Poster No. P2-654

Adherence to growth hormone therapy: comparison of electronic auto-injection to non-electronic injection devices

Mia Trendafilow[1] and Klaus K P Hartmann[1]

[1]Medical Center for Childhood and Adolescence in Pediatric Endocrinology and Diabetology, 60594, Frankfurt, Germany

BACKGROUND

- Recombinant human growth hormone (r-hGH) is used to promote growth in children with conditions such as GH deficiency (GHD), Turner syndrome (TS), chronic renal failure (CRF) and to treat children born small for gestational age (SGA) who fail to demonstrate catch-up growth.[1]
- easypod™ is a hidden-needle auto-injector device that records the date and time of injection, prescribed dose (mg), injected dose (mg) and injection status (dose setting, performed, missed or partial injection). Due to the registration of each r-hGH injection, patient adherence can be monitored accurately.[2]
- We previously have reported that patients under r-hGH therapy using easypod™ as their electronic injection device showed a high adherence (AD) rate.[3,4]
- In addition we reported that patients using a non-electronic device (NEL) for r-hGH administration had a similar high AD rate to patients using the easypod™ electronic device.[4]

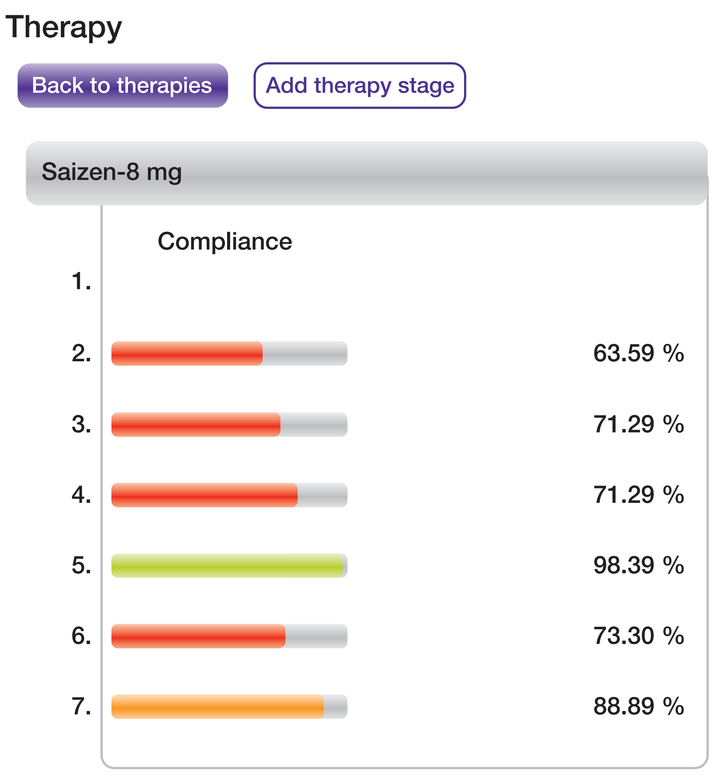
OBJECTIVES

- To evaluate AD rates of r-hGH treatment under everyday conditions and to calculate the amount of r-hGH administered using the easypod™ or a NEL device.

