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The role of growth hormone device optimization in patient-reported outcomes: real-world evidence from South Korea

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ABSTRACT

Background: Growth hormone (GH) treatment preference and adherence are affected by delivery device convenience, injection-site pain, confidence in correct dose administration, and device satisfaction. This survey investigated if switching device to NordiFlex[®] improved treatment experience in pediatric patients in South Korea.

Design and methods: Patients aged 4–≤18 years were surveyed. Participants were NordiFlex[®] users who previously used NordiLet[®]/other devices. Participants compared preference, self-reported adherence, satisfaction, perceived ease of use, and device subjective benefits (across four domains: *ease of use, self-efficacy, minimal disruption of daily life, positive feelings about injections*) of NordiFlex[®] vs. previous device.

Results: Ninety-four patients were enrolled, of which 91.5% previously used NordiLet[®]. Significantly more patients preferred, and were more satisfied with NordiFlex[®] vs. previous device; mean score: 0.65 (95% confidence interval [CI]:0.41;0.88) and 0.61 (95% CI:0.36;0.85), respectively. Participants reported greater perceived ease of use (0.49 [95% CI:0.26;0.72]) and fewer missed injections (0.20 [95% CI:0.06;0.34], with NordiFlex[®] vs. previous device. Bivariate analysis showed significant associations between preference for NordiFlex[®] and higher scores on *self-efficacy, ease of use, minimal disruption of daily life*, and *positive feelings about injection* (all p < 0.001).

Conclusion: These results suggest that improvements in device features could be associated with improved treatment experience.

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KEYWORDS

Adherence; burden of treatment; growth hormone delivery device; patientreported outcomes; patient preference; patient satisfaction

1. Introduction

Growth hormone (GH) therapy is approved to promote growth in children with short stature affected by conditions like growth hormone deficiency (GHD), idiopathic short stature (ISS), small for gestational age (SGA), Noonan syndrome (NS), SHOX deficiency, Prader-Willi syndrome (PWS), Turner syndrome, or chronic renal disease [1–5].

Daily subcutaneous injections are required, often over many years, to promote linear growth. For example, in children with GHD, treatment may start in early infancy and continue until adult height is achieved [4]. However, the necessity for daily injections may lead to suboptimal adherence, which may result in decreased efficacy and increased healthcare expenditure.

Non-adherence is documented in as many as 77% of adolescents [6]; height velocity is compromised in patients who have suboptimal adherence [6–9]. There are also economic costs associated with suboptimal adherence. These include direct costs including those owing to additional diagnostic procedures, wasted medicines, increased GH dosage (with the added increased risk of adverse effects), increased hospitalization, and/or additional drugs or the introduction of other therapeutic interventions [10–12].

Inherent treatment burden that exists in the long-term administration of GH treatment (which could reduce the final efficacy of treatment) includes: the frequency and route of injections, the complexity of the injection regimen, injection pain, difficulties associated with the injection device (such as the need to reconstitute the GH), the patient's or caregivers' lack of understanding of the benefits of treatment, formulary/ insurance changes, the administration burden of long-term therapy, and inadequate patient education [6,12–15].

There are several device-related factors that could potentially improve adherence to GH treatment. These include perceived device convenience, acceptability of and satisfaction with the device, reduction of injection pain or discomfort, storage flexibility, and confidence of having administered the right dose [16–18]. To increase choice and satisfy patient needs, several pen devices for administering GH have been

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developed [18–22], with features such as needle-free injection technology [19], electronic injection [20], and features to ease user experience, such as prefilled GH injection devices and liquid formulations that do not require reconstitution [18].

In 2002, Norditropin[®] NordiLet[®] (Novo Nordisk A/S, Bagsvaerd, Denmark) was the first prefilled multidose GH injection pen device to be approved in Europe. It received regulatory approval in South Korea in 2004. Norditropin NordiFlex[®] (Novo Nordisk A/S, Bagsvaerd, Denmark; approved in South Korea in 2018) was designed to further improve on Norditropin[®] NordiLet[®], with features to further alleviate injection burden and improve treatment experience (Appendix A). Like Norditropin[®] NordiLet[®], Norditropin NordiFlex® is prefilled with a liquid formulation of GH to eliminate the need for reconstitution prior to use. Furthermore, Norditropin NordiFlex® is quick and easy to set up for injection, and requires less injection force than previous devices, enabling children to inject themselves [23,24]. All of these properties were designed to improve comfort and adherence to treatment, since patient autonomy has been found to be a positive factor in adherence to GH therapy [13,25].

Results from a Phase IV multicenter prospective study in France showed that Norditropin NordiFlex[®] was safe and easy to use, and most patients preferred it to their previous device [24].

This questionnaire-based cross-sectional survey was conducted to evaluate patient-reported satisfaction and ease-ofuse with Norditropin NordiFlex® compared with the last GH device used prior to switching in pediatric and adolescent patients who were prescribed treatment with Norditropin® ([GH] somatropin, Novo Nordisk A/S, Denmark) in routine clinical care in South Korea.

The primary objective of the survey was to examine if respondents preferred their current GH therapy device (Norditropin NordiFlex®) to the previous device (Norditropin® NordiLet® or other GH devices). Secondary objectives included examining the difference in self-reported adherence, satisfaction, and perceived ease of use with Norditropin NordiFlex® compared with the previous device.

2. Patients and methods

2.1. Study design

This was a cross-sectional survey of pediatric and adolescent patients (and/or their caregivers/legally authorized representatives [LARs]) who had been switched to GH therapy with Norditropin NordiFlex® from Norditropin NordiLet® or another GH injection device. The survey was conducted between January 2019 and July 2019 at eight outpatient pediatric clinics in South Korea. Patients were recruited via convenience sampling during regularly scheduled clinic visits.

During these visits, participating physicians identified potential participants, and at the end of the visit, the physician introduced the survey and explained its details to the patient and his/her caregiver/LAR. For children aged 4 to 6 years old, the caregiver/LAR signed the informed consent form. For those aged between 7 and 17 years old, written informed consent was obtained from the patient's caregiver/LAR and the assent form or informed consent form was obtained from children who met the age requirement of each site's Institutional Review Board guidelines. Written informed consent was obtained from participants who were aged 18 years.

Prior to study initiation, the protocol, amendments, informed consent and assent forms were reviewed and approved by the independent ethics committee of the respective study site. The study was conducted in accordance with the protocol and implemented according to the consensus ethical principles derived from international guidelines, including the Declaration of Helsinki and Council for International Organizations of Medical Sciences International Ethical Guidelines, applicable International Council for Harmonization (ICH) Guidelines for Good Pharmacoepidemiology Practices, and other applicable laws and regulations.

2.2. Participants

Patients aged 4 to ≤ 18 years who were current users of Norditropin NordiFlex[®] for 4 to ≤ 12 weeks (initial protocol) at the time of enrollment, and had used another GH device (Norditropin[®] NordiLet[®] or any other GH device) for at least 3 months before switching to Norditropin NordiFlex[®] were eligible to participate.

Owing to the observational nature of the study, the majority of patients who were potentially eligible to participate in this survey had already been switched from their previous device to Norditropin NordiFlex[®] by the time that ethics committee approvals were received and the study sites were ready to enroll patients. Thus, these patients could not be enrolled into the study, limiting the overall number of patients that could participate in the survey. In order to mitigate this limitation and to ensure an appropriate level of statistical power, the protocol was amended to extend the use of Norditropin NordiFlex[®] from 4 to \leq 12 weeks to 4–24 weeks. Enrollment was stopped when no additional patients met the expanded time-related inclusion criterion.

Patients aged 4 to 17 years old were to be accompanied by a LAR to give consent, and the caregiver who administered the injections, if different to the LAR.

Patients who had previously participated in this survey, or who had received any investigational drug within the past 6 months, or had a serious comorbidity or other circumstances that would interfere with adherence to GH therapy, or a physical or mental incapacity (as determined by physicians) interfering with capability to participate in the survey were excluded.

2.3. Assessments/data collection

The survey comprised three parts: A, B, and C (**Appendix B**). Part A contained questions about the patient's clinical and medical information, and was completed by the attending physician. Part B was a self-administered survey that contained questions about the demographic characteristics of the caregiver or LAR. Part C was a 25-item questionnaire (completed by the administrator of GH) assessing primary and secondary outcomes (preference for, satisfaction, perceived ease of use and adherence with Norditropin NordiFlex® compared with the previous GH device) as well as subjective benefits of GH device features, categorized under four domains: *self-efficacy*, *ease of use, minimal disruption of daily life*, and *positive feelings about injection*. These subjective benefits were based on a conceptual model of the factors influencing preference for GH delivery devices (**Figure 1**).

Except for two questions relating to participant classification and adherence on the basis of participants' recall of missed injections in a typical month, participants responded on a 5-point Likert scale: 1, strongly disagree; 2, disagree; 3, no difference; 4, agree; 5, strongly agree. An option of 'not sure' (0) was also provided.

If a participant was unable to choose an option or provide an answer in the survey, the researcher did not coerce the participant to answer the question. All questionnaires were developed in English and were then translated to Korean. Face validity of the survey was assessed by two practicing investigators before rolling out to participants.

No qualitative data were collected in this study.

2.4. Data analysis

Primary and secondary outcome data were categorized as dependent variables. Participant clinical and/or demographic data, as well as data relating to the subjective benefits of GH device features, were categorized as independent variables.

All scores on the Likert scale were transformed from 1 to 5, to standardized scores ranging from -2 to 2 accordingly. '0' responses were replaced with the median score. As the number of items in each domain varied from one another, the total scores were averaged by the number of items within each domain and reported as mean and standard deviation (SD) in order to facilitate interpretation. This resulted in a score of -2 to 2 per domain per patient. Scores from dependent variables were transformed into binary (>0 vs. \leq 0) and ternary variables (>0 vs. 0 vs. <0).

As the study inclusion criteria extended the maximum use of Norditropin NordiFlex® from 12 weeks to 24 weeks, there was a potential for recall bias. This was examined with a sensitivity analysis by comparing preference for, and selfreported adherence with, Norditropin NordiFlex[®] between patients who used Norditropin NordiFlex[®] for 4 to \leq 12 weeks vs. those who used it for >12 weeks.

STATA version 15 (StataCorp LLC, College Station, Texas, USA) was used to analyze the data.

2.5. Statistical methods

Sample size calculation: it was assumed that approximately 64% of users would prefer Norditropin NordiFlex®, based on findings from Tauber and colleagues [24]. With a power of 80% and statistical significance set at 5%, and accounting for potential omitted responses, a sample size of 120 participants who had previously used Norditropin® NordiLet® and 120 participants who had previously used other GH devices were estimated.

Descriptive statistics were used to summarize the main participant demographic characteristics. The mean scores of the dependent variables were compared to the hypothesized value of zero using a one-sided one-sample t-test. Statistical significance level was set at p < 0.05 and power at 80%. Bivariate associations between the dependent and independent variables were performed. Continuous variables were reported as mean (SD) and median (interquartile range), where appropriate. Categorical variables were reported as n (%) and the differences were tested using a chi-square test.

Differences between participants who preferred Norditropin NordiFlex[®] and those who did not were tested using a t-test if the distribution was normal, or a Mann-Whitney U test if the data were not normally distributed.

The contribution of each independent variable on the preference for Norditropin NordiFlex[®] was assessed using multivariate logistic regression accounting for age, sex, height SDS at the point of the survey, and the ratio of duration of treatment with Norditropin NordiFlex[®] to total duration of GH treatment. As the majority of patients previously used Norditropin[®] NordiLet[®] (n = 86) and only eight patients used other devices before Norditropin NordiFlex[®], preference



Figure 1. The conceptual model used to identify factors associated with GH device preference GH, growth hormone; GHD, growth hormone deficiency.

was assessed using a multivariate model that included all participants.

Independent variables that had a statistical significance level of p < 0.1 were included in the multivariate logistic regression model using the backward stepwise removal method. Odds ratios were calculated with 95% Cls.

For the recall bias sensitivity analysis, the percentage of patients who preferred Norditropin NordiFlex[®], as well as the percentage of the patients who missed fewer injections with Norditropin NordiFlex[®], were compared between patients who used Norditropin NordiFlex[®] for 4 to ≤ 12 weeks and those who used the device for >12 to ≤ 24 weeks.

The internal consistency of the items within each domain was assessed using Cronbach's alpha, except for items in the *positive feelings about injections* domain, which were assessed using kappa statistics. Cronbach's alpha values were above the threshold of 0.70 for all three domains (range 0.81–0.92), showing high internal consistency. The two items in *positive feelings about injections* also had a good correlation, with a kappa of 0.79.

No transformation for missing data was required, as all participants provided responses to all survey items.

3. Results

3.1. Patient caregiver/LAR characteristics

A total of 94 patients were enrolled in the survey. Participant demographics and clinical characteristics are described in **Table 1**.

3.2. Primary and secondary outcomes

A significantly greater proportion of participants preferred and were more satisfied with Norditropin NordiFlex[®] compared with the previous device, with mean-standardized scores of 0.65 (95% Cl: 0.41;0.88) and 0.61 (95% Cl: 0.36;0.85), respectively. Similarly, participants reported higher perceived ease of use and fewer missed injections with Norditropin NordiFlex[®] compared with the previous device, with mean standardized scores of 0.49 (95% Cl: 0.26;0.72) and 0.20 (95% Cl: 0.06;0.34), respectively.

Categorization of outcome data as ternary variables showed that more than half of the participants showed a preference for, and had greater satisfaction with Norditropin NordiFlex[®] compared to the previous device (**Figure 2**). Less than 20% of participants preferred or were more satisfied with their previous device. About half of participants perceived Norditropin NordiFlex[®] to be easier to use than their previous device. 15% of participants reported missing fewer injections with Norditropin NordiFlex[®] than with their previous device, and only 3% reported missing fewer injections with their previous device compared with Norditropin NordiFlex[®].

3.3. Preference for Norditropin NordiFlex®

 Table 2 shows the bivariate associations between patient and caregiver/LAR characteristics and preference for Norditropin

Table 1. Patient and caregiver/LAR demographics.

Patients ($N = 94$)	
Age (years), mean (SD)	11.0 (2.0)
Child ^a , n (%)	47 (50.0)
Adolescent ^b , n (%)	47 (50.0)
Sex, n (%)	
Male	34 (36.2)
Female	60 (63.8)
Duration of treatment (years), mean (SD)	2.2 (1.6)
Diagnosis, n (%)	
More severe condition	21 (22.3)
Growth hormone deficiency	/ (/.4)
Small for gestational age	13 (13.8)
Noonan syndrome	(.)
Less severe condition	/3 (//./)
Familial chart stature	50 (55.2) 15 (15.9)
Processions publicity	12 (12.0)
Others ^c	3 (3.3)
No family history of CH disorders n (%)	3 (3.2) 94 (100 0)
Height at diagnosis (cm) mean (SD)	174 A (17 1)
Height SDS at diagnosis (cm), mean (SD)	-10(13)
Weight at diagnosis (kg) mean (SD)	27 3 (10 3)
Weight SDS at diagnosis, mean (SD)	-0.6(1.1)
Height at the point of the survey (cm), mean (SD)	141.3 (13.8)
Height SDS at the point of the survey, mean (SD)	-0.4 (0.9)
Weight at the point of the survey (kg), mean (SD)	37.6 (11.3)
Weight SDS at the point of the survey, mean (SD)	-0.2 (0.8)
Injection administrator, n (%)	
Patient	8 (8.5)
Caregiver/LAR	86 (91.5)
Last device used before Norditropin NordiFlex [®] , n (%)	
Norditropin [®] NordiLet [®]	86 (91.5)
Others"	8 (8.5)
Duration of use of Norditropin NordiFlex [®] at the point of	17.1 (5.8)
survey (weeks), mean (SD)	
No. of injections missed in a typical month, n (%)	0C (01 E)
< > LIMES	6 (6 4)
S-S times	0 (0.4)
Caregivers/LAPs (N = 94)	2 (2.1)
	42.0 (4.0)
Age (years), mean (SD)	43.8 (4.0)
Sex, II (%)	5 (5 2)
Fomale	20 (04 7)
Highest academic qualification n (%)	09 (94.7)
High School	6 (6 4)
University or college	36 (38 3)
Other	10 (10.6)
Preferred not to answer	42 (44.7)
Annual household income in KRW, n (%)	()
<50 million	9 (9.6)
50 million to <70 million	14 (14.6)

^aAge ≤11 years for girls and age ≤12 years for boys, ^bAge >11 years for girls and age >12 years for boys, ^cIncludes hypothyroidism, failure to thrive and constitutional delay of growth and puberty, ^dPrefilled Eutropin[®], Growtropin[®] II, Saizen[®] Easypod[®], Genotropin[®] GoQuick[®]

70 million or more

Preferred not to answer

16 (16.7)

55 (57.3)

GH, growth hormone; KRW, South Korean won; LAR, legally authorized representative; SD, standard deviation; SDS, standard deviation score.

