Original article

User trial of Easypod™, an electronic autoinjector for growth hormone

Essai auprès des utilisateurs de l’Easypod™, un auto-injecteur électronique pour l’hormone de croissance

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Résumé

Objectif. – Un nouveau dispositif d’injection électronique, l’Easypod™, a été développé pour administrer l’hormone de croissance. Cette étude a évalué l’utilisation de ce dispositif dans la pratique courante. Matériels et méthodes. – Nous rapportons les résultats obtenus du bras français (un seul site) d’une étude internationale ouverte non contrôlée. Les patients sont des enfants utilisant déjà, ou sur le point d’utiliser, la thérapie par l’hormone de croissance. Les enfants ont utilisé le dispositif Easypod™ pendant 60 jours. Les principales mesures du résultat sont l’impression qualitative générale produite par le dispositif chez les patients ou, le cas échéant, les parents et l’évaluation de l’utilité des caractéristiques du dispositif après 15 jours d’utilisation, évaluée au moyen d’un questionnaire. Résultats. – Au quinzième jour, tous les participants (20/20) ont indiqué qu’ils avaient une « bonne » ou « très bonne » impression du dispositif Easypod™. Tous les participants ont indiqué par un score si l’affichage du médicament restant dans la cartouche, la posologie préprogrammée, les instructions sur écran et la fixation automatique de l’aiguille étaient « utiles » ou « très utiles ». Les signaux sonores/visuels du dispositif et la profondeur et la vitesse d’injection adaptées à chaque patient ont chacun été cotés comme « utiles » ou « très utiles » par 19/20 participants et le détecteur cutané, la vitesse d’insertion de l’aiguille adaptée à chaque patient et la confirmation de l’injection de la dose ont, chacun aussi, été cotés de la sorte par 18/20 participants. L’affichage électronique de la date et de l’heure de la dernière injection et l’historique de la dose ont été jugés « utiles » ou « très utiles » par 17/20 et 15/20 participants, respectivement. Au soixantième jour, 17/17 répondants ont exprimé qu’ils préféraient continuer à utiliser le dispositif. Conclusions. – Ces résultats prouvent que les caractéristiques de l’Easypod™ sont considérées comme utiles dans la pratique systématique et que la majorité des participants ont exprimé le désir de continuer à utiliser le dispositif.

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Abstract

Objective. – A new electronic injection device, the Easypod™, has been developed to administer growth hormone (GH). This study assessed the use of this device in common practice. Materials and methods. – Results are from the French arm (one centre) of an international, open-label, uncontrolled study. Subjects were children already using, or about to start, GH therapy. Children used the Easypod™ device for 60 days. The main outcome measures were patients’ or, if appropriate, their parents’ qualitative overall impression of the device and the usefulness of its features after 15 days’ use, as evaluated by questionnaire. Results. – At day 15, all participants (20/20) described their overall impression of the Easypod™ device as “good” or “very good”. All participants rated the display of the remaining drug in the cartridge, the preprogrammed dosing, the onscreen instructions and the automatic-needle attachment as “useful” or “very useful”. The device’s audible/visible signals and customisable injection depth and speed were each rated as “useful” or “very useful” by 19/20 participants and the skin sensor, customisable needle-insertion speed and dose-injection confirmation were each rated as such by 18/20 participants. Electronic display of the date and time of the last injection and the dose history were considered “useful” or “very useful” by 17/20 and 15/20 participants, respectively. At day 60, 17/17 respondents expressed a preference for continuing to use the device.

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1. Introduction

Growth-hormone deficiency (GHD) in children is characterised by short stature and low-growth velocity [1,2]. Recombinant human-growth hormone (r-hGH) is an effective treatment for children with GHD and is also indicated for those born small for gestational age or who have Turner’s syndrome or chronic-renal failure [3]. GH therapy usually requires daily injections on a long-term basis [4]. The importance of frequent, continued r-hGH injections has led to research into easier methods of administration to facilitate treatment acceptance by patients. Several devices for r-hGH delivery are available in France, as shown in Table 1. Injection techniques have changed from the intramuscular to the subcutaneous route and injection devices have evolved from conventional syringes and needles to injection-pen and needle-free devices, which have all improved adherence to treatment [5–8]. Nonadherence is associated with poor clinical outcomes, lower quality of life and higher-healthcare costs [6,9,10].