METHODS

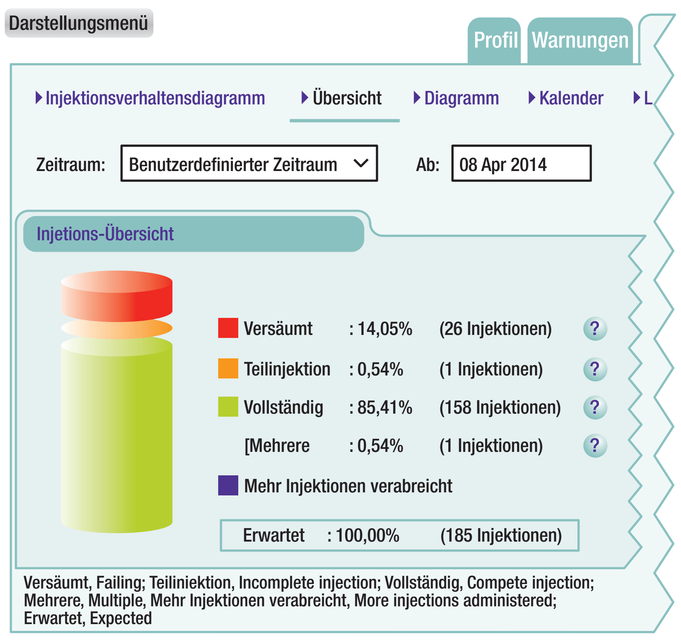
- Retrospective, observational, open-label, non-controlled study in patients receiving r-hGH, either by the easypod™ or a NEL device.
- Patients were treated with r-hGH using either easypod™ or NEL devices.
- For patients using NEL devices, AD was determined by the ratio of provided vials to prescribed dose x duration of observation period (days)
- Data collection and calculation of adherence using the vial consuming method was performed by PAEDLOGIC software (www.paedlogic.com). (**Figure 1**)

Figure 1. Calculation of AD via Paedlogic software



- r-hGH dose and injection time were measured automatically by the easypod™ electronic injection device.
- Adherence data were collected from pediatric patients receiving r-hGH therapy using the easypod™ injection device in conjunction with the easypod-connect software (Version 2.0) (**Figure 2**)
- easypod™ data from patients attending 11 paediatric endocrinology centers in Germany from October 2009 to May 2011 were uploaded to the internet-based Saizen® electronic data capture system (SAIZEN-EDC).
- easypod: data collection and calculation of adherence using the vial consumption method; analysis of data from patients recruited only from one center (medikijz, Frankfurt)
- Data from patients using the NEL injection device were collected only from one center (medikijz, Frankfurt).

Figure 2. Calculation of AD via Easypod-connect software



RESULTS

- In total, 250 patients (99 female, 151 male) received r-hGH using easypod™. The observation period was 2.8 ± 2.3 years after start of GH therapy. The average age at the start of r-hGH therapy was 9.1 ± 3.6 years.
- In contrast, 294 patients (133 female, 161 male) using different NEL devices (needle injection or non-needle injection systems) were observed over a time period of 2.2 ± 1.2 years after start of GH therapy. The age of these patients at the start of r-hGH therapy was 11.3 ± 5.7 years. (**Table 1**).

Table 1. Characterisation of patients using easypod™ or NEL devices for r-hGH injection

Number of patients	Age at start of therapy (yrs)	Duration of therapy (yrs)
easypod 251	9.1 ± 3.6	2.8 ± 2.3
NEL 294	11.3 ± 5.7	2.2 ± 1.2

- Modified analysis according to the criteria of Cutfield et al.[5] indicated that there was a higher observed proportion of over-adherent NEL patients (AD >110%; **Table 2**). These results indicate that patients using the NEL device showed an over-AD due to wastage of r-hGH. This could be due to two reasons:
  - 1. Non emptying of r-hGH vials or
  - 2. Storage mismanagement of the r-hGH vials.

Table 2. Adherence rates in patients using easypod™ or NEL devices

Mean AD rate	easypod™ (% of patients)[a]	NEL (% of patients)[b]
>110% (wastage of r-hGH)	0	15.5
85.7–110%	72.5	58.8
57.1–85.7%	26.3	24.6
<57.1%	1.2	1.1

a: determined by electronic registration
b: calculated by the ratio of provided vials to prescribed dose x duration of observation period (days).