NordiFlex[®]. Patients who preferred Norditropin NordiFlex[®] had a longer duration of GH treatment before switching, compared with those who expressed no preference or preferred the previous device (2.5 years vs. 1.8 years, p = 0.040). Additionally, respondents were significantly more likely to prefer Norditropin NordiFlex[®] if patients were diagnosed with a more severe condition (GHD, SGA, NS) compared to those who were diagnosed with a less severe condition (ISS,



Figure 2. Primary and secondary outcomes: GH device preference, satisfaction, perceived ease of use and missing fewer injections (N = 94) GH, growth hormone.

Table 2 Divariate accordiations between	nations and caregiver/LAD characteristics a	ad proforance for Norditronin NordiFlov®
Iddle Z. Divariate associations between	patient and caregiver/LAR characteristics a	in preference for Noraltrophi NoralFlex ^o .

	Preference for NordiFlex®ª (n = 53)	No difference or preference for previous device ^b (n = 41)	<i>p</i> -value
	Patients		-
Age (years), mean (SD)	11.0 (1.6)	11.0 (2.5)	0.994
Child ^c , n (%)	30 (63.8)	17 (36.2)	
Adolescent ^d , n (%)	23 (48.9)	24 (51.1)	0.112
Sex, n (%)			0.612
Male	18 (52.9)	16 (47.1)	
Female	35 (58.3)	25 (41.7)	
Duration of treatment (years), mean (SD)	2.5 (1.8)	1.8 (1.2)	0.040
Diagnosis, n (%)			0.038 ^f
More severe condition	16 (76.2)	5 (23.8)	
Growth hormone deficiency	6 (85.7)	1 (14.3)	
Small for gestational age	9 (69.2)	4 (30.8)	
Noonan syndrome	1 (100.0)	0 (0.0)	
Less severe condition	37 (50.7)	36 (49.3)	
Idiopathic short stature	21 (42.0)	29 (58.0)	
Familial short stature	9 (75.0)	3 (25.0)	
Precocious puberty	7 (87.5)	1 (12.5)	
Others ^e	0 (0.0)	3 (100.0)	
No family history of GH disorders, n (%)	53 (56.4)	41 (43.6)	N/A
Height at diagnosis (cm), mean (SD)	121.8 (15.8)	127.7 (18.4)	0.094
Height SDS at diagnosis, mean (SD)	-1.2 (1.3)	-0.8 (1.3)	0.167
Weight at diagnosis (kg), mean (SD)	25.8 (8.9)	29.4 (11.6)	0.093
Weight SDS at diagnosis, mean (SD)	-0.7 (1.3)	-0.5 (0.9)	0.427
Height at the point of the survey (cm), mean (SD)	140.2 (11.7)	142.6 (16.2)	0.414
Height SDS at the point of the survey, mean (SD)	-0.6 (0.9)	-0.2 (0.9)	0.067
Weight at the point of the survey (kg), mean (SD)	36.9 (10.3)	38.5 (12.6)	0.479
Weight SDS at the point of the survey, mean (SD)	-0.3 (0.9)	-0.2 (0.8)	0.514
Injection administrator, n (%)			0.715
Patient	5 (62.5)	3 (37.5)	
Caregiver/LAR	48 (55.8)	38 (44.2)	
Last device used before Norditropin NordiFlex [®] , n (%)			0.064 ^h
Norditropin [®] NordiLet [®]	46 (53.5)	40 (46.5)	
Others ^g	7 (87.5)	1 (12.5)	
Duration of use of Norditropin NordiFlex® at the point	16.6 (5.6)	17.7 (6.1)	0.372
of survey (weeks), mean (SD)			
	Caregivers/LARs		
Age (vears) mean (SD)	A3 5 (A 2)	44.2 (3.8)	0 380
Age (years), mean (SD)	43.3 (4.2)	44.2 (5.8)	0.360
Mala	2 (60.0)	2 (40.0)	0.007
Fomalo	5 (00.0)	2 (40.0)	
Highest academic qualification in (%)	50 (50.2)	37 (4 3.0)	0 3 2 5
High School	5 (92 2)	1 (16 7)	0.525
Liniversity or college	ט (02,5) כר (61 1)	1 (10.7) 14 (20 0)	
Othor	22 (01.1) A (40.0)	14 (30.9) 6 (60.0)	
Dreferred pot to answer	4 (40.0) 22 (52 A)	0 (00.0)	
	22 (32.4)	20 (47.0)	

(Continued)

Table 2. (Continued).

	Preference for NordiFlex ^{®a} (n = 53)	No difference or preference for previous device ^b (n = 41)	<i>p</i> -value
	Patients		
Annual household income in KRW, n (%)			0.583
<50 million	6 (66.7)	3 (33.3)	
50 million to <70 million	7 (50.0)	7 (50.0)	
70 million or more	7 (43.8)	9 (56.3)	
Preferred not to answer	33 (60.0)	22 (44.0)	

^aStandardized score of preference toward NordiFlex[®] >0, ^bStandardized score of preference toward NordiFlex[®] ≤ 0 , ^cAge ≤ 11 years for girls and age ≤ 12 years for boys, ^dAge >11 years for girls and age >12 years for boys, ^eIncludes hypothyroidism, failure to thrive and constitutional delay of growth and puberty, ^fp-value for comparison between 'more severe condition' and 'less severe condition', ^gPrefilled Eutropin[®], Growtropin[®] II, Saizen[®] Easypod[®], Genotropin[®] GoQuick[®], ^hp-value for comparison between 'Norditropin[®] NordiLet[®]' and 'Others'

GH, growth hormone; KRW, South Korean won; LAR, legally authorized representative; SD, standard deviation; SDS, standard deviation score.

familial short stature [FSS], precocious puberty, others) (76.2% vs. 50.7%, p = 0.038). No significant associations were identified for age, sex, height, and weight at diagnosis, height SDS and weight SDS at diagnosis, height and weight at the point of the survey, height SDS and weight SDS at the point of the survey, administrator of injection, last device used before Norditropin NordiFlex[®], and duration of Norditropin NordiFlex[®] use. There were no significant associations between caregiver/LAR characteristics and preference for Norditropin NordiFlex[®].

Respondents who preferred Norditropin NordiFlex[®] had higher standardized scores on *self-efficacy* (1.33 [0.69] vs. 0.41 [0.87]), *ease of use* (1.14 [0.75] vs. 0.02 [0.82]), *minimal disruption of daily life* (0.67 [0.88] vs. -0.18 [0.49]), and *positive feelings about injection* (0.58 [0.85] vs. -0.24 [0.63]) compared with those who reported no difference or preferred the previous device (all p < 0.001) (**Figure 3A**).

3.3.1. Subgroup analyses of participants who used Norditropin NordiFlex® for 4 to ≤ 12 weeks and those who used it for >12 weeks

There was no significant difference in GH device preference between those who used Norditropin NordiFlex[®] for 4 to ≤ 12 weeks and those who used it for >12 weeks (64.0% vs. 53.6%, p = 0.370).

3.3.2. Multivariate analysis of factors associated with preference for Norditropin NordiFlex®

Multivariate analysis (accounting for age, sex, height SDS at the point of the survey and the ratio of duration of treatment with Norditropin NordiFlex® to total duration of GH treatment) showed that higher scores of *ease of use* (adjusted odds ratio [OR] [95% CI]: 3.77 [1.04;13.57]; p = 0.042) and *minimal disruption of daily life* (adjusted OR [95% CI]: 5.05 [1.09;23.25]; p = 0.038) were significantly associated with preference for Norditropin NordiFlex®.

However, the observed associations with *self-efficacy* (adjusted OR [95% CI]: 1.10 [0.38;3.21]) and *positive feelings about injection* (adjusted OR [95% CI]: 1.63[0.44;6.01]) were no longer statistically significant (p > 0.05).

3.4. Satisfaction with Norditropin NordiFlex®

Patients who experienced greater satisfaction with Norditropin NordiFlex[®] had longer duration of GH treatment before switching, compared with those who experienced no difference or were more satisfied with the previous device (2.5 years vs. 1.8 years, p = 0.03). Additionally, patients with a relatively more severe diagnosis also showed significantly higher satisfaction with Norditropin NordiFlex[®] vs. the previous device (81.0% vs. 49.3%, p = 0.01). There were no significant associations between caregiver/LAR characteristics and satisfaction with Norditropin NordiFlex[®] (**Table 3**).

Respondents who were more satisfied with Norditropin NordiFlex[®] had higher standardized scores on *self-efficacy* (1.35 [0.66] vs. 0.40 [0.89]), *ease of use* (1.19 [0.67] vs. -0.01 [0.83]), *minimal disruption of daily life* (0.67 [0.86] vs. -0.18 [0.53]), and *positive feelings about injection* (0.60 [0.82] vs. -0.27 [0.65]) compared with those who reported no difference or were more satisfied with the previous device (all p < 0.001) (**Figure 3B**).

3.5. Perceived ease of use with Norditropin NordiFlex®

Similarly, patients who perceived Norditropin NordiFlex[®] to be easier to use were significantly more likely to have been receiving GH treatment for a longer period of time before switching, compared with those who perceived no difference or perceived the previous device to be easier to use (2.6 years vs. 1.9 years, p = 0.03) and diagnosed with a relatively more severe condition (66.7% vs. 39.7%, p = 0.029). There were no significant associations between caregiver/LAR characteristics and perceived ease of use with Norditropin NordiFlex[®] (**Table 4**).

Respondents who perceived Norditropin NordiFlex® to be easier to use vs their previous device had higher standardized scores on *self-efficacy* (1.51 [0.61] vs. 0.45 [0.82]), *ease of use* (1.33 [0.61] vs. 0.10 [0.82]), *minimal disruption of daily life* (0.77 [0.87] vs. -0.09 [0.59]), and *positive feelings about injection* (0.70 [0.87] vs. -0.18 [0.64]) compared with those who reported no difference or perceived the previous



Figure 3. Associations between domains of subjective benefits and preference for (A), satisfaction with (B), perceived ease of use (C), and self-reported adherence (D) with Norditropin NordiFlex[®].

device to be easier to use vs Norditropin NordiFlex[®] (all p < 0.001) (Figure 3C).

3.6. Self-reported adherence with Norditropin NordiFlex®

Patients who missed fewer injections with Norditropin NordiFlex[®] (compared with those who reported no difference or missed fewer injections with the previous device)

were more likely to be: i) a child rather than an adolescent (25.5% vs. 4.3%, p = 0.008); ii) diagnosed with a relatively more severe medical condition (33.3% vs. 9.6%, p = 0.007); iii) shorter and smaller at diagnosis (height 112.4 cm vs. 126.5 cm, p = 0.004; weight 21.4 kg vs. 28.4 kg, p = 0.018); and iv) shorter at the point of the survey (height 132.9 cm vs 142.7 cm, p = 0.014; height SDS -0.9 vs. -0.3, p = 0.027) (**Table 5**).

Table 3. Bivariate associations between patient and caregiver/LAR characteristics and satisfaction with Norditropin NordiFlex®.

