3 months of the period (Table 2). The rate of adherence was significantly higher in treatment-naïve patients than in treatment-experienced patients (89.7% vs 81.7%; $P=0.0062$)⁶. The Easypod™ Connect Observational study (ECOS) included 2,403 patients enrolled in 23 countries and started in 2010 to evaluate the level of adherence in patients receiving rhGH via easypod™¹⁰. According to the 2014 interim analysis, height velocity at the start of GH treatment was 4.5 cm/year for Growth Hormone-deficient patients. After 1 year, height velocity had increased up to 7.9 cm/year with a 93.0% adherence rate with easypod™. The correlation between adherence rate and change in height/height velocity was only weakly positive ($P=0.084, 0.132$). It could have been weakened by the inclusion of older children who had undergone previous GH therapy¹⁰.

Although a direct association between height velocity and the use of easypod™ has not been established, easypod™ contributed to the high adherence rates of GH therapy of 87.5% and 93% in Bozzola et al.'s study and the ECOS, respectively, compared with the non-adherence rate of up to 82% in a systemic review by Fisher et al.^{2,6,10} The positive effects of easypod™ on adherence may result in patients reaching their growth potential and maximizing the effects of GH therapy. Additionally, patients' acceptance of easypod™ suggests easypod™ is a good treatment choice for patients for improving adherence to GH therapy⁶.

Conclusion

Suboptimal adherence to GH therapy is a common problem that results in reduced height velocity in patients with growth disorders. High adherence rates were observed in patients using easypod™. Easypod™ is an easy/quick-to-use device that had high acceptability to patients⁶. For clinicians, its automatic recording features allow the elimination of adherence as a cause of

suboptimal GH therapy response and more informed treatment decisions. Therefore, easypod™ could be considered one of the clinician's choices in helping patients with suboptimal response to GH therapy.

More than a device change should be made to improve adherence, but easypod™ could be one of the preferred choices for improving patients' adherence and treatment outcomes. Further studies assessing different interventions for motivating patients with easypod™ and the association between the use of easypod™ and treatment outcome would be helpful in practice.

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