- To check the second possible reason, we compared the amount of r-hGH which is electronically recorded by easypod™ with the prescribed and delivered amount of r-hGH (Saizen®) as vials for this device.
- 53 easypod™ patients (recruited only from one center, see Methods) were observed over a time period of 2.2 ± 1.0 years receiving r-hGH via the electronic device easypod (**Table 3**). During this time period these patients injected on average 947.8 ± 413.1 mg growth hormone. During the same time period, these patients consumed on average 983 ± 404.35 r-hGH. These results indicated that 3.8 % of the prescribed r-hGH was lost during this time.
- To compare these results with the data of the NEL devices we analyzed the AD of easypod™ patients in the same manner as the AD for the NEL patients (see Methods). These results showed that 28.3 % of the easypod™ patients had an AD rate >110 % (**Table 4**).
- These data are comparable to the results of the patients using the NEL device (**Tables 2 and 4**).

Table 3. Consumption of r-hGH as electronically registered via easypod™ in comparison with the actual number of r-hGH vials prescribed and delivered

Number of patients	Duration of therapy (yrs)	Electronic registration of consumption of r-hGH	Consumption of r-hGH vials (mg)	Ratio of consumed vials/electronic registration of consumption
53	2.2 ± 1.0	947 ± 413.1	983 ± 404.4	1.038

Table 4: Consumption of r-hGH of patients using easypod™ or NEL devices. Determination of AD rate by NEL method

Number of patients	Proportion of patients with an AD >110% (%)	Proportion of wasted r-hGH for patients with AD >110% (%)	Overall wasted r-hGH (%)
easypod 53	28.3	16.3	4.6
NEL 294	15.5	18.0	2.8

- The calculation of the overall amount of GH consumption for these patients showed that 4.6% of the r-hGH amount was wasted by easypod™ patients. This was the result of inadequate vial storage management. In comparison 2.8 % of all administered r-hGH amount was lost by mismanagement by patients use of the NEL devices.

CONCLUSIONS

- **Both groups of patients using either NEL or easypod™ device show a similar high AD rate.**
- **Electronic measurement by easypod™ of AD has the advantage of direct detection of actual AD rate.**
- **Both groups also show an increased wastage of r-hGH although patients using easypod were younger and the sample size for this calculation was smaller than that for the patients using the NEL devices.**
- **Our results indicate that this is due to mismanagement of the r-hGH vials.**
- **To avoid wastage of r-hGH an electronic network should be established between pharmacy and patients for supporting management of r-hGH vials.**
- **Electronic connection from easypod-connect and Paedlogic software will be necessary to improve detection of wastage of r-hGH.**
- **Individual re-education of patients with low AD rate or increased wastage of r-hGH will be very important to adjust individual r-hGH dose for achieving optimal final height.**

REFERENCES

1. Richmond E, Rogol AD. *Endocr Dev* 2010; 18:92–108.
2. Dahlgren J. *Expert Rev Med Devices* 2008; 5:297–304.
3. Hartmann K et al. *Horm Res Paediatr* 2013; 80:1–5.
4. Trendafilow M et al. Poster presented at the 9th Joint Meeting of Paediatric Endocrinology; September 2013; Milan, Italy (P2-d1-958)
5. Cutfield WS et al. *PLoS One*. 2011 Jan 31;6:e16223.

ACKNOWLEDGEMENTS

The trial was financially supported by Merck GmbH Serono GmbH, Germany. The authors would like to thank patients and their families, investigators, co-investigators and the study teams at each of the participating centers and at Merck KGaA, Darmstadt, Germany.

The author thanks the SAIZEN-EDC Study Group (Germany) for providing the patient data.

Medical writing assistance was provided by David Candlish, inScience Communications, Tattenhall, UK and funded by Merck KGaA, Darmstadt, Germany. Merck has reviewed the poster but was not involved in the contents.

DISCLOSURES

KKPH has received Honoraria as an Advisory Board member and consultant to Merck KGaA, Darmstadt, Germany and has been sponsored to attend scientific meetings by the company.

To view the e-Poster, scan the QR code or go to:
http://medpub-poster.merckgroup.com/ESPE2016_P2.654.pdf

Presented at ESPE, Paris, 10-12 September, 2016

55ESPE 654--P2

Growth

David Candlish

DOI: 10.3252/pso.eu.55ESPE.2016

Poster presented at: ESPE 2016 PARIS

PosterSessionOnline.com