Patients Age (years), mean (SD) 11.0 (1.8) 11.0 (2.4) 0.928 Adde (years), mean (SD) 28 (59.6) 19 (40.4) 0.242 Adde scent ¹ , n (%) 25 (53.2) 22 (46.8) 0.242 Male 18 (52.9) 16 (47.1) 0.030 Male 18 (52.9) 16 (47.1) 0.030 Duration of treatment (years), mean (SD) 2.5 (1.8) 18 (1.2) 0.030 Diagnosis, n (%) 0.010 4 (19.1) 0.010 Growth hormone deficiency 6 (85.7) 1 (14.3) 11.0 (2.0) Small for gestational age 10 (76.9) 3 (23.1) 10.000 Less severe condition 36 (49.3) 37 (50.7) 10.000 Idiopathic short stature 28 (66.7) 4 (33.3) 10.000 Precoclous puberty 6 (75.0) 2 (25.0) 0.152 Others ⁴ 0.0.0 3 (100.0) 0.092 Weight at diagnosis, mean (SD) -12 (1.3) -0.8 (1.4) 0.182 Veight at diagnosis, mean (SD) -07 (13. -0.5 (0.9)		More satisfied with NordiFlex ^{®a} (n = 53)	No difference or more satisfied with previous device ^b $(n = 41)$	<i>p</i> -value
lage (years), mean (SD) 11.0 (1.8) 11.0 (2.4) 0.928 Childr, n (%) 26 (S5.6) 19 (40.4) 0.242 Adolescent ⁴ , n (%) 25 (S3.2) 22 (46.8) 0.412 Male 18 (52.9) 16 (47.1) 0.612 Pernale 35 (S8.3) 25 (41.7) 0.030 Duation of treatment (years), mean (SD) 2.5 (1.8) 1.8 (1.2) 0.030 More severe condition 17 (81.0) 4 (19.1) 0.010 Growth hormone deficiency 6 (85.7) 1 (14.3) 0.010 Small for gestational age 10 (76.9) 3 (23.1) 0.000 Less severe condition 36 (49.3) 37 (50.7) 1 I diopathic short stature 8 (66.7) 4 (33.3) Precolous puberty 6 (75.0) 2 (25.0) Others* ⁶ 0 (0.0) 3 (100.0) N N No A (43.6) N/A Height at diagnosis, mean (SD) -12.7 (1.3) -0.8 (1.4) 0.182 No (5.2) 0.002 Weight at diagnosis, mean (SD) -12.7 (1.3) -0.8 (1.4) 0.182 No (5.2) 0.520 Weight at diagnosi		Patients		
Child's (n (%) Adolescent', n (%) 28 (59.6) 19 (40.4) (40.4) 0.242 Sex, n (%) 25 (53.2) 22 (46.8) 0.612 Male 18 (52.9) 16 (47.1) 0.030 Duration of treatment (years), mean (SD) 2.5 (1.8) 1.8 (1.2) 0.030 Diagnosis, n (%) 0.010' 4 (19.1) 0.010' Growth hormone deficiency 6 (85.7) 1 (14.3) 5mail for gestational age 10 (76.9) 3 (23.1) Noona syndrome 1 (100.0) 0 (0.0) 12 (56.0) 14 (36.1) VA I diopathic short stature 2.2 (44.0) 2.8 (56.0) 2 (25.0) 0 (0.0) 3 (100.0) No No cans syndrome 6 (75.0) 2 (25.0) 0 (0.0) 3 (100.0) NA Precocious puberty 6 (75.0) 2 (25.0) 0 (0.0) 3 (100.0) NA No fight short stature 8 (66.7) 4 (3.36) NA Height stop of GH disorders, n (%) 53 (56.4) 41 (43.6) NA Height stop of GH disorders, n (%) 53 (56.4) 41 (43.6) NA Height stop and fight spins (man (SD) -0.7 (13) -0.8 (1.4) <td< td=""><td>Age (years), mean (SD)</td><td>11.0 (1.8)</td><td>11.0 (2.4)</td><td>0.928</td></td<>	Age (years), mean (SD)	11.0 (1.8)	11.0 (2.4)	0.928
$ \begin{array}{cccc} Adolescent0, n (%) & 25 (32,2) & 22 (4.6.8) & 0.612 \\ \hline Male & 18 (52.9) & 16 (47.1) & 0.612 \\ \hline Male & 35 (58.3) & 25 (41.7) & 0.030 \\ \hline Duration of treatment (years), mean (SD) & 2.5 (1.8) & 1.8 (1.2) & 0.030 \\ \hline More severe condition & 17 (81.0) & 4 (19.1) & 0.010^{10} & 0.010^{10} & 0.010^{10} & 0.001 & 0.001 & 0.001 & 0.001 & 0.001 & 0.001 & 0.001 & 0.0000 & 0.000 & 0.0000 & 0.0000 & 0.0000 & 0.0000 & 0.0000 & 0.0000$	Child ^c , n (%)	28 (59.6)	19 (40.4)	0.242
Sex, n %b) 0.612 Male 16 (47.1) Female 35 (58.3) 25 (41.7) Duration of treatment (years), mean (SD) 2.5 (1.8) 1.8 (1.2) 0.030 Diagnosis, n (%b) 0.0101 4 (19.1) 0.0101 Growth hormone deficiency 6 (85.7) 1 (14.3) 0.0101 Small for gestational age 10 (76.9) 3 (23.1) 0.000 Less severe condition 36 (49.3) 37 (50.7) 1 Idiopathic short stature 22 (44.0) 28 (56.0) - Familial short stature 8 (66.7) 4 (33.3) - Precocious puberty 6 (75.0) 2 (25.0) 0.00.0 Others* 0 (0.0) 3 (100.0) NA Neight at diagnosis (m, mean (SD) 12 17 (16.0) 127 8 (18.2) 0.152 Height at diagnosis (m, mean (SD) -0.7 (1.3) -0.5 (0.9) 0.427 Height at diagnosis (m, mean (SD) -0.7 (1.3) -0.5 (0.9) 0.220 Weight SDS at diagnosis, mean (SD) -0.2 (0.9) -0.2 (0.8) 0.979	Adolescent ^d , n (%)	25 (53.2)	22 (46.8)	0.242
Male 16 (52.9) 16 (47.1) Fenale 35 (58.3) 25 (41.7) Duration of treatment (years), mean (SD) 2.5 (1.8) 1.8 (1.2) 0.030 Diagnosis, n (%) 0.010 ⁴ 0.010 ⁴ 0.010 ⁴ More severe condition 17 (81.0) 4 (19.1) 0.010 ⁴ Growth hormone deficiency 6 (85.7) 1 (14.3) 5.031 Small for gestational age 10 (76.9) 3 (23.1) 1.000.0 Less severe condition 36 (49.3) 37 (50.7) 1.000.0 Idiopathic short stature 22 (44.0) 28 (56.0) 2.025.0 Others ⁶ 0 (0.0) 3 (100.0) 0.00.0 0.00.0 No family history of GH disorders, n (%) 53 (56.4) 41 (43.6) N/A Height SDS at diagnosis, mean (SD) -12.1 (1.3) -0.8 (1.4) 0.182 Weight SDS at the point of the survey (man, mean (SD) -0.5 (0.9) -0.5 (0.9) 0.220 Weight SDS at the point of the survey (kg), mean (SD) -0.2 (0.9) -0.2 (0.8) 0.979 Injection administrator, n (%) 5 (62.5)	Sex, n (%)			0.612
Female 25 (58.3) 25 (41.7) Duration of treatment (years), mean (SD) 2.5 (1.8) 1.8 (1.2) 0.030 Diagnosis, n (%) 0.010 ⁴ 0.010 ⁴ 0.010 ⁴ More severe condition 17 (81.0) 4 (19.1) 0.030 ⁴ Growth hormone deficiency 6 (85.7) 114.3 0.010 ⁴ Noona syndrome 1 (10.0) 0 (0.0) 0.00 Less severe condition 36 (49.3) 37 (50.7) 140.3 Idiopatitic short stature 22 (44.0) 28 (56.0) 7.8 Precoclous puberty 6 (75.0) 2 (25.0) 0.00.0 Others ⁴ 0 (0.0) 3 (100.0) N/A Height at diagnosis (m), mean (SD) 121.7 (16.0) 122.78 (18.2) 0.152 Height at diagnosis (magnosis (magnosis), mean (SD) -0.7 (1.3) -0.5 (0.9) 0.467 Height SDS at diagnosis (magnosis (m), mean (SD) 140.5 (12.4) 142.2 (15.5) 0.556 Height SDS at the point of the survey, mean (SD) -0.7 (1.3) -0.5 (0.9) 0.220 Weight SDS at diagnosis, mean (SD) 37 (20.5)	Male	18 (52.9)	16 (47.1)	
Duration of treatment (years), mean (SD) 2.5 (1.8) 1.8 (1.2) 0.030 Diagnosis, n (%) 0.010 0.010 More severe condition 17 (81.0) 4 (19.1) Growth hormone deficiency 6 (85.7) 1 (14.3) Small for gestational age 10 (76.9) 3 (23.1) Noonan syndrome 1 (100.0) 0 (0.0) Less severe condition 36 (49.3) 37 (50.7) Idiopathic short stature 8 (66.7) 4 (33.3) Precocious puberty 6 (75.0) 2 (25.0) Others ⁶ 0 (0.0) 3 (100.0) No family history of GH disorders, n (%) 53 (56.4) 41 (43.6) N/A Height at diagnosis (m), mean (SD) -12 (1.3) -0.8 (1.4) 0.182 Weight at diagnosis, mean (SD) -0.7 (1.3) -0.5 (0.9) 0.467 Height SDS at diagnosis, mean (SD) -0.2 (0.9) -0.3 (0.9) 0.220 Weight SD S at the point of the survey (mean (SD) -0.2 (0.9) -0.2 (0.8) 0.979 Inglite short the survey (mean (SD) -0.2 (0.9) -0.2 (0.8) 0.979	Female	35 (58.3)	25 (41.7)	
Diagnosis, n (%) 0.010' More severe condition 17 (81.0) 4 (19.1) Growth hormone deficiency 6 (85.7) 1 (14.3) Small for gestational age 10 (76.9) 3 (23.1) Noonan syndrome 1 (100.0) 0 (0.0) Less severe condition 36 (49.3) 37 (50.7) Idiopatitic short stature 22 (44.0) 28 (56.0) Familial short stature 8 (66.7) 4 (33.3) Precocious puberty 6 (75.0) 2 (25.0) Others* 0 (0.0) 3 (100.0) No faily history of GH disorders, n (%) 53 (56.4) 41 (43.6) N/A Height SDS at diagnosis (m, mean (SD) 121.7 (16.0) 122.8 (18.2) 0.152 Weight at diagnosis (m, mean (SD) -0.7 (1.3) -0.5 (0.9) 0.467 Height SDS at diagnosis (m, mean (SD) -0.7 (1.3) -0.5 (0.9) 0.220 Weight SDS at the point of the survey, mean (SD) -0.2 (0.9) -0.2 (0.8) 0.979 Ingitic and ministrator, n (%) 7 2 (0.5.) 3 (37.5) 0.6467 Weight SDS at the point	Duration of treatment (years), mean (SD)	2.5 (1.8)	1.8 (1.2)	0.030
More severe condition 17 (81.0) 4 (19.1) Growth hormone deficiency 6 (85.7) 1 (14.3) Small for gestational age 10 (76.9) 3 (23.1) Noonan syndrome 1 (100.0) 0 (0.0) Less severe condition 36 (49.3) 37 (50.7) Idiopathic short stature 22 (44.0) 28 (56.0) Familial short stature 8 (66.7) 4 (33.3) Precocious puberty 6 (75.0) 2 (25.0) Others ⁶ 0 (0.0) 3 (100.0) No family history of GH disorders, n (%) 53 (56.4) 41 (43.6) N/A Height at diagnosis (cm), mean (SD) -12 (1.3) -0.8 (1.4) 0.186 Weight at diagnosis, mean (SD) -27 (8.9) 29.4 (11.6) 0.092 Weight SDS at diagnosis, mean (SD) -0.7 (1.3) -0.5 (0.9) 0.467 Height SDS at the point of the survey, mean (SD) -0.5 (0.9) -0.2 (0.8) 0.979 Injection administrator, n (%) 72 (10.5) 38 (12.4) 0.723 Height SDS at the point of the survey, mean (SD) -0.2 (0.9) -0.2 (0.8) 0.979 <td>Diagnosis, n (%)</td> <td></td> <td></td> <td>0.010'</td>	Diagnosis, n (%)			0.010'
Growth hormone deficiency 6 (85.7) 1 (14.3) Small for gestational age 10 (76.9) 3 (23.1) Noonan syndrome 1 (100.0) 0 (0.0) Less severe condition 36 (49.3) 37 (50.7) Idiopatitic short stature 22 (44.0) 28 (56.0) Familial short stature 8 (66.7) 4 (33.3) Precocious puberty 6 (75.0) 2 (25.0) Others* 0 (0.0) 3 (100.0) No family history of GH disorders, n (%) 53 (56.4) 41 (43.6) N/A Height at diagnosis (m, mean (SD) 12.17 (15.0) 127.8 (18.2) 0.152 Weight SDS at diagnosis, mean (SD) -0.7 (1.3) -0.8 (1.4) 0.166 Weight SDS at diagnosis, mean (SD) -0.7 (1.3) -0.5 (0.9) 0.467 Height SDS at the point of the survey mean (SD) -0.2 (0.9) -0.2 (0.8) 0.979 Weight SDS at the point of the survey mean (SD) -0.2 (0.9) -0.2 (0.8) 0.979 Injection administrator, n (%) -0.2 (0.9) -0.2 (0.8) 0.979 Patient 5 (62.5) 3 (37.5)	More severe condition	17 (81.0)	4 (19.1)	
Small for gestational age 10 (76.9) 3 (23.1) Noonan syndrome 1 (100.0) 0 (0.0) Less severe condition 36 (49.3) 37 (50.7) Idiopathic short stature 22 (44.0) 28 (56.0) Familial short stature 8 (66.7) 4 (33.3) Precocious puberty 6 (75.0) 2 (25.0) Others* 0 (0.0) 3 (100.0) No family history of GH disorders, n (%) 53 (56.4) 41 (43.6) N/A Height at diagnosis (cm), mean (SD) 121.7 (16.0) 127.8 (18.2) 0.152 Height SDS at diagnosis, mean (SD) -12 (1.3) -0.8 (1.4) 0.186 Weight SDS at diagnosis, mean (SD) -0.7 (1.3) -0.5 (0.9) 0.467 Height SDS at the point of the survey (mn), mean (SD) -0.5 (0.9) -0.3 (0.9) 0.220 Weight SDS at the point of the survey, mean (SD) -0.2 (0.9) -0.2 (0.8) 0.979 Ipection administrator, n (%) 37.2 (10.5) 38.1 (12.4) 0.723 Weight SDS at the point of the survey, mean (SD) -0.2 (0.9) -0.2 (0.8) 0.979 Ipection administrator, n (%) 7 (87.5) 1 (12.5) 0.664 ^h	Growth hormone deficiency	6 (85.7)	1 (14.3)	
Noonan syndrome 1 (100.0) 0 (0.0) Less severe condition 36 (49.3) 37 (50.7) Idiopathic short stature 22 (44.0) 28 (56.0) Familial short stature 8 (66.7) 4 (33.3) Precocious puberty 6 (75.0) 2 (25.0) Others ⁶ 0 (0.0) 3 (100.0) No family history of GH disorders, n (%) 53 (56.4) 41 (43.6) N/A Height ta diagnosis (m), mean (SD) 121.7 (16.0) 127.8 (18.2) 0.152 Height SDS at diagnosis, mean (SD) -1.2 (1.3) -0.8 (1.4) 0.186 Weight at diagnosis (m), mean (SD) -0.7 (1.3) -0.5 (0.9) 0.467 Height SDS at diagnosis, mean (SD) -0.7 (1.3) -0.5 (0.9) 0.467 Height SDS at the point of the survey, mean (SD) -0.2 (0.9) -0.3 (0.9) 0.220 Weight SDS at the point of the survey, mean (SD) -0.2 (0.9) -0.2 (0.8) 0.979 Injection administrator, n (%) 72 (10.5) 38.1 (12.4) 0.723 Weight SDS at the point of the survey, mean (SD) -0.2 (0.9) -0.2 (0.8) 0.9791	Small for gestational age	10 (76.9)	3 (23.1)	
Less severe condition 36 (49.3) 37 (50.7) Idiopathic short stature 22 (44.0) 28 (56.0) Familial short stature 8 (66.7) 4 (33.3) Precocious puberty 6 (75.0) 2 (25.0) Others ⁶ 0 (0.0) 3 (100.0) No family history of GH disorders, n (%) 53 (56.4) 41 (43.6) N/A Height at diagnosis (cm), mean (SD) -1.2 (1.3) -0.8 (1.4) 0.186 Weight SD st diagnosis, mean (SD) -0.7 (1.3) -0.5 (0.9) 0.467 Height SD st diagnosis, mean (SD) -0.7 (1.3) -0.5 (0.9) 0.467 Height SD st diagnosis, mean (SD) -0.2 (0.9) -0.3 (0.9) 0.220 Weight SD st the point of the survey (mean (SD) -0.2 (0.9) -0.2 (0.8) 0.979 Injection administrator, n (%) 0 -0.2 (0.9) -0.2 (0.8) 0.979 Injection administrator, n (%) -0.2 (0.9) -0.2 (0.8) 0.979 Injection administrator, n (%) -0.2 (0.9) -0.2 (0.8) 0.979 Injection administrator, n (%) -0.2 (0.9) -0.2 (0.8) 0.064	Noonan syndrome	1 (100.0)	0 (0.0)	
Idiopathic short stature 22 (44.0) 28 (56.0) Familial short stature 8 (66.7) 4 (33.3) Precocious puberty 6 (75.0) 2 (25.0) Others ⁶ 0 (0.0) 3 (100.0) No family history of GH disorders, n (%) 53 (56.4) 41 (43.6) N/A Height at diagnosis (cm), mean (SD) 121.7 (16.0) 127.8 (18.2) 0.152 Height SDS at diagnosis, mean (SD) -1.2 (1.3) -0.8 (1.4) 0.062 Weight at diagnosis (kg), mean (SD) -0.7 (1.3) -0.5 (0.9) 0.467 Height SDS at diagnosis, mean (SD) -0.5 (0.9) -0.3 (0.9) 0.220 Weight SDS at the point of the survey (cm), mean (SD) -0.5 (0.9) -0.2 (0.9) -0.2 (0.9) 0.220 Weight SDS at the point of the survey, mean (SD) -0.5 (0.9) -0.2 (0.8) 0.979 Injection administrator, n (%) 37.2 (10.5) 38.1 (12.4) 0.723 Weight SDS at the point of the survey, mean (SD) -0.2 (0.9) -0.2 (0.8) 0.979 Injection administrator, n (%) - 0.064 ^h 0.064 ^h Norditropin® NordiFlex®	Less severe condition	36 (49.3)	37 (50.7)	
Familial short stature 8 (66.7) 4 (33.3) Precocious puberty 6 (75.0) 2 (25.0) Others ⁶ 0 (0.0) 3 (100.0) No family history of GH disorders, n (%) 53 (56.4) 41 (43.6) N/A Height at diagnosis (mn, mean (SD) 1217 (16.0) 127.8 (18.2) 0.152 Height at diagnosis (kg), mean (SD) -1.2 (1.3) -0.8 (1.4) 0.186 Weight SDS at diagnosis, mean (SD) -0.7 (1.3) -0.5 (0.9) 0.467 Height at the point of the survey (cm), mean (SD) 140.5 (12.4) 142.2 (15.5) 0.560 Height SDS at the point of the survey, mean (SD) -0.5 (0.9) -0.3 (0.9) 0.220 Weight SDS at the point of the survey, mean (SD) -0.2 (0.9) -0.2 (0.8) 0.979 Injection administrator, n (%) 0.715 38.1 (12.4) 0.723 Patient 5 (62.5) 3 (37.5) 0.208 0.979 Injection administrator, n (%) 7 (87.5) 1 (12.5) 0.064 ^h Norditropin® NordiLet [®] 7 (87.5) 1 (12.5) 0.212 Duration of use of NordiFlex [®] at the point of survey 43.6 (4.2) 44.0 (3.8) 0.604	Idiopathic short stature	22 (44.0)	28 (56.0)	
Precocious puberty 6 (75.0) 2 (25.0) Others ⁶ 0 (0.0) 3 (100.0) No family history of GH disorders, n (%) 53 (56.4) 41 (43.6) N/A Height at diagnosis (cm), mean (SD) 121.7 (16.0) 127.8 (18.2) 0.152 Height SDS at diagnosis, mean (SD) -1.2 (1.3) -0.8 (1.4) 0.082 Weight at diagnosis (kg), mean (SD) -0.7 (1.3) -0.5 (0.9) 0.467 Height SDS at diagnosis, mean (SD) -0.7 (1.3) -0.5 (0.9) 0.467 Height SDS at the point of the survey (mean (SD) 140.5 (12.4) 142.2 (15.5) 0.560 Height SDS at the point of the survey, mean (SD) -0.2 (0.9) -0.2 (0.8) 0.979 Injection administrator, n (%) 37.2 (10.5) 38.1 (12.4) 0.723 Patient 5 (62.5) 3 (37.5) 2 2 Caregiver/LAR 48 (55.8) 38 (44.2) 0.064 ^h Norditropin [®] NordiLet [®] n (%) 0.064 ^h 0.064 ^h Nerditropin [®] NordiFlex [®] at the point of survey 16.3 (5.5) 18.2 (6.0) 0.112 Uast device	Familial short stature	8 (66.7)	4 (33.3)	