A recent survey identified which attributes of an r-hGH device were deemed most important to patients, parents, physicians and nurses who had experience with administration of GH [11]. The five most important features were reliability, ease of use, lack of pain during injection, safety in use and storage and the number of steps to prepare the device before use. Patients and nurses rated ease of use and convenience as the most important factors to consider. Both patients and parents needed to be reassured that the treatment was being injected properly and to have a confirmation that the correct dose had been administered. Adherence monitoring was also an important consideration, especially for physicians and nurses. Importantly, at the time of the survey in 2006, no device was able to monitor or confirm dose administration.

To optimise the treatment of patients receiving r-hGH (Saizen®, Merck Serono International S.A., Geneva, Switzerland), a new electronic injection device, the Easypod™ (Merck Serono International S.A.), has been developed for the injection of r-hGH. The device has a number of unique features, such as recording the dosing history and preprogrammed dosing, which prevent dosing errors and simplify the dosing schedule. It has a digital display to show the dose that has been preselected by the physician, the confirmation of the dose administered and the remaining doses in the cartridge. The needle, which remains within the needle cap during the attachment and detachment steps, is hidden from sight at all times and the injection depth, speed and time can be programmed to suit each user. An electronic skin-sensor detects the distance of the device from the skin, allowing for more accurate needle insertion. Following injection, the remaining r-hGH is stored safely within the device for later use. The device is designed to give children increased autonomy in administering their GH treatment, which is an important element for treatment adherence [12].

We report results from a study that evaluated the use of this injection device in common practice. Patients, or their parents, were asked to assess the features of the device. Nurses and physicians were also asked to evaluate the training process and device set-up.

2. Patients

Participants for the study (NCT00450190) were recruited from Finland, France, Norway, Sweden and Switzerland. Results from the French interventional study are presented here. Results from patients recruited in the other countries are presented elsewhere [13]. Patients who were treatment-naive or pretreated with r-hGH for growth disorders in registered paediatric indications were eligible for the study.

A total of 20 children entered the study at the hôpital des Enfants, service d’endocrinologie pédiatrique in Toulouse, France, in 2006. Exclusion criteria included a known hypersensitivity to somatropin or any of the excipients, the presence of epiphyseal fusion, active neoplasia, history of intracranial hypertension with papilloedema, diabetes mellitus, severe congenital malformations, severe psychomotor retardation, chronic infectious disease, known renal insufficiency or hepatic disease, current congestive heart failure, untreated hypertension and serious chronic oedema. Patients were also excluded if they had been using concomitant levothyroxine or corticoid treatment (other than substitutive, topical or inhaled treatment) or had previous or ongoing treatment with sex-steroid therapy or any therapy that could influence growth, including GH-releasing factor and long-duration corticosteroid therapy.

The study was conducted in accordance with the Declaration of Helsinki and was approved by the institution’s committee on human research. Written consent was obtained from the parents or legal guardians of the children at the beginning of the study or directly from the children if they were able to understand the trial.

3. Study design

This was an open-label, uncontrolled, interventional trial of the use in common practice of the Easypod™ electronic
Table 1
Comparison of growth hormone-delivery devices available in France
Comparaison des dispositifs pour l’administration de l’hormone de croissance disponible en France