Others ⁵ 0 (0.0) 3 (100.0) No family history of GH disorders, n (%) 53 (56.4) 41 (43.6) N/A Height at diagnosis (cm), mean (SD) 121.7 (16.0) 127.8 (18.2) 0.152 Height at diagnosis, mean (SD) -1.2 (1.3) -0.8 (1.4) 0.186 Weight SDS at diagnosis, mean (SD) -0.7 (1.3) -0.5 (0.9) 0.467 Height at the point of the survey, mean (SD) -0.5 (0.9) -0.3 (0.9) 0.220 Weight SDS at the point of the survey, mean (SD) -0.5 (0.9) -0.3 (0.9) 0.220 Weight SDS at the point of the survey, mean (SD) -0.2 (0.9) -0.2 (0.8) 0.979 Injection administrator, n (%) -0.6 (5.5) 3 (37.5) 0.664 ^h Norditropin® NordiFlex®, n (%) -0.6 (5.5) 1 (12.5) 0.064 ^h Norditropin® NordiFlex®, n (%) -0.63 (5.5) 1 (2.5) 0.064 ^h Norditropin® NordiFlex® at the point of survey 16.3 (5.5) 1 (2.5) 0.112 Duration of use of NordiFlex® at the point of survey 1 (6.3 (5.5) 1 (2.5) 0.867 Male 3 (60.0) 2 (40.0)	Precocious puberty	6 (75.0)	2 (25.0)	
No family history of GH disorders, n (%) 53 (56.4) 41 (43.6) N/A Height at diagnosis (cm), mean (SD) 121.7 (16.0) 127.8 (18.2) 0.152 Height SDS at diagnosis, mean (SD) -1.2 (1.3) -0.8 (1.4) 0.186 Weight SDS at diagnosis, mean (SD) -0.7 (1.3) -0.5 (0.9) 0.467 Height SDS at the point of the survey (cm), mean (SD) 140.5 (12.4) 142.2 (15.5) 0.560 Height SDS at the point of the survey, mean (SD) -0.5 (0.9) -0.3 (0.9) 0.220 Weight SDS at the point of the survey, mean (SD) -0.2 (0.9) -0.2 (0.8) 0.979 Injection administrator, n (%) -0.2 (0.9) -0.2 (0.8) 0.979 Injection administrator, n (%) -0.6 (5.5) 3 (37.5) 0.715 Patient 5 (62.5) 3 (37.5) 0.064 ^h Norditropin® NordiEle®, n (%) -0.645 0.064 ^h Norditropin® NordiFlex® at the point of survey 16.3 (5.5) 18.2 (6.0) 0.064 ^h Weight SDS at the point of survey 16.3 (5.5) 18.2 (6.0) 0.064 ^h Norditropin % NordiFlex® at the point of survey 16.3 (5.5) 18.2 (6.0) 0.064 ^h Nale<	Others	0 (0.0)	3 (100.0)	
Height at diagnosis (cm), mean (SD) 121.7 (16.0) 127.8 (18.2) 0.152 Height SDS at diagnosis, mean (SD) -1.2 (1.3) -0.8 (1.4) 0.186 Weight at diagnosis (kg), mean (SD) 25.7 (8.9) 29.4 (11.6) 0.092 Weight SDS at diagnosis, mean (SD) -0.7 (1.3) -0.5 (0.9) 0.467 Height SDS at the point of the survey, (cm), mean (SD) 140.5 (12.4) 142.2 (15.5) 0.560 Height SDS at the point of the survey, mean (SD) -0.5 (0.9) -0.3 (0.9) 0.220 Weight at the point of the survey, mean (SD) -0.2 (0.9) -0.2 (0.8) 0.979 Injection administrator, n (%) 0.262.5) 3 (37.5) 0.715 Caregiver/LAR 48 (55.8) 38 (44.2) 0.064 ^h Norditropin® NordiFlex®, n (%) 0.064 ^h 0.064 ^h Norditropin® NordiFlex® at the point of survey 16.3 (5.5) 18.2 (6.0) 0.112 (weeks), mean (SD) 3 (60.0) 2 (40.0) 0.867 0.867 Male 3 (60.0) 2 (40.0) 0.3667 0.325 Male 3 (60.0) 2 (40.0) 0.325 0.325 Male 3 (60.0)	No family history of GH disorders, n (%)	53 (56.4)	41 (43.6)	N/A
Height SDS at diagnosis, mean (SD) -1.2 (1.3) -0.8 (1.4) 0.186 Weight at diagnosis (mean (SD) 25.7 (8.9) 29.4 (11.6) 0.092 Weight SDS at diagnosis, mean (SD) -0.7 (1.3) -0.5 (0.9) 0.467 Height at the point of the survey (cm), mean (SD) 140.5 (12.4) 142.2 (15.5) 0.560 Height SDS at the point of the survey, mean (SD) -0.5 (0.9) -0.3 (0.9) 0.220 Weight SDS at the point of the survey, mean (SD) -0.2 (0.9) -0.2 (0.8) 0.979 Injection administrator, n (%) 0.220 0.2 (0.8) 0.979 Injection administrator, n (%) 0.2 (0.9) -0.2 (0.8) 0.715 Patient 5 (62.5) 3 (37.5) 0.064 ^h Norditropin® NordiLet® 46 (53.5) 40 (46.5) 0.064 ^h Norditropin® NordiLet® 7 (87.5) 1 (12.5) 0.112 Duration of use of NordiFlex® at the point of survey 16.3 (5.5) 18.2 (6.0) 0.867 Male 3 (60.0) 2 (40.0) 0.867 0.867 Male 3 (60.0) 2 (40.0) 0.867 0.325 High School 5 (83.3) 1 (16.7)<	Height at diagnosis (cm), mean (SD)	121.7 (16.0)	127.8 (18.2)	0.152
Weight at diagnosis (kg), mean (SD) 25.7 (8.9) 29.4 (11.6) 0.092 Weight SDS at diagnosis, mean (SD) -0.7 (1.3) -0.5 (0.9) 0.467 Height at the point of the survey (cm), mean (SD) 140.5 (12.4) 142.2 (15.5) 0.560 Height SDS at the point of the survey, mean (SD) -0.5 (0.9) -0.3 (0.9) 0.220 Weight SDS at the point of the survey, mean (SD) -0.2 (0.9) -0.2 (0.8) 0.979 Injection administrator, n (%) 0.715 $3(37.5)$ 0.715 Patient 5 (62.5) 3 (37.5) 0.764^h Last device used before Norditropin NordiFlex®, n (%) 0.064^h 0.064^h Norditropin® NordiLet® 7 (87.5) 1 (12.5) 0.064^h Uweeks), mean (SD) 43.6 (4.2) 44.0 (3.8) 0.604^h Vereexs, mean (SD) 43.6 (4.2) 44.0 (3.8) 0.604^h Sex, n (%) 0.867 0.867 0.867 Male 3 (60.0) 2 (40.0) 0.867 High School 5 (83.3) 1 (16.7) 0.325 High School 5 (83.3) 1 (16.7) 0.325 <	Height SDS at diagnosis, mean (SD)	-1.2 (1.3)	-0.8 (1.4)	0.186
Weight SDS at diagnosis, mean (SD) -0.7 (1.3) -0.5 (0.9) 0.467 Height at the point of the survey (cm), mean (SD) 140.5 (12.4) 142.2 (15.5) 0.560 Weight At the point of the survey, mean (SD) -0.5 (0.9) -0.3 (0.9) 0.220 Weight At the point of the survey, mean (SD) 37.2 (10.5) 38.1 (12.4) 0.723 Weight SDS at the point of the survey, mean (SD) -0.2 (0.9) -0.2 (0.8) 0.979 Injection administrator, n (%) 0.220 0.715 0.715 Patient 5 (62.5) 3 (37.5) 0.715 Caregiver/LAR 48 (55.8) 38 (44.2) 0.064^h Norditropin® NordiLet® 46 (53.5) 40 (46.5) 0.064^h Norditropin® NordiLet® 46 (53.5) 18.2 (6.0) 0.112 Caregiver/LAR Advise of NordiFlex® at the point of survey 16.3 (5.5) 18.2 (6.0) 0.604^h Nordiclet® 0.604^h 0.867^h Male 3 (60.0) 2 (40.0) 0.867^h Male 3 (60.0) 2 (40.0) 0.325^h Female	Weight at diagnosis (kg), mean (SD)	25.7 (8.9)	29.4 (11.6)	0.092
Height at the point of the survey (cm), mean (SD) 140.5 (12.4) 142.2 (15.5) 0.560 Height SDS at the point of the survey, mean (SD) -0.5 (0.9) -0.3 (0.9) 0.220 Weight at the point of the survey (kg), mean (SD) 37.2 (10.5) 38.1 (12.4) 0.723 Weight SDS at the point of the survey, mean (SD) -0.2 (0.9) -0.2 (0.8) 0.979 Injection administrator, n (%) -0.2 (0.9) -0.2 (0.8) 0.979 Patient 5 (62.5) 3 (37.5) 0.715 Caregiver/LAR 48 (55.8) 38 (44.2) 0.064 ^h Norditropin® NordiLet® 7 (87.5) 1 (12.5) 0.064 ^h Norditropin® NordiFlex® at the point of survey 16.3 (5.5) 18.2 (6.0) 0.112 Caregiver/LARs Age (years), mean (SD) 43.6 (4.2) 44.0 (3.8) 0.604 Sex, n (%) 0.562 39 (43.8) 0.867 Male 3 (60.0) 2 (40.0) 0.867 Female 50 (56.2) 39 (43.8) 0.325 Highest academic qualification, n (%) 0.325 0.325 0.325 Highest academic qualification, n (%) 5	Weight SDS at diagnosis, mean (SD)	-0.7 (1.3)	-0.5 (0.9)	0.467
Height SDS at the point of the survey, mean (SD) -0.3 (0.9) -0.3 (0.9) 0.220 Weight at the point of the survey (kg), mean (SD) 37.2 (10.5) 38.1 (12.4) 0.723 Weight SDS at the point of the survey, mean (SD) -0.2 (0.9) -0.2 (0.8) 0.979 Injection administrator, n (%) 0.715 0.715 0.715 Patient 5 (62.5) 3 (37.5) 0.064 ^h Caregiver/LAR 48 (55.8) 38 (44.2) 0.064 ^h Norditropin® NordiLet® 46 (53.5) 40 (46.5) 0.064 ^h Norditropin® NordiFlex® at the point of survey 16.3 (5.5) 18.2 (6.0) 0.112 Caregivers/LARs Age (years), mean (SD) 43.6 (4.2) 44.0 (3.8) 0.604 Sex, n (%) 0.867 0.867 0.867 Male 3 (60.0) 2 (40.0) 0.867 Female 50 (56.2) 39 (43.8) 0.325 Highest academic qualification, n (%) 0.325 0.325 0.325 High School 5 (83.3) 1 (16.7) 0.325 University or college 22 (61.1) 14 (38.9) 0.00 <td>Height at the point of the survey (cm), mean (SD)</td> <td>140.5 (12.4)</td> <td>142.2 (15.5)</td> <td>0.560</td>	Height at the point of the survey (cm), mean (SD)	140.5 (12.4)	142.2 (15.5)	0.560
Weight at the point of the survey (kg), mean (SD) $37.2 (10.5)$ $38.1 (12.4)$ 0.723 Weight SDS at the point of the survey, mean (SD) $-0.2 (0.9)$ $-0.2 (0.8)$ 0.979 Injection administrator, n (%) 0.715 0.715 0.715 Patient $5 (62.5)$ $3 (37.5)$ 0.715 Caregiver/LAR $48 (55.8)$ $38 (44.2)$ 0.064^h Norditropin® NordiLet® $46 (53.5)$ $40 (46.5)$ 0.064^h Norditropin® NordiFlex®, n (%) 0.064^h 0.064^h 0.064^h Weeks), mean (SD) $7 (87.5)$ $1 (12.5)$ 0.112 Caregivers/LARs Age (years), mean (SD) $43.6 (4.2)$ $44.0 (3.8)$ 0.604 Sex, n (%) 0.867 0.867 0.867 Male $3 (60.0)$ $2 (40.0)$ 0.325 High School $5 (83.3)$ $1 (16.7)$ 0.325 High School $5 (83.3)$ $1 (16.7)$ 0.325 Other $44.0 0.9$ $6 (60.9)$ 0.604	Height SDS at the point of the survey, mean (SD)	-0.5 (0.9)	-0.3 (0.9)	0.220
Weight SDS at the point of the survey, mean (SD) -0.2 (0.9) -0.2 (0.8) 0.979 Injection administrator, n (%) 0.715 0.715 Patient 5 (62.5) 3 (37.5) Caregiver/LAR 48 (55.8) 38 (44.2) Last device used before Norditropin NordiFlex®, n (%) 0.064 ^h 0.064 ^h Norditropin® NordiLet® 46 (53.5) 40 (46.5) Others ⁹ 7 (87.5) 1 (12.5) Duration of use of NordiFlex® at the point of survey (weeks), mean (SD) 16.3 (5.5) 18.2 (6.0) Others ⁹ 7 (87.5) 1 (12.5) Others ⁹ 0.604 (weeks), mean (SD) 43.6 (4.2) 44.0 (3.8) 0.604 Sex, n (%) Others Male 3 (60.0) 2 (40.0) 0.867 Male 3 (60.0) 2 (40.0) 0.325 Highest academic qualification, n (%) 0.325 0.325 0.325 High School 5 (83.3) 1 (16.7) 0.325 High School 22 (61.1) 14 (38.9) 0.400	Weight at the point of the survey (kg), mean (SD)	37.2 (10.5)	38.1 (12.4)	0./23
Injection administrator, n (%) 0.715 Patient 5 (62.5) 3 (37.5) Caregiver/LAR 48 (55.8) 38 (44.2) Last device used before Norditropin NordiFlex®, n (%) 0.064 ^h Norditropin® NordiLet® 46 (53.5) 40 (46.5) Others ⁹ 7 (87.5) 1 (12.5) Duration of use of NordiFlex® at the point of survey (weeks), mean (SD) 16.3 (5.5) 18.2 (6.0) 0.112 Caregivers/LARs Age (years), mean (SD) 43.6 (4.2) 44.0 (3.8) 0.604 Sex, n (%) 0.3867 Male 3 (60.0) 2 (40.0) 0.867 Female 50 (56.2) 39 (43.8) 0.325 High School 5 (83.3) 1 (16.7) 0.325 High School 5 (83.3) 1 (16.7) 14 (38.9) Other 22 (61.1) 14 (38.9) 0.00	Weight SDS at the point of the survey, mean (SD)	-0.2 (0.9)	-0.2 (0.8)	0.979
Patient 5 (62.5) 3 (37.5) Caregiver/LAR 48 (55.8) 38 (44.2) Last device used before Norditropin NordiFlex®, n (%) 0.064 ^h Norditropin® NordiLet® 46 (53.5) 40 (46.5) Others ⁹ 7 (87.5) 1 (12.5) Duration of use of NordiFlex® at the point of survey (weeks), mean (SD) 16.3 (5.5) 18.2 (6.0) Caregivers/LARs Age (years), mean (SD) 43.6 (4.2) 44.0 (3.8) 0.604 Sex, n (%) 0.8677 Male 3 (60.0) 2 (40.0) Female 50 (56.2) 39 (43.8) Highest academic qualification, n (%) 0.325 High School 1 (16.7) University or college 22 (61.1) 14 (38.9)	Injection administrator, n (%)		2 (27 5)	0.715
Caregiver/LAR 48 (55.8) 38 (44.2) Last device used before Norditropin NordiFlex®, n (%) 0.064 ^h Norditropin® NordiLet® 46 (53.5) 40 (46.5) Others ⁹ 7 (87.5) 1 (12.5) Duration of use of NordiFlex® at the point of survey 16.3 (5.5) 18.2 (6.0) (weeks), mean (SD) 43.6 (4.2) 44.0 (3.8) 0.604 Sex, n (%) 0.867 Male 3 (60.0) 2 (40.0) Female 50 (56.2) 39 (43.8) Highest academic qualification, n (%) 0.325 High School 5 (83.3) 1 (16.7) University or college 22 (61.1) 14 (38.9) Other 6 (60.0) 6 (60.0)	Patient Granding (LAD	5 (62.5)	3 (37.5)	
Last device used before Norditropin NordiFlex®, n (%) 0.064" Norditropin® NordiLet® 46 (53.5) 40 (46.5) Others ⁹ 7 (87.5) 1 (12.5) Duration of use of NordiFlex® at the point of survey 16.3 (5.5) 18.2 (6.0) (weeks), mean (SD) 43.6 (4.2) 44.0 (3.8) 0.604 Sex, n (%) 0.867 0.867 Male 3 (60.0) 2 (40.0) 0.867 Female 50 (56.2) 39 (43.8) 0.325 Highest academic qualification, n (%) 5 (83.3) 1 (16.7) 0.325 High School 5 (83.3) 1 (16.7) 0.325 Other 22 (61.1) 14 (38.9) 0.604	Caregiver/LAR	48 (55.8)	38 (44.2)	o o c dh
Norditropino Norditropino <t< td=""><td>Last device used before Norditropin NordiFlex®, n (%)</td><td></td><td>10 (16 5)</td><td>0.064</td></t<>	Last device used before Norditropin NordiFlex®, n (%)		10 (16 5)	0.064
Outlets ²⁻ 7 (87.5) 1 (12.5) Duration of use of NordiFlex® at the point of survey (weeks), mean (SD) 16.3 (5.5) 18.2 (6.0) Caregivers/LARs Age (years), mean (SD) 43.6 (4.2) 44.0 (3.8) 0.604 Sex, n (%) 0.867 0.867 Male 3 (60.0) 2 (40.0) 0.867 Female 50 (56.2) 39 (43.8) 0.325 Highest academic qualification, n (%) 0.325 0.325 High School 5 (83.3) 1 (16.7) University or college 22 (61.1) 14 (38.9) Other 6 (60.0) 6 (60.0)	Noraitropin® NoraiLet®	46 (53.5)	40 (46.5)	
Duration of use of NordiFiex® at the point of survey 16.3 (5.3) 18.2 (6.0) (weeks), mean (SD) Caregivers/LARs Age (years), mean (SD) 43.6 (4.2) 44.0 (3.8) 0.604 Sex, n (%) 0.867 Male 3 (60.0) 2 (40.0) Female 50 (56.2) 39 (43.8) Highest academic qualification, n (%) 0.325 High School 5 (83.3) 1 (16.7) University or college 22 (61.1) 14 (38.9) Other 6 (60.0) 6 (60.0)	Others [®]	/ (8/.5)	1 (12.5)	
Caregivers/LARs 0.112 Age (years), mean (SD) 43.6 (4.2) 44.0 (3.8) 0.604 Sex, n (%) 0.867 0.867 Male 3 (60.0) 2 (40.0) 0.867 Female 50 (56.2) 39 (43.8) 0.325 Highest academic qualification, n (%) 0.325 1 (16.7) 0.325 University or college 22 (61.1) 14 (38.9) 0.400	Survey (weeks) mean (CD)	10.3 (5.5)	18.2 (6.0)	0 1 1 2
Caregivers/LARs Age (years), mean (SD) 43.6 (4.2) 44.0 (3.8) 0.604 Sex, n (%) 0.867 Male 3 (60.0) 2 (40.0) Female 50 (56.2) 39 (43.8) Highest academic qualification, n (%) 0.325 High School 5 (83.3) 1 (16.7) University or college 22 (61.1) 14 (38.9) Other 6 (60.0) 6 (60.0)	(weeks), mean (SD)			0.112
Age (years), mean (SD) 43.6 (4.2) 44.0 (3.8) 0.604 Sex, n (%) 0.867 Male 3 (60.0) 2 (40.0) Female 50 (56.2) 39 (43.8) Highest academic qualification, n (%) 0.325 High School 5 (83.3) 1 (16.7) University or college 22 (61.1) 14 (38.9)		Caregivers/LARs		
Sex, n (%) 0.867 Male 3 (60.0) 2 (40.0) Female 50 (56.2) 39 (43.8) Highest academic qualification, n (%) 0.325 High School 5 (83.3) 1 (16.7) University or college 22 (61.1) 14 (38.9) Other 6 (60.0)	Age (years), mean (SD)	43.6 (4.2)	44.0 (3.8)	0.604
Male 3 (60.0) 2 (40.0) Female 50 (56.2) 39 (43.8) Highest academic qualification, n (%) 0.325 High School 5 (83.3) 1 (16.7) University or college 22 (61.1) 14 (38.9) Other 6 (60.0)	Sex, n (%)			0.867
Female 50 (56.2) 39 (43.8) Highest academic qualification, n (%) 0.325 High School 5 (83.3) 1 (16.7) University or college 22 (61.1) 14 (38.9) Other 6 (60.0)	Male	3 (60.0)	2 (40.0)	
Highest academic qualification, n (%) 0.325 High School 5 (83.3) 1 (16.7) University or college 22 (61.1) 14 (38.9) Other 4 (40.0) 6 (60.0)	Female	50 (56.2)	39 (43.8)	
High School 5 (83.3) 1 (16.7) University or college 22 (61.1) 14 (38.9) Other 4 (40.0) 6 (60.0)	Highest academic qualification, n (%)			0.325
University or college 22 (61.1) 14 (38.9) Other 4 (40.0) 6 (40.0)	High School	5 (83.3)	1 (16.7)	
Other $4 (40.0)$ 6 (60.0)	University or college	22 (61.1)	14 (38.9)	
Guier 4 (40.0) 0 (60.0)	Other	4 (40.0)	6 (60.0)	
Preferred not to answer 22 (52.4) 20 (47.6)	Preferred not to answer	22 (52.4)	20 (47.6)	
Annual household income in KRW, n (%) 0.851	Annual household income in KRW, n (%)			0.851
<50 million 5 (55.6) 4 (44.4)	<50 million	5 (55.6)	4 (44.4)	
50 million to <70 million 7 (50.0) 7 (50.0)	50 million to <70 million	7 (50.0)	7 (50.0)	
70 million or more 8 (50.0) 8 (50.0)	70 million or more	8 (50.0)	8 (50.0)	
Preferred not to answer 33 (60.0) 22 (40.0)	Preferred not to answer	33 (60.0)	22 (40.0)	

^aStandardized score of satisfaction with NordiFlex[®] >0, ^bStandardized score of satisfaction with NordiFlex[®] ≤0, ^cAge ≤11 years for girls and age ≤12 years for boys, ^dAge >11 years for girls and age >12 years for boys, ^eIncludes hypothyroidism, failure to thrive and constitutional delay of growth and puberty, ^fp-value for comparison between 'more severe condition' and 'less severe condition', ^gPrefilled Eutropin[®], Growtropin[®] II, Saizen[®] Easypod[®], Genotropin[®] GoQuick[®], ^hp-value for comparison between 'Norditropin[®] NordiLet[®] and 'Others'

GH, growth hormone; KRW, South Korean won; LAR, legally authorized representative; SD, standard deviation; SDS, standard deviation score.

Patients missed fewer injections with Norditropin NordiFlex® if they had previously used other GH devices other than Norditropin® NordiLet® (Norditropin® NordiLet®: 9.3% vs. other GH devices: 75.0%, p < 0.001). Those that used Norditropin NordiFlex® for a shorter period (14.3 weeks vs. 17.6 weeks, p = 0.045) were also more likely to miss fewer injections. The difference in the number of injections missed in a typical month between the two groups was not statistically significant (**Table 5**).

With respect to caregivers/LARs, there were notable differences in education level and annual household income between those that reported missing fewer injections with Norditropin NordiFlex[®] and those that did not (**Table 5**).

Respondents who reported missed fewer injections with Norditropin NordiFlex[®] had higher standardized scores on *self-efficacy* (1.81 [0.39] vs. 0.78 [0.88]), *ease of use* (1.74 [0.47] vs. 0.48 [0.89]), *minimal disruption of daily life* (1.70 [0.46] vs. 0.05 [0.63]), and *positive feelings about injection* (1.71 [0.54] vs. -0.04 [0.61]) compared with those who reported no difference or missed fewer injections with the previous device (all p < 0.001) (**Figure 3D**).

Table 4. Bivariate associations between patient and caregiver/LAR characteristics and perceived ease of use with Norditropin NordiFlex®

	Perceived NordiFlex ^{®a} to be easier to use (n = 43)	No difference or perceived previous device ^b to be easier to use (n = 51)	<i>p</i> -value
	Patients		
Age (years), mean (SD)	10.9 (1.6)	11.0 (2.4)	0.884
Child ^c , n (%)	25 (53.2)	22 (46.8)	0 1 47
Adolescent ^d , n (%)	18 (38.3)	29 (61.7)	0.147
Sex, n (%)			
Male	16 (47.1)	18 (52.9)	0.847
Female	27 (45.0)	33 (55.0)	
Duration of treatment (years), mean (SD)	2.6 (2.0)	1.9 (1.2)	0.030
Diagnosis, n (%)			0.029 ^e
More severe condition	14 (66.7)	7 (33.3)	
Growth hormone deficiency	4 (57.1)	3 (42.9)	
Small for gestational age	9 (69.2)	4 (30.8)	
Noonan syndrome	1 (100.0)	0 (0.0)	
Less severe condition	29 (39.7)	44 (60.3)	
Idiopathic short stature	18 (36.0)	32 (64.0)	
Familial short stature	7 (58.3)	5 (41.7)	
Precocious puberty	4 (50.0)	4 (50.0)	
Others [†]	0 (0.0)	3 (100.0)	
No family history of GH disorders, n (%)	43 (45.7)	51 (54.3)	N/A
Height at diagnosis (cm), mean (SD)	121.7 (16.1)	126.7 (17.8)	0.159
Height SDS at diagnosis, mean (SD)	-1.1 (1.4)	-0.9 (1.2)	0.484
Weight at diagnosis (kg), mean (SD)	25.6 (9.0)	28.8 (11.1)	0.133
Weight SDS at diagnosis, mean (SD)	-0.7 (1.4)	-0.6 (0.9)	0.673
Height at the point of the survey (cm), mean (SD)	140.4 (11.3)	142.0 (15.7)	0.568
Height SDS at the point of the survey, mean (SD)	-0.5 (1.0)	-0.4 (0.9)	0.516
Weight at the point of the survey (kg), mean (SD)	37.0 (10.3)	38.1 (12.2)	0.657
Weight SDS at the point of the survey, mean (SD)	-0.2 (1.0)	-0.2 (0.8)	0.862
Injection administrator, n (%)			0.625
Patient	3 (37.5)	5 (62.5)	
Caregiver/LAR	40 (46.5)	46 (53.5)	
Last device used before Norditropin NordiFlex [®] , n (%)			0.082"
NordiLet®	37 (43.0)	49 (57.0)	
Others ⁹	6 (75.0)	2 (25.0)	
Duration of use of NordiFlex [®] at the point of survey	16.4 (5.3)	17.7 (6.2)	0.300
(weeks), mean (SD)			
	Caregivers/LARs		
Age (years), mean (SD)	43.7 (4.5)	43.9 (3.6)	0.823
Sex, n (%)	- />	- ()	0.511
Male	3 (60.0)	2 (40.0)	
Female	40 (44.9)	49 (55.1)	
Highest academic qualification, n (%)	. (- ()	0.714
High School	4 (66.7)	2 (33.3)	
University or college	17 (47.2)	19 (52.8)	
Other	4 (40.0)	6 (60.0)	
Preferred not to answer	18 (42.9)	24 (57.1)	
Annual household income in KRW, n (%)		2 (22 2)	0.499
<50 million	6 (66./)	3 (33.3)	
SU million to $ million$	5 (35./)	9 (64.3)	
/U million or more	8 (50.0)	8 (50.0)	
Preierred not to answer	24 (43.6)	31 (50.4)	

^aStandardized score of satisfaction with NordiFlex[®] >0, ^bStandardized score of satisfaction with NordiFlex[®] ≤0, ^cAge ≤11 years for girls and age <12 years for boys, ^dAge >11 years for girls and age >12 years for boys, ^ep-value for comparison between 'more severe condition' and 'less severe condition', ¹Includes hypothyroidism, failure to thrive and constitutional delay of growth and puberty, ^gPrefilled Eutropin[®], Growtropin[®] II, Saizen[®] Easypod[®], Genotropin[®] GoQuick[®], ^hp-value for comparison between 'Norditropin[®] NordiLet[®]' and 'Others'

GH, growth hormone; KRW, South Korean won; LAR, legally authorized representative; SD, standard deviation; SDS, standard deviation score.

3.6.1 Subgroup analyses of participants who used Norditropin NordiFlex® for 4 to \leq 12 weeks and those who used it for >12 weeks

Patients who used Norditropin NordiFlex[®] for a longer period were less likely to report missing fewer injections (>12 weeks: 10.1% vs. $4-\le 12$ weeks: 28.0%, p = 0.032).

3.7. Mean standardized scores of subjective benefits of GH device features

Figure 4 shows forest plots of the mean standardized scores for individual subjective benefits of GH device features, as well as the overall mean score for each of the four domains of subjective benefits. Respondents' opinions were in favor Table 5. Bivariate associations between patient and caregiver/LAR characteristics and self-reported adherence with Norditropin NordiFlex®.