<table>
<thead>
<tr>
<th>Device type</th>
<th>Device</th>
<th>Device features</th>
<th>r-hGH</th>
<th>Manufacturer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Electronic injector</td>
<td>Easypod®</td>
<td>Electronic autoinjector. Dose programmed. Adjustable injection depth. Hidden needle. Lyophilised r-hGH is reconstituted using Click.easy® device</td>
<td>Saizen®</td>
<td>Merck Serono</td>
</tr>
<tr>
<td>Autoinjector pen</td>
<td>One.clickTM</td>
<td>Multi-use autoinjector pen. Dose dialled. Adjustable injection depth. Hidden needle. Lyophilised r-hGH is reconstituted using Click.easy® device</td>
<td>Saizen®</td>
<td>Merck Serono</td>
</tr>
<tr>
<td>Injector pen</td>
<td>Genotonorm® Pen</td>
<td>Multi-use pen in two sizes. Needle guard. Dose dialled before each injection. Digital dose-display window. Lyophilised r-hGH is mixed in a two-chamber cartridge</td>
<td>Genotropin®</td>
<td>Pfizer</td>
</tr>
<tr>
<td>HumatroPen®</td>
<td></td>
<td>Multi-use pen. Hidden dose. Dose dialled. Digital display of dose selected. Lyophilised r-hGH must be reconstituted before use</td>
<td>Humatrope®</td>
<td>Eli Lilly</td>
</tr>
<tr>
<td>NordiPen®</td>
<td></td>
<td>Multi-use pen. Dose dialled before each injection. Prefilled cartridge contains premixed liquid r-hGH. Can be used with an optional guard to hide the needle and autoinserter mechanism (NordiPenmate®)</td>
<td>Norditropin®</td>
<td>Novo Nordisk</td>
</tr>
<tr>
<td>Nutropin AQ Pen®</td>
<td></td>
<td>Multi-use pen. Dose dialled before each injection or dose recall function used. Digital dose display. Optional needle shield. Prefilled cartridge contains premixed liquid r-hGH</td>
<td>Nutropin AQ®</td>
<td>Ipsen/Genetech</td>
</tr>
<tr>
<td>Needle-free injector</td>
<td>Omnitrope Pen L</td>
<td>Multi-use pen. Dose dialled before each injection with audible clicks</td>
<td>Omnitrone®</td>
<td>Becton Dickinson</td>
</tr>
<tr>
<td>Cool.clickTM</td>
<td></td>
<td>Needle-free device. Dose dialled before each use. Lyophilised r-hGH is reconstituted using Click.easy® device</td>
<td>Saizen®</td>
<td>Merck Serono</td>
</tr>
<tr>
<td>Zomajet® 2</td>
<td></td>
<td>Needle-free device. Dose dialled before each use. Lyophilised r-hGH must be reconstituted before use</td>
<td>Zomacton®</td>
<td>Ferring</td>
</tr>
<tr>
<td>Genotonorm ZipTipTM</td>
<td></td>
<td>Needle-free device. Lyophilised r-hGH is mixed in a two-chamber cartridge</td>
<td>Genotropin®</td>
<td>Pfizer</td>
</tr>
<tr>
<td>Syringe and needle</td>
<td>Genotonorm Miniquick®</td>
<td>Single-use, disposable syringe. Available in doses 0.2–2.0 mg in 0.2 mg steps. Lyophilised r-hGH is mixed in a two-chamber cartridge</td>
<td>Genotropin®</td>
<td>Pfizer</td>
</tr>
<tr>
<td>ND®</td>
<td></td>
<td>Lyophilised powder must be reconstituted before use</td>
<td>Maxomaf®</td>
<td>Sanofi-Aventis</td>
</tr>
</tbody>
</table>

r-hGH: recombinant human-growth hormone.

* Only available in France.

Table 2
Comparison of features between the Easypod® electronic-injection device and autoinjectors used previously by patients in this study
Comparaison de caractéristiques entre le dispositif à injection électronique Easypod® et des auto-injecteurs utilisés précédemment par des patients lors de cette étude

<table>
<thead>
<tr>
<th>Device</th>
<th>Easypod®</th>
<th>Cool.clickTM</th>
<th>One.clickTM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hidden needle</td>
<td>✓</td>
<td>n/a</td>
<td>✓</td>
</tr>
<tr>
<td>Adjustable-injection depth</td>
<td>✓</td>
<td>n/a</td>
<td>✓</td>
</tr>
<tr>
<td>Preset dosing</td>
<td>✓</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Electronic display</td>
<td>✓</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Injection log/adherence monitoring</td>
<td>✓</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Skin sensor</td>
<td>✓</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Dose confirmation</td>
<td>✓</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>One-step drug administration</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>

n/a: not applicable as the Cool.clickTM device is needle free.

autoinjector in children treated with r-hGH (Saizen®) over a period of two months. As the study endpoint was the ease of use and acceptance of the device, patient growth data were not collected. The r-hGH was supplied as a multidose preparation in glass vials containing 24 IU (8 mg) of r-hGH. The solvent for reconstitution was supplied in cartridges containing metacresol 0.3% (w/v) water for injection. The r-hGH and solvent cartridge were preassembled in the reconstitution device – Click.easy® (Merck Serono International S.A.). Treatment was administered subcutaneously once daily, generally in the evening. Recommended injection sites were the outside of the abdomen, the upper outer buttoc and the upper outer thigh, with site selection depending on what the patient was accustomed to. The weekly dose of r-hGH was calculated based on the patient’s pathology and weight, and the number of injections (six or seven injections per week) was chosen according to the physician’s usual practice. Prior to beginning the injections, children and their parents were provided with an instruction manual and training in the use of the device. At the end of the study (day 60), patients were required to return all of the partially used and unused r-hGH, as well as the device. Patients then continued GH treatment using their previous device – One.clickTM or Cool.clickTM (both Merck Serono International S.A.) (Table 2).