Patients Age of patient (years), mean (SD) 10.2 (1.3) 11.1 (2.1) 0.103 Child', n (%) 12 (2.5.5) 35 (74.5) 0.003 Add address, n (%) 2 1.1 (2.1) 0.103 Mail address, n (%) 2 2.1 (1.5) 0.355 Duration of treatment (years), mean (SD) 2.4 (2.2) 2.1 (1.5) 0.0355 Duration of treatment (years), mean (SD) 2.4 (2.2) 2.1 (1.5) 0.0355 Duration of treatment (years), mean (SD) 2.4 (2.2) 2.1 (1.5) 0.0355 Duration of treatment (years), mean (SD) 2.4 (2.2) 2.1 (1.5) 0.0355 Duration of treatment (years), mean (SD) 2.1 (1.5) 0.0355 Colspan="2">Colspan="2">0.000 1.1 (2.0) 4.4 (8.0) 4.9 (2.2) Duration of treatment (years, n (%)		Missed fewer injections with NordiFlex ^{®a} (n = 14)	No difference or missed fewer injections with previous device ^b (n = 80)	<i>p</i> -value
Age of patient (years), mean (SD) 10.2 (1.3) 11.1 (2.1) 0.103 Child', n (%) 12 (25.5) 35 (74.5) 0.008 Adolescent ¹ , n (%) 2 (4.3) 45 (95.7) 0.069 Male 5 (14.7) 29 (85.3) 0.969 Male 5 (14.7) 29 (85.3) 0.007 Penale 9 (15.0) 51 (85.0) 0.007 More severe condition 7 (33.3) 14 (66.7) 0.007 Growth hormone deficiency 3 (42.9) 4 (57.1) 0.007 More severe condition 7 (9.6) 66 (90.4) 0.000 Growth hormone deficiency 3 (25.0) 9 (75.0) 9 Precodeus puberty 0 (0.0) 8 (100.0) 0 0 Others' 0 (0.0) 8 (100.0) 0 0 0 Others' 0 (0.0) 1124 (15.8) 126 (16.6) 0.004 Neghty Starture 14 (8.5) 2.84 (10.3) 0.037 Weight Adagnosis, mean (SD) -1.6 (1.6) -0.9 (1.3) 0.076 Weight Adagnosis (mean (SD) -0.3 (0.8) -0.6 (1.0) 0.391		Patients		
Child', n (%) 12 (25) 35 (745) 0.008 Sex of patient, n (%) 2 (4.3) 45 (95.7) 0.869 Male 5 (14.7) 29 (85.3) 0.007 Female 9 (15.0) 51 (85.0) 0.007 Duration of treatment (years), mean (SD) 2.8 (2.2) 2.1 (1.5) 0.007* More severe condition 7 (33.3) 14 (65.7) 0.007* Small for gestational age 4 (30.8) 9 (62.2) 0.007* Nonoan syndrome 0 (0.0) 1 (10.00) 1 Less severe condition 7 (9.6) 66 (90.4) 1 Idiopathic short stature 4 (8.0) 46 (92.0) 1 Fermilal short stature 3 (25.0) 9 (75.0) Precocjous puberty 0 (0.0) 8 (100.0) No family history of 6H disorders, n (%) 14 (14.9) 80 (85.1) NA Height at diagnosis (man, neo SD) -16 (1.6) -09 (1.3) 0.076 Weight at diagnosis (man, neo SD) 2.23 (9.8) 3.85 (11.4) 0.031 Weight at diagnosis, mean (SD) -0.0 (1.8)	Age of patient (years), mean (SD)	10.2 (1.3)	11.1 (2.1)	0.103
Addecem ⁴ , n (%) 2 (4.3) 4 (95.7) 0000 Male 5 (14.7) 29 (85.3) 0.669 Male 5 (14.7) 29 (85.3) 0.699 Duration of treatment (yeas), mean (SD) 2.8 (2.2) 2.1 (1.5) 0.135 Duration of treatment (yeas), mean (SD) 2.8 (2.2) 2.1 (1.5) 0.007° More severe condition 7 (33.3) 14 (66.7) 0.0007° Growth hormone deficiency 3 (42.9) 4 (57.1) 0.0007° Noonan syndrome 0.00.0 1 (1000.0) 1 (1000.0) 1 (1000.0) Construction 7 (9.6) 66 (90.4) 1 (1000.0) 1 (1000.0) Orten's 0 (0.0) 8 (100.0) 0 (100.0) 1 (100.0) 0.076 Orten's 0 (0.0) 1 (12.4 (15.8) 1.25 (16.6) 0.044 0.014 0.014 0.014 0.014 0.014 0.014 0.014 0.014 0.014 0.014 0.014 0.014 0.014 0.014 0.014 0.010 0.010 0.010 0.016 0.010	Child ^c , n (%)	12 (25.5)	35 (74.5)	0.000
Sex of patient, n (%) 0.669 Male 5 (14.7) 29 (83.) Female 9 (15.0) 51 (85.0) Duardino of treatment (years), mean (SD) 2.8 (2.2) 2.1 (1.5) 0.007° More severe condition 7 (33.3) 14 (66.7) 0.007° Growth hormone deficiency 3 (42.9) 4 (57.1) 0.007° Small for greatizational age 4 (30.8) 9 (62.2) 1.000.0 Less severe condition 7 (9.6) 66 (90.4) 1.000.0 Idiopathic short stature 4 (8.0) 46 (92.0) 1.000.0 Precocjous puberty 0 (0.0) 8 (100.0) 0.000.0 Others* 0 (0.0) 3 (100.0) 0.004 Height t 3 (agnosis, mean (SD) -1.6 (1.6) -0.9 (1.3) 0.076 Weight t 3 (agnosis, mean (SD) -0.0 (1.8) -0.6 (1.0) 0.018 Weight t 3 (agnosis, mean (SD) -0.0 (1.8) -0.2 (0.8) 0.24 Weight t3 S at diagnosis, mean (SD) -0.0 (0.8) -0.2 (0.8) 0.24 Weight 3DS at tagnosis, mean (SD) -0.4 (1.0)	Adolescent ^d , n (%)	2 (4.3)	45 (95.7)	0.008
Main 5 (147) 29 (85.3) Fernale 9 (15.0) 2.8 (2.2) 2.1 (1.5) 0.135 Diganosis, n (%) 0.007" 0.007" 0.007" More severe condition 7 (33.3) 14 (66.7) 0.007" Growth hormone deficiency 3 (42.9) 4 (57.1) Small for gestational age 4 (30.8) 9 (69.2) Nooran syndrome 0 (0.0) 1 (100.0) 1 (100.0) 1 (100.0) 1 (100.0) Less severe condition 7 (9.6) 66 (90.4) 4 (14.9) 80 (85.1) NA No family history of CH disorders, n (%) 14 (14.9) 80 (85.1) NA No family history of CH disorders, n (%) 1124 (15.8) 126.5 (16.6) 0.004 Weight ta diagnosis, mean (SD) 21.4 (8.5) 28.4 (10.3) 0.018 Weight ta diagnosis (man (SD) 22.9 (8.0) 14.27 (14.1) 0.014 Height th the point of the survey, mean (SD) -0.9 (1.8) -0.6 (1.0) 0.99 Weight ta the point of the survey, mean (SD) -0.4 (1.0) 4 (10.0) 2.2 (0.8) 0.340 <t< td=""><td>Sex of patient, n (%)</td><td></td><td></td><td>0.969</td></t<>	Sex of patient, n (%)			0.969
Female 9 (15.0) 21 (15) 0.037 Diagnosis, n (%) 0.007* 0.007* More severe condition 7 (33.3) 14 (66.7) Growth hormone deficiency 3 (42.9) 4 (15.71) Small for gestational age 4 (30.8) 9 (69.2) Noonan syndrome 0 (0.0) 1 (100.0) Less severe condition 7 (9.6) 66 (00.4) Familial short stature 3 (25.0) 9 (75.0) Precocious puberty 0 (0.0) 8 (100.0) Otramity history of GH disorders, n (%) 14 (14.9) 80 (85.1) N/A Height SDS at diagnosis, mean (SD) 11.24 (15.8) 12.26 (16.6) 0.004 Weight at diagnosis (main, mean (SD) 21.4 (8.5) 2.84 (10.3) 0.018 Weight SDS at diagnosis, mean (SD) -0.4 (1.6) -0.9 (1.8) 0.014 Height SDS at beyons (FG) -0.4 (1.0) -0.2 (0.8) 0.309 0.027 Weight SDS at beyons (FG) -0.4 (1.0) -0.2 (0.8) 0.309 0.027 Weight SDS at the point of the survey, mean (SD) -0.4 (1.0) -0.	Male	5 (14.7)	29 (85.3)	
Duration of treatment (years), mean (SD) 2.8 (2.2) 2.1 (1.5) 0.135 Diagnosis, (P6) 0.007 ⁺ 0.007 ⁺ More severe condition 7 (33.3) 14 (66.7) Growth homone deficiency 3 (42.9) 4 (57.1) Snall for gestational age 4 (30.8) 9 (69.2) Nooran syndrome 0 (0.0) 1 (100.0) Less severe condition 7 (9.6) 66 (90.4) Idopathis kort stature 3 (25.0) 9 (75.0) Precoclous puberty 0 (0.0) 8 (100.0) Others' 0 (0.0) 8 (100.0) No family history of GH disorders, n (%) 112.4 (15.8) 12.65 (16.6) 0.004 Height SDS at diagnosis, mean (SD) -1.6 (1.6) -0.9 (1.3) 0.076 Weight at diagnosis (man (SD) 21.4 (8.5) 28.4 (10.3) 0.018 Weight at the point of the survey, mean (SD) -0.4 (1.8) -0.6 (1.0) 0.039 Height SDS at diagnosis, mean (SD) -0.4 (1.0) 8 (100.0) 0.216 Cargiver/LAR 14 (16.3) 72 (83.7) -0.001 ^h Veie	Female	9 (15.0)	51 (85.0)	
Diagnosis, n (%) 0.007 ^k More sever condition 7 (33.3) 14 (66.7) Growth hormone deficiency 3 (42.9) 4 (57.1) Small for gestational age 4 (30.8) 9 (69.2) Noonan syndrome 0 (0.0) 1 (100.0) Less sever condition 7 (9.6) 66 (90.4) Idiopathic short staure 4 (80.0) 46 (92.0) Familia bhort staure 3 (25.0) 9 (75.0) Precolous puberty 0 (0.0) 8 (100.0) Other 0 (0.0) 126.5 (16.6) 0.04 Height at diagnosis (cm), mean (SD) -1.4 (15.6) -0.9 (1.3) 0.075 Weight SDS at diagnosis, mean (SD) -1.4 (15.6) -0.9 (1.3) 0.076 Weight SDS at diagnosis (cm), mean (SD) -0.2 (1.8) -0.6 (1.0) 0.3 (1.0) 0.3 (1.0) Usepits SDS at diagnosis (cm), mean (SD) -0.2 (1.8) -0.0 (1.0) 0.3 (0.0) 0.2 (2.8) Usepits SDS at diagnosis (cm), mean (SD) -0.2 (2.8) -0.3 (0.9) 0.2 (2.8) Usepits CDS at diagnosis (cm), mean (SD) -0.2 (2.8) -0.2 (0.8)	Duration of treatment (years), mean (SD)	2.8 (2.2)	2.1 (1.5)	0.135
More severe condition 7 (33.3) 14 (66.7) Growth hormone deficiency 3 (429) 4 (57.1) Small for gestational age 4 (30.8) 9 (69.2) Noonan syndrome 0 (0.0) 1 (100.0) Less severe condition 7 (9.6) 66 (90.4) Idiopathic short stature 4 (80.0) 46 (92.0) Familial short stature 3 (25.0) 9 (75.0) Precocious puberty 0 (0.0) 3 (100.0) Others 0 (80.0) 3 (100.0) No family history of GH disorders, n (%) 14 (14.9) 30 (85.1) N/A Height SDS at diagnosis, mean (SD) -1.6 (1.6) -0.9 (1.3) 0.018 Weight SDS at diagnosis, mean (SD) -0.8 (1.0) -0.31 0.014 Height SDS at diagnosis, mean (SD) -0.9 (1.8) -0.2 (0.8) 0.32 (1.0) Weight at diagnosis, mean (SD) -0.9 (0.8) -0.3 (0.9) 0.027 Weight at the point of the survey, mean (SD) -0.2 (0.8) 3.83 (1.4) 0.059 Weight at the point of the survey, flagn enant (SD) -0.2 (0.8) 3.2 (1.4) 0.059	Diagnosis, n (%)			0.007 ^e
Growth hormone deficiency 3 (42.9) 4 (57.1) Small for gestational age 4 (38.08) 9 (69.2) Noonan syndrome 0 (0.0) 1 (100.0) Less severe condition 7 (9.6) 66 (90.4) Idiopathic short stature 3 (25.0) 9 (75.0) Precocious puberty 0 (0.0) 8 (100.0) Others' 0 (0.0) 8 (100.0) No family history of GH disorders, n (%) 14 (14.9) 80 (85.1) NA Height At diagnosis, mem (5D) -1.6 (1.6) -0.9 (1.3) 0.076 Weight SDS at diagnosis, mem (5D) -0.9 (1.8) -0.6 (1.0) 0.391 Height At the point of the survey, mem (5D) -0.9 (0.8) -0.3 (0.9) 0.027 Weight SDS at the point of the survey, mean (SD) -0.4 (1.0) -0.2 (0.8) 0.340 Ipetion administrator, n (%) 14 (16.3) 72 (83.7) -0.001 ^h Veight SDS at the point of the survey, mean (SD) -0.4 (1.0) -0.2 (0.8) 0.340 Ipetion administrator, n (%) 0 (0.0) & (100.0) 6 (100.0) Leight SDS at the point of the survey, th	More severe condition	7 (33.3)	14 (66.7)	
Small for gestational age 4 (30.8) 9 (69.2) Noonan syndrome 0 (0.0) 1 (100.0) Less severe condition 7 (9.6) 66 (90.4) Idiopathic short stature 4 (80.0) 46 (92.0) Prececious puberty 0 (0.0) 8 (100.0) Others ¹ 0 (0.0) 8 (100.0) No family history of GH disorders, n (%b) 14 (14.9) 80 (85.1) N/A Height at diagnosis (m, mean (SD) -1.6 (1.6) -0.9 (1.3) 0.0018 Weight SDS at diagnosis, mean (SD) -1.6 (1.6) -0.9 (1.3) 0.018 Weight SDS at diagnosis (m, mean (SD) -0.2 (1.8) -0.6 (1.0) 0.391 Weight SDS at diagnosis (m, mean (SD) -0.2 (8.8) -0.3 (0.9) 0.027 Weight SDS at the point of the survey (cm), mean (SD) -0.2 (8.8) -0.3 (0.9) 0.027 Weight SDS at the point of the survey, mean (SD) -0.4 (1.0) -0.2 (0.8) 0.340 Injection administrator, n(%) - - - 0.001 Veight at the point of the survey, mean (SD) -0.4 (1.0) 72 (8.7) - - </td <td>Growth hormone deficiency</td> <td>3 (42.9)</td> <td>4 (57.1)</td> <td></td>	Growth hormone deficiency	3 (42.9)	4 (57.1)	
Noonan syndrome 0 (0.0) 1 (100.0) Less sever condition 7 (9.6) 66 (90.4) Idiopathic short stature 4 (8.0) 46 (92.0) Familial short stature 3 (25.0) 9 (75.0) Precocious puberty 0 (0.0) 3 (100.0) No family history of GH disorders, n (%) 14 (14.9) 80 (85.1) N/A Height at diagnosis, (end), mean (SD) 112.4 (15.8) 126.5 (16.6) 0.0076 Weight st diagnosis, mean (SD) -1.6 (1.6) -0.9 (1.3) 0.076 Weight st diagnosis, mean (SD) -1.6 (1.6) -0.9 (1.3) 0.076 Weight SDS at diagnosis, mean (SD) -0.9 (1.8) -0.6 (1.0) 0.391 Height at the point of the survey, (end), mean (SD) -0.9 (0.8) -0.3 (0.9) 0.027 Weight SDS at the point of the survey, mean (SD) -0.4 (1.0) -0.2 (0.8) 0.340 Injection administrator, n (%) -0.4 (1.0) -0.2 (0.8) 0.340 Patient 0.00 8 (100.0) 0.216 Caregiver/LAR 0.001 2 (28.7) -0.01 ^h Duration	Small for gestational age	4 (30.8)	9 (69.2)	
Less severe condition 7 (9.6) 66 (90.4) Idiopathic short stature 4 (80) 46 (92.0) Precocious puberty 0 (0.0) 8 (100.0) Others' 0 (0.0) 8 (100.0) Others' 0 (0.0) 3 (100.0) No family history of GH disorders, n (%) 14 (14.9) 80 (85.1) N/A Height at diagnosis (m, mean (SD) -1.5 (1.6) -0.9 (1.3) 0.004 Weight at diagnosis (m, mean (SD) -1.4 (4.5.5) 2.8.4 (10.3) 0.018 Weight SD's at diagnosis, mean (SD) -0.9 (1.8) -0.6 (1.0) 0.391 Weight SD's at diagnosis, mean (SD) -0.9 (1.8) -0.6 (1.0) 0.391 Weight SD's at the point of the survey, mean (SD) -0.9 (0.8) -3.8 (0.9) 0.027 Weight SD's at the point of the survey (m), mean (SD) 2.2.3 (9.8) 3.8.5 (11.4) 0.059 Weight SD's at the point of the survey, mean (SD) -0.4 (0.0) -2.0 (0.0) 0.216 Caregiver/LAR 0 (0.0) 8 (100.0) 0.216 -2.2 (0.8) 0.340 Injection administrator, n (%) (6.75.0)	Noonan syndrome	0 (0.0)	1 (100.0)	
Idiopathic short stature 4 (8.0) 46 (92.0) Familia short stature 3 (25.0) 9 (75.0) Precocious puberty 0 (0.0) 8 (100.0) Others ⁵ 0 (0.0) 3 (100.0) No family history of GH disorders, n (%) 14 (14.9) 80 (85.1) N/A Height to Sta diagnosis, remain (SD) -1.5 (1.6) -0.9 (1.3) 0.076 Weight to Sta diagnosis, remain (SD) -0.9 (1.8) -0.6 (1.0) 0.311 Height to Sta diagnosis, remain (SD) -0.9 (1.8) -0.6 (1.0) 0.311 Height to Sta the point of the survey, mean (SD) -0.9 (1.8) -0.3 (0.9) 0.027 Weight to Sta the point of the survey, mean (SD) -0.2 (0.8) 0.330 0.027 Weight SDS at the point of the survey, mean (SD) -0.2 (1.8) -0.3 (0.9) 0.027 Weight SDS at the point of the survey, mean (SD) -0.2 (1.8) -0.3 (0.9) 0.027 Weight SDS at the point of the survey, mean (SD) -0.2 (0.8) 0.340 0.14 Ipection administrator, n (%) 6 (75.0) 2 (25.0) 0.001 0.001 Caregiver/LAR<	Less severe condition	7 (9.6)	66 (90.4)	
Familial short stature 3 (25.0) 9 (75.0) Precocious pubery 0 (0.0) 8 (100.0) Others' 0 (0.0) 3 (100.0) No family history of GH disorders, n (%) 14 (14.9) 80 (85.1) N/A Height at diagnosis (m, mean (SD) -1.6 (1.6) -0.9 (1.3) 0.076 Weight at diagnosis (m, mean (SD) -1.6 (1.6) -0.9 (1.3) 0.076 Weight at diagnosis (m, mean (SD) -0.9 (1.8) -0.6 (1.0) 0.331 Height at the point of the survey, mean (SD) -0.9 (0.8) -0.3 (0.9) 0.027 Weight SDS at the point of the survey, mean (SD) -0.9 (0.8) -0.3 (0.9) 0.027 Weight SDS at the point of the survey, mean (SD) -0.4 (1.0) -0.2 (0.8) 0.340 Injection administrator, n (%) 72 (83.7) - - Patient 0 (0.0) 8 (100.0) 0.216 Caregiver/LAR 14 (16.3) 72 (83.7) - Last device use before Norditepin NordiFlex®, n (%) - - - Norditropin NordiFlex® at the point of the survey 14 (16.3) 72 (83.7) - - Norditropin NordiFlex® at the poi	Idiopathic short stature	4 (8.0)	46 (92.0)	
Precocious puberty 0 (0.0) 8 (100.0) Others ¹ 0 (0.0) 3 (100.0) No family history of GH disorders, n (%) 14 (14.9) 80 (85.1) N/A Height SDS at diagnosis, (cm), mean (SD) 112.4 (15.8) 126.5 (16.6) 0.004 Weight SDS at diagnosis, mean (SD) 21.4 (8.5) 28.4 (10.3) 0.018 Weight SDS at diagnosis, mean (SD) -0.9 (1.8) -0.6 (1.0) 0.391 Height at the point of the survey (cm), mean (SD) 132.9 (8.0) 142.7 (14.1) 0.014 Height SDS at the point of the survey, mean (SD) -0.4 (1.0) -0.2 (0.8) 0.309 Meight SDS at the point of the survey, mean (SD) -0.4 (1.0) -0.2 (0.8) 0.340 Injection administrator, n (%) 14 (16.3) 72 (83.7) Patient 0 (0.0) 8 (100.0) 2.010 ⁻¹ Nordfitorpin NordiFlex [®] at the point of the survey 14.3 (6.2) 72 (83.7) Caregiver/LAR 14 (16.3) 72 (83.7) Vereight SDS at the point of the survey 14.3 (6.2) 72 (63.0)	Familial short stature	3 (25.0)	9 (75.0)	
Others ¹ 0 (0.0) 3 (100.0) No family history of GH disorders, n (%) 14 (14.9) 80 (85.1) N/A Height at diagnosis (gn, mean (SD) 112.4 (15.8) 126.5 (16.6) 0.004 Height SDS at diagnosis (gn, mean (SD) -1.6 (1.6) -0.9 (1.3) 0.076 Weight at diagnosis (gn, mean (SD) 21.4 (8.5) 28.4 (10.3) 0.018 Weight SDS at diagnosis (gn, mean (SD) -0.9 (1.8) -0.6 (1.0) 0.331 Height at the point of the survey, mean (SD) -0.9 (0.8) -0.3 (0.9) 0.027 Weight SDS at the point of the survey, mean (SD) -0.4 (1.0) -0.2 (0.8) 0.340 Injection administrator, n (%) Patient 0 (0.0) 8 (100.0) 0.216 Caregiver/LAR 14 (16.3) 72 (83.7) -0.001 ^h Norditropin® NordiLet® 6 (75.0) 2 (25.0) -0.465 -0.465 Outers ⁴ 14 (16.3) 72 (83.7) -0.465 -0.465 (wesk), mean (SD) 43 (6.2) 17.6 (5.6) 0.045 -0.465 Caregivers/LAR 14 (16.3) <t< td=""><td>Precocious puberty</td><td>0 (0.0)</td><td>8 (100.0)</td><td></td></t<>	Precocious puberty	0 (0.0)	8 (100.0)	
No family history of GH disorders, n (%) 14 (14.9) 80 (85.1) NVA Height at diagnosis (cm), mean (SD) 112.4 (15.8) 126.5 (16.6) 0.004 Weight SDS at diagnosis, mean (SD) -1.6 (1.6) -0.9 (1.3) 0.076 Weight SDS at diagnosis, mean (SD) 21.4 (8.5) 28.4 (10.3) 0.018 Weight SDS at diagnosis, mean (SD) -0.9 (1.8) -0.6 (1.0) 0.391 Height At the point of the survey (cm), mean (SD) 23.2 (9.8) 38.5 (11.4) 0.059 Weight SDS at the point of the survey, mean (SD) -0.9 (0.8) -0.2 (0.8) 0.340 Injection administrator, n (%) -0.2 (0.8) 0.340 0.027 Patient 0 (0.0) 8 (100.0) 0.216 Caregiver/LAR 14 (16.3) 72 (83.7) 2 (25.0) Duration of use of Nordiflex® at the point of the survey 14.3 (6.2) 17.6 (5.6) 0.045 (weeks), mean (SD) 43.6 (5.2) 43.8 (3.8) 0.894 As vice used before Nordiflex® at the point of the survey 14.1 (16.3) 72 (83.7) 0.465 St ines 0 (0.0) 2 (100.0) 2 (100.0) 2 (100.0) 2 (100.0) 2 (100.0)	Others ^f	0 (0.0)	3 (100.0)	
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	No family history of GH disorders, n (%)	14 (14.9)	80 (85.1)	N/A
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	Height at diagnosis (cm), mean (SD)	112.4 (15.8)	126.5 (16.6)	0.004
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	Height SDS at diagnosis, mean (SD)	-1.6 (1.6)	-0.9 (1.3)	0.076
Weight SDS at diagnosis, mean (SD) $-0.9 (1.8)$ $-0.6 (1.0)$ 0.391 Height at the point of the survey (cm), mean (SD) $132.9 (8.0)$ $142.7 (14.1)$ 0.014 Height SDS at the point of the survey, mean (SD) $-0.9 (0.8)$ $-0.3 (0.9)$ 0.027 Weight SDS at the point of the survey, mean (SD) $-0.4 (1.0)$ $-0.2 (0.8)$ 0.340 Injection administrator, n (%) $0 (0.0)$ $8 (100.0)$ 0.216 Caregiver/LAR 14 (16.3) 72 (83.7) $< 0.001^h$ Last device used before Norditropin NordiFlex®, n (%) $0 (0.0)$ $2 (25.0)$ 0.045 Norditropin® NordiLet® $6 (75.0)$ $2 (25.0)$ 0.045 Weeksh, mean (SD) $0 (0.0)$ $6 (100.0)$ $2 (100.0)$ No. of injections missed in a typical month, n (%) (0.0) $2 (100.0)$ 0.465 < 3 times	Weight at diagnosis (kg), mean (SD)	21.4 (8.5)	28.4 (10.3)	0.018
$\begin{array}{c c c c c c c } \mbox{Height at the point of the survey (cm), mean (SD) 132.9 (8.0) 142.7 (14.1) 0.014 \\ \mbox{Height SDS at the point of the survey, (sD) 2.3 (9.8) 38.5 (11.4) 0.059 \\ \mbox{Weight sDS at the point of the survey, mean (SD) -0.4 (1.0) -0.2 (0.8) 0.340 \\ \mbox{Injection administrator, n (%) & 0.000 8 (100.0) 0.216 \\ \mbox{Caregiver/LAR } & 14 (16.3) 72 (83.7) & -0.4 (1.0) & -0.2 (0.8) 0.201^{h} \\ \mbox{Norditropin @ NordilLet^@ 0 (0.0) 8 (100.0) 0.216 \\ \mbox{Caregiver/LAR } & 14 (16.3) 72 (83.7) & -0.01^{h} \\ \mbox{Norditropin @ NordilLet^@ 0 the survey (14.3 (6.2) 17.6 (5.6) 0.045 \\ (weeks), mean (SD) & 0.000 2 (100.0) & 0.000 & 0.045 \\ (weeks), mean (SD) & 144 (16.3) 72 (83.7) & -0.465 \\ \mbox{Caregiver/LAR } & 0 (0.0) & 6 (100.0) & 0.045 \\ (weeks), mean (SD) & 0.000 & 2 (100.0) & 0.045 \\ (weeks), mean (SD) & 0.000 & 2 (100.0) & 0.045 \\ \mbox{Weeks} & 0 (0.0) & 0.00 & 0.000 & 0.000 \\ \mbox{S times } & 0 (0.0) & 0.000 & 0.000 & 0.000 \\ \mbox{S times } & 0 (0.0) & 0.000 & 0.000 & 0.000 \\ \mbox{S times } & 0 (0.0) & 0.000 & 0.000 & 0.000 \\ \mbox{S times } & 0 (0.0) & 0.000 & 0.000 & 0.000 & 0.000 \\ \mbox{S times } & 0 (0.0) & 0.000 & 0.000 & 0.000 & 0.000 & 0.000 & 0.000 \\ \mbox{S times } & 0 (0.0) & 0.000 &$	Weight SDS at diagnosis, mean (SD)	-0.9 (1.8)	-0.6 (1.0)	0.391
Height SDS at the point of the survey, mean (SD) $-0.9 (0.8)$ $-0.3 (0.9)$ 0.027 Weight SDS at the point of the survey (kg), mean (SD) $22.3 (9.8)$ $38.5 (11.4)$ 0.059 Weight SDS at the point of the survey, mean (SD) $-0.4 (1.0)$ $-0.2 (0.8)$ 0.340 Injection administrator, n (%) no.01 $8 (100.0)$ 0.216 Caregiver/LAR 14 (16.3) 72 (83.7) Last device used before Norditropin NordiFlex®, n (%) 8 (9.3) 78 (90.7) Norditropin® NordiFlex® at the point of the survey 14.3 (6.2) 17.6 (5.6) 0.045 (weeks), mean (SD) 0.000 6 (170.0) 2 (25.0) 0.465 Caregivers/LAR 14 (16.3) 72 (83.7) 0.465 <3 times	Height at the point of the survey (cm), mean (SD)	132.9 (8.0)	142.7 (14.1)	0.014
Weight at the point of the survey (kg), mean (SD) 32.3 (9.8) 38.5 (11.4) 0.059 Weight SDS at the point of the survey, mean (SD) -0.4 (1.0) -0.2 (0.8) 0.340 Injection administrator, n (%) 0 (0.0) 8 (100.0) 0.216 Patient 0 (0.0) 8 (100.0) 0.216 Caregiver/LAR 14 (16.3) 72 (83.7) Last device used before Norditropin NordiFlex®, n (%) . Norditropin® NordiLet® 6 (75.0) 2 (25.0) . Duration of use of NordiFlex® at the point of the survey 14.3 (6.2) 17.6 (5.6) 0.045 (weeks), mean (SD) 3 to 5 times 0 (0.0) 6 (100.0) 2 (100.0) > 5 times 0 (0.0) 2 (100.0) . . . Age (years), mean (SD) 43.6 (5.2) 43.8 (3.8) 0.894 . Sex, n (%)	Height SDS at the point of the survey, mean (SD)	-0.9 (0.8)	-0.3 (0.9)	0.027
Weight SDS at the point of the survey, mean (SD) -0.4 (1.0) -0.2 (0.8) 0.340 Injection administator, n (%) 0 (0.0) 8 (100.0) 0.216 Patient 0 (0.0) 8 (100.0) 0.216 Caregiver/LAR 14 (16.3) 72 (83.7) Norditropin® Norditet® 8 (9.3) 78 (90.7) Others ⁹ 6 (75.0) 2 (25.0) Duration of use of NordiFlex® at the point of the survey 14.3 (6.2) 17.6 (5.6) 0.045 (weeks), mean (SD) 0.00) 6 (100.0) 6 (100.0) No. of injections missed in a typical month, n (%)	Weight at the point of the survey (kg), mean (SD)	32.3 (9.8)	38.5 (11.4)	0.059
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	Weight SDS at the point of the survey, mean (SD)	-0.4 (1.0)	-0.2 (0.8)	0.340
Patient 0 (0.0) 8 (100.0) 0.216 Caregiver/LAR 14 (16.3) 72 (83.7)	Injection administrator, n (%)			
$\begin{array}{c c} Caregiver/LAR & 14 (16.3) & 72 (83.7) \\ Last device used before NordiiTopin NordiFlex®, n (%) & 0.001^h \\ Norditropin® NordiiLet® & 8 (9.3) & 78 (90.7) \\ Others^9 & 6 (75.0) & 2 (25.0) \\ \end{array} \\ \begin{array}{c} 0.001^h \\ Verkers^9 & 6 (75.0) & 2 (25.0) \\ \hline \\ 0.011 \\ Verkers^0 & 0.005 \\ \hline \\ (weeks), mean (SD) & 0.045 \\ \hline \\ verkers, mean (SD) & 0.000 & 6 (100.0) \\ >5 times & 0 (0.0) & 6 (100.0) \\ >5 times & 0 (0.0) & 2 (100.0) \\ \hline \\ $	Patient	0 (0.0)	8 (100.0)	0.216
Last device used before Norditropin NordiFlex®, n (%) <0.001 ^h Norditropin® NordiLet® 8 (9.3) 78 (90.7) Otters ⁹ 6 (75.0) 2 (25.0) Duration of use of NordiFlex® at the point of the survey 14.3 (6.2) 17.6 (5.6) 0.045 (weeks), mean (SD) 0.00) 6 (100.0) 0.465 <3 times	Caregiver/LAR	14 (16.3)	72 (83.7)	
Norditropin® NordiLet® 8 (9.3) 78 (90.7) Others ⁹ 6 (75.0) 2 (25.0) Duration of use of NordiFlex® at the point of the survey (weeks), mean (SD) 14.3 (6.2) 17.6 (5.6) 0.045 No. of injections missed in a typical month, n (%) 0 (0.0) 6 (10.0) 0.465 < 3 times	Last device used before Norditropin NordiFlex®, n (%)			<0.001 ^h
Others 6 (75.0) 2 (25.0) Duration of use of NordiFlex® at the point of the survey (weeks), mean (SD) 14.3 (6.2) 17.6 (5.6) 0.045 No. of injections missed in a typical month, n (%) 0.465 0.465 <3 times	Norditropin [®] NordiLet [®]	8 (9.3)	78 (90.7)	
Duration of use of NordiFlex® at the point of the survey (weeks), mean (SD) 14.3 (6.2) 17.6 (5.6) 0.045 No. of injections missed in a typical month, n (%) 0.465 0.465 <3 times	Others ^g	6 (75.0)	2 (25.0)	
(weeks), mean (SD) 0.465 No. of injections missed in a typical month, n (%) 0.465 <3 times	Duration of use of NordiFlex [®] at the point of the survey	14.3 (6.2)	17.6 (5.6)	0.045
No. of injections missed in a typical month, n (%) 0.465 <3 times	(weeks), mean (SD)			
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	No. of injections missed in a typical month, n (%)			0.465
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	<3 times	14 (16.3)	72 (83.7)	
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	3 to 5 times	0 (0.0)	6 (100.0)	
Caregivers/LARs Age (years), mean (SD) 43.6 (5.2) 43.8 (3.8) 0.894 Sex, n (%) 0.742 0.742 Male 1 (20.0) 4 (80.0) 0.742 Female 13 (14.6) 76 (85.4) 0.011 Highest qualification, n (%) 0.011 High School 3 (50.0) 3 (50.0) 3 (50.0) University or college 6 (16.7) 30 (83.3) 0.011 Others 3 (30.0) 7 (70.0) 0.052 < 50 million 4 (44.4) 5 (55.6) 0.052 < 50 million to <70 million 1 (7.1) 13 (92.9) 0.052 < 70 million or more 3 (18.8) 13 (81.3) Preferred not to answer 6 (10.9) 49 (89.1)	>5 times	0 (0.0)	2 (100.0)	
Age (years), mean (SD) $43.6 (5.2)$ $43.8 (3.8)$ 0.894 Sex, n (%) 0.742 Male 1 (20.0) 4 (80.0) Female 13 (14.6) 76 (85.4) Highest qualification, n (%) 0.011 High School 3 (50.0) 3 (50.0) University or college 6 (16.7) 30 (83.3) Others 3 (30.0) 7 (70.0) Prefer not to answer 2 (4.8) 40 (95.2) Annual household income in KRW, n (%) 0.052 <50 million		Caregivers/LARs		
Sex, n (%) 0.742 Male 1 (20.0) 4 (80.0) Female 13 (14.6) 76 (85.4) Highest qualification, n (%) 0.011 High School 3 (50.0) 3 (50.0) University or college 6 (16.7) 30 (83.3) Others 3 (30.0) 7 (70.0) Prefer not to answer 2 (4.8) 40 (95.2) Annual household income in KRW, n (%) 0.052 <50 million	Age (years), mean (SD)	43.6 (5.2)	43.8 (3.8)	0.894
Male 1 (20.0) 4 (80.0) Female 13 (14.6) 76 (85.4) Highest qualification, n (%) 0.011 High School 3 (50.0) 3 (50.0) University or college 6 (16.7) 30 (83.3) Others 3 (30.0) 7 (70.0) Prefer not to answer 2 (4.8) 40 (95.2) Annual household income in KRW, n (%) 0.052 <50 million	Sex. n (%)	1010 (012)		0.742
Highest qualification, n (%) 13 (14.6) 76 (85.4) Highest qualification, n (%) 0.011 High School 3 (50.0) 3 (50.0) University or college 6 (16.7) 30 (83.3) Others 3 (30.0) 7 (70.0) Prefer not to answer 2 (4.8) 40 (95.2) Annual household income in KRW, n (%) 0.052 <50 million	Male	1 (20.0)	4 (80.0)	017 12
Highest qualification, n (%) 0.011 High School 3 (50.0) 3 (50.0) University or college 6 (16.7) 30 (83.3) Others 3 (30.0) 7 (70.0) Prefer not to answer 2 (4.8) 40 (95.2) Annual household income in KRW, n (%) 0.052 <50 million	Female	13 (14.6)	76 (85.4)	
High School 3 (50.0) 3 (50.0) University or college 6 (16.7) 30 (83.3) Others 3 (30.0) 7 (70.0) Prefer not to answer 2 (4.8) 40 (95.2) Annual household income in KRW, n (%) 0.052 <50 million	Highest gualification, n (%)			0.011
University or college 6 (16.7) 30 (83.3) Others 3 (30.0) 7 (70.0) Prefer not to answer 2 (4.8) 40 (95.2) Annual household income in KRW, n (%) 0.052 <50 million	High School	3 (50.0)	3 (50.0)	01011
Others 3 (30.0) 7 (70.0) Prefer not to answer 2 (4.8) 40 (95.2) Annual household income in KRW, n (%) 0.052 <50 million	University or college	6 (16.7)	30 (83.3)	
Prefer not to answer 2 (4.8) 40 (95.2) Annual household income in KRW, n (%) 0.052 <50 million	Others	3 (30.0)	7 (70.0)	
Annual household income in KRW, n (%) 0.052 <50 million	Prefer not to answer	2 (4.8)	40 (95.2)	
<50 million	Annual household income in KRW, n (%)	_ ()		0.052
50 million to <70 million	<50 million	4 (44,4)	5 (55.6)	
70 million or more 3 (18.8) 13 (81.3) Preferred not to answer 6 (10.9) 49 (89.1)	50 million to <70 million	1 (7.1)	13 (92.9)	
Preferred not to answer 6 (10.9) 49 (89.1)	70 million or more	3 (18.8)	13 (81.3)	
	Preferred not to answer	6 (10.9)	49 (89.1)	

^aStandardized score of satisfaction with NordiFlex[®] >0, ^bStandardized score of satisfaction with NordiFlex[®] ≤0, ^cAge ≤11 years for girls and age ≤12 years for boys, ^dAge >11 years for girls and age >12 years for boys, ^ep-value for comparison between 'more severe condition' and 'less severe condition', ^fIncludes hypothyroidism, failure to thrive and constitutional delay of growth and puberty, ^gPrefilled Eutropin[®], Growtropin[®] II, Saizen[®] Easypod[®], Genotropin[®] GoQuick[®], ^hp-value for comparison between 'Norditropin[®] NordiLet[®]' and 'Others'

GH, growth hormone; KRW, South Korean won; LAR, legally authorized representative; SD, standard deviation; SDS, standard deviation score.

of Norditropin NordiFlex[®] across the majority of measures. For two subjective benefits, 'NordiFlex[®] is easier to hold' and 'With NordiFlex[®], it is easier to press the dose button,' the difference was not statistically significant. Preference for Norditropin NordiFlex[®] was less pronounced on subjective benefits in the *positive feelings about injection* domain.

4. Discussion

A growing body of evidence suggests that device-related factors can play a role in improving adherence to GH treatment. Norditropin NordiFlex® introduced a number of key improvements compared with Norditropin® NordiLet®, including no requirement for dose conversion, a dose



Figure 4. Forest plots of mean (95% CI) standardized scores of subjective benefits of GH device features categorized by domain: self-efficacy (A), ease of use (B), minimal disruption of daily life (C), and positive feelings about injection (D).

indicator window, finer dose increments, and a soft push button. Previous studies evaluating patients' self-reported preference for Norditropin NordiFlex[®] compared to other devices, showed favorable outcomes for Norditropin NordiFlex[®] [18,23,24,26].

This survey assessed the patients' and caregivers' opinions regarding the subjective benefits of Norditropin NordiFlex® after switching from their previous device (primarily Norditropin® NordiLet®) in a real-world setting. To quantify the impact of this switch, a conceptual model (grounded on available evidence) that categorized subjective benefits under four domains (*self-efficacy, ease of use, minimal disruption of daily life,* and *positive feelings about injection*) was developed. Assessment of the subjective benefits showed that items within each domain had a high internal consistency.

Participants reported a greater preference for and satisfaction, improved perceived ease of use, and self-reported adherence with Norditropin NordiFlex[®], compared with the previous GH device. This suggests that feature improvements in Norditropin NordiFlex[®] were associated with improved patient treatment experience. Furthermore, preference for Norditropin NordiFlex[®] was positively associated with the four domains of subjective benefits. Multivariate analysis showed that preference for Norditropin NordiFlex[®] was still significantly associated with *ease of use* and *minimal disruption of daily life*, while associations with *self-efficacy* and *positive feelings about the injection* were no longer statistically significant, after controlling for age, sex, height SDS at the point of the survey and the ratio of duration of treatment with Norditropin NordiFlex[®] to total duration of GH treatment.

Patients with a relatively more severe diagnosis (e.g. GHD, SGA, NS), showed a stronger preference for Norditropin NordiFlex[®] vs. patients with a less severe diagnosis (e.g. ISS, FSS, precocious puberty, others). Additionally, these patients (as well as those with a longer duration of GH treatment) reported a higher perceived ease of use, and greater satisfaction with Norditropin NordiFlex[®] compared with the previous

device. These findings suggest that patients with a relatively more severe diagnosis may be more sensitive to (and gain a greater advantage from) device features that improve their treatment experience compared with patients with a relatively less severe diagnosis.

Furthermore, patients with a relatively more severe diagnosis as well as those with a longer duration of GH treatment or lower height SDS at the point of survey, may be more acutely aware of the impact of adherence on outcomes, and/ or may experience challenges with their GH treatment device. Devices that can improve these patients' treatment experiences are likely to be viewed favorably.

Standardized scores of the individual subjective benefits of GH device features showed that, overall, participants preferred Norditropin NordiFlex® to the previous device across the majority of measures. Respondents strongly favored Norditropin NordiFlex® on the 'Read the dose,' 'Correct the dose' and 'Select the dose' items within the ease of use domain, as well as the 'Selecting the right dose' and 'Administering the right dose' items within the self-efficacy domain. Dose selection can have a two-fold impact on patient experience. In terms of ease of use, device improvements that facilitate dose selection can make the injection process easier for the patient or caregiver. Similarly, from a self-efficacy perspective, device improvements that enhance confidence when selecting the correct GH dose can empower patients to self-inject. The large dose window with Norditropin NordiFlex® may have provided patients with additional dose clarity vs. their previous device. Bagnasco and colleagues [17] found that among patients who reported being confident of having administered the correct GH dose, a significantly larger proportion of them was adherent to treatment. This suggests that features that increase a patient's or caregiver's confidence in administering the correct dose of GH could, in turn, have a positive impact on adherence.

Previous research has shown that refrigeration of GH products, especially when traveling away from home, was perceived to be a substantial burden by both patients and caregivers [14]. In the same study, the majority of patients and caregivers indicated a wish for a treatment that could be stored outside the refrigerator for longer periods of time, while almost half of the patients and caregivers expressed a preference for a treatment that did not require reconstitution.

Both Norditropin NordiFlex® and Norditropin® NordiLet® are prefilled injector pens with liquid GH using histidine buffer that can be stored at room temperature for 3 weeks after the first use. These features are absent from most of the other devices previously used by the respondents in this survey. These devices typically require reconstitution (e.g., Genotropin[®] GoQuick[®]), refrigerated (e.g., storage Genotropin[®] GoQuick[®]), cartridge replacement (e.g., Saizen[®] easypod®), or extra care as it is electronic (e.g., Saizen® easypod®). Also, devices which are relatively large could be perceived as less discreet (e.g., Saizen® easypod®, Genotropin® GoQuick®). In this survey, respondents indicated only a marginal improvement in favor of Norditropin NordiFlex® on items within the minimal disruption of daily life domain, and had similar positive feelings towards injection for Norditropin NordiFlex[®] compared with their previous device. These domains are influenced by device features that are common

to both Norditropin NordiFlex[®] and Norditropin[®] NordiLet[®]. It is plausible that these results are a reflection of the high proportion of patients who switched to Norditropin NordiFlex[®] from Norditropin[®] NordiLet[®]. Given the high proportion of patients who previously used Norditropin[®] NordiLet[®], it is also plausible that the small improvement in the *minimal disruption of daily life* domain is directly associated with feature enhancements in Norditropin NordiFlex[®] compared with Norditropin[®] NordiLet[®]. It may be possible that a larger difference in these domains could have been observed had there been more participants switching from a device other than Norditropin[®] NordiLet[®]. This needs to be evaluated in future studies.

Some patients, particularly those with smaller hands, may have needed to grip Norditropin NordiFlex® from a higher position to compensate for the slightly larger dimensions (150 vs. 144 mm in length, and 15 vs. 13 mm in diameter, respectively), and longer push button travel at maximum dose (~33 vs. ~16 mm, respectively) compared with Norditropin® NordiLet® (**Appendix A**). However, the standardized scores of the individual subjective benefits observed in this survey suggest that the impact of these small differences in size may have been mitigated by the reduction in pressure required to press the push button of Norditropin NordiFlex® compared with the previous device. The two subjective benefits, 'NordiFlex® is easier to hold' and 'With NordiFlex®, it is easier to press the dose button' within the *ease of use* domain, were not statistically significantly in favor of Norditropin NordiFlex® or the previous device.

This survey assessed self-reported adherence as a relative measure of injections missed with Norditropin NordiFlex® vs. the previous device. As the survey design did not allow for adherence data to be collected before and after patients switched devices, adherence was assessed on the basis of patients' recall of missed injections with the current device in comparison with the previous device. The conceptual model suggested that treatment experience improvement across the four domains of subjective benefits could have an indirect effect on adherence.

Self-reported adherence results showed that patients who missed fewer injections with Norditropin NordiFlex® vs. the previous device were more likely to be children (rather than adolescents) diagnosed with a relatively more severe condition, be shorter in height at diagnosis and at the point of survey, have a lower weight at diagnosis, and have a lower height SDS at the point of survey. Considering the relatively low number of the patients who used other devices before Norditropin® NordiLet®, it is difficult to make a meaningful interpretation of this finding. The results also showed that the difference in the number of injections missed in a typical month between the two groups was not statistically significant. However, it is not possible to meaningfully interpret this observation, as only eight patients reported suboptimal adherence. Differences were observed in the educational level and annual household income between caregivers/LARs who injections with Norditropin missing fewer reported NordiFlex® and those that did not. A meaningful interpretation of this finding was not possible owing to the large proportion of caregivers/LARs who chose not to disclose their education level and household income.

Results from the subgroup analysis suggest that patients who used Norditropin NordiFlex[®] for 4 to ≤12 weeks were less likely to report missing fewer injections (vs. the previous device) compared with patients who used Norditropin NordiFlex® for >12 weeks. This observation could be potentially accounted for by two reasons. First, previous studies have reported different effects of duration of treatment on adherence; some studies [7,17,27] reported a negative impact, while others [28,29] did not observe any relation. Bagnasco et al. [17] also reported the impact of 'Duration of use of current device' on adherence where the non-adherence was significantly more in patients using their current device for more than one year compared to less than 6 months. While one cannot confidently exclude the impact of duration of using Norditropin NordiFlex® on the observed difference, the size of this impact might be minimal in light of the evidence from Bagnasco et al. [17]. Secondly, and more plausibly, patients or caregivers/LARs could have experienced a recall bias with respect to adherence levels with the previous device.

As self-reported adherence was based solely on recollection, it is possible that patients or caregivers/LARs could have erroneously attributed better levels of adherence with the previous device than was actually the case. Furthermore, respondents who used Norditropin NordiFlex® for a longer period of time could have had less recollection about the level of adherence with their previous device compared with those who used NordiFlex® for a shorter period. Further research with a larger sample size will be required to clarify this result.

Bivariate analysis revealed a statistically significant positive association between all four domains of subjective benefits and self-reported adherence. A multivariate analysis was not performed owing to the small number of participants who reported missing fewer injections with Norditropin NordiFlex®. The adherence results from this survey suggest that minimal improvement in device features (that are not related to drug formulation) may have a positive effect on adherence. Furthermore, they are qualitatively similar to those reported by Bagnasco and colleagues (2010), who found that factors, such as level of confidence in administering the right dose, as well as convenience and overall satisfaction with the GH device, were associated with adherence.

It was not possible to establish whether other factors affected adherence in this study, as the design of the survey was developed around the primary outcome of 'preference.' Nevertheless, treating physicians should consider other factors (e.g. psychosocial factors [30], motivation [31], the patient's or carer's knowledge and understanding of the condition, the quality of the HCP-patient relationship [32], as well as education on the positive effects of GH treatment [33]) that may influence adherence to treatment.

4.1. Study limitations

This survey was affected by some limitations. It was not possible to assess the satisfaction level of patients who were unaccompanied by their caregiver/LAR, owing to informed consent requirements. This group of patients could exhibit greater independence compared with patients that were accompanied by their caregiver/LAR.

This study relied largely on participants' self-reported data and could be potentially biased by social desirability. Nonetheless, questions related to the evaluation of device features are unlikely to be affected by this bias. Adherence to treatment was also self-reported as the majority of the devices used by the study participants did not have electronic monitoring capability, which could have potentially provided more objective adherence data.

Factors that could have played a role in device preference (e.g., disease awareness, patient-physician relationship) were not measured in this survey. Additionally, as the study had a cross-sectional design, the temporal association could not be established.

As the majority of patients used Norditropin® NordiLet® before switching to Norditropin NordiFlex®, it was not possible to compare the impact of some GH product-specific characteristics (such as storage flexibility and liquid formulation), or to perform exploratory subanalyses based on prior device group.

It was not possible to collect data or draw conclusions on the potential impact of factors that could influence device preference or acceptance, like the clinic setting or time of the appointment. This was due to limitations that are intrinsic to the design of survey-driven studies and differences between study centers that could not be controlled for. In this study, it was only possible to enroll 94 patients. Thus, it was not possible to stratify patients by previous device. Therefore, although number of participants allowed for the analysis of the primary endpoint, it was not possible to perform further comparative analyses between Norditropin NordiLet[®] and the other previously used devices.

Finally, a larger study with a prospective design to test the observed relations with a comprehensive multivariate model could have provided broader insight into the impact of GH device improvements on patients' treatment experience and clinical outcomes.

4.2. Study strengths

This is one of the very few studies conducted in Asia that assesses the preference of GH devices for pediatric patients with growth disorders. The multi-center design allowed for a wider range of patients, thereby increasing the generalizability of the results.

The potential risk of recall bias among participants [34] was mitigated by limiting the recall period to 24 weeks. Additionally, a sensitivity analysis was undertaken to compare the data on preference between those who used Norditropin NordiFlex® for 4 to \leq 12 weeks and those who used it for >12 weeks.

The medicinal product and formulation were identical between the new device (Norditropin NordiFlex®) and the previous device in the majority of participants (Norditropin® NordiLet®). This allowed the detection of device-related impact on treatment experience while minimizing any potential confounds related to differences in formulation.

5. Conclusions

Participants in this survey reported greater preference and satisfaction, improved perceived ease of use, and self-reported adherence to Norditropin NordiFlex®, compared to the previous device. Of the subjective benefits of device features, *ease of use*, and *minimal disruption of daily life* domains were significantly associated with preference for Norditropin NordiFlex®.

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Author contributions

All authors were involved in the conduct of the study and data collection, drafting, critical revision, and final approval of the version of the paper to be published. All authors agree to be accountable for all aspects of the work.

Data availability statement

The data that support the findings of this study are available on request from the corresponding author (WYC). The data contain information that could compromise research participant privacy/consent are therefore not publicly available.

Geolocation information

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