3.1. Study endpoints

The primary endpoint was the participants’ (patients or their parents) qualitative overall impression of the ease of use and features of the device after 15 days of use, as evaluated by questionnaire. Secondary endpoints, all of which were assessed using the questionnaire, included participants’ opinions after
the initial training and after use of the device for 60 days and evaluation of nurse/physician opinions on the device set-up and the training process. Assessing the safety during the treatment and follow-up periods of the study was also a secondary endpoint.

3.2. Training and assessments

Participants attended the clinic at the inclusion visit (day 1) and after 60 days of using the device (day 60). They were contacted by telephone at days 15 and 90. At the inclusion visit, participants were given training in how to set up and use the device by either a nurse or physician. The nurse or physician used the questionnaire (Table 3) to collect participants’ feedback and record their own opinions on device handling and ease of training. At day 15, the nurse or physician telephoned the participant to obtain their qualitative overall impression of the device and assessment of the device’s features (Table 3). At day 60, overall comments about the use of the device and the usefulness of each device function were collected (Table 3). All patients had a post-treatment safety assessment at day 90, 30 days after use of the device was terminated. The nurse or physician contacted the participant by telephone to ask about any adverse events that had occurred during the study period.

3.3. Data analyses

For this report, comparative descriptive analyses were performed from the French arm of the multinational study. Only available data points have been included in these analyses and no adjustment was made for missing data.

4. Results

4.1. Patient characteristics

Ten female children (age range: 6 to 15 years) and 10 male children (age range: 8 to 16 years) were enrolled. The mean (standard deviation [S.D.]) age was 11.30 (2.66) years. Of the 20 patients, 18 were available for follow-up at day 60; the reasons for the two withdrawals were problems with the device in one child and needle-phobia in another.

All patients were receiving r-hGH (Saizen®) treatment at enrolment. Six of the children had experience with the Cool.click™ needle-free device and the remaining 14 with the One.click™ device. The mean (S.D.) age of the devices used at enrolment was 2.40 (1.42) years. In 65% of cases, the parent prepared or assisted with the preparation of the device; the injection was performed by or with the assistance of a parent in 65% of cases. The mean (S.D.) prescribed dose was 1.14 (0.32) mg/day.

4.2. Participant assessments

Initial training: the mean (S.D.) time to train participants on all features of the device was 48.00 (16.34) minutes. The setting up of the device and dose programming were each described as “easy” by the nurses and physicians for 19/20 participants. All of the nurses and physicians set the amount of r-hGH to be delivered by the device by inputting the dose required in milligrams.

Initial impressions: immediately after training, cartridge loading was rated as “easy” or “very easy” by 19/20 participants and the injection process by 17/18 (n = 2 missing), whereas needle attachment and menu navigation were rated as “easy” or
“very easy” by 18/20 participants. Device handling was considered “easy” by 15/16 participants (n = 4 missing). Needle detachment had the most “difficult” ratings (7/20), but was considered “easy” by 12/20 and “very easy” by 1/20.

Day 15: all participants rated the device as “good” (7/20) or “very good” (13/20) when asked for their overall impression.

Of the device features, related to the injection process (automatic needle attachment and customisable needle insertion speed, drug injection speed and injection depth), automatic needle attachment was rated most highly, with 9/20 participants regarding this feature as “useful” and 11/20 participants regarding it as “very useful” (Fig. 1). Both the display of the remaining drug in the cartridge and the preprogrammed dosing were rated as “useful” or “very useful” by 20/20 participants (Fig. 1). The feature of the graphical interface rated most highly was the onscreen instructions, which was rated as “useful” or “very useful” by 20/20 participants (Fig. 1). The feature of the graphical interface rated most highly was the onscreen instructions, which was rated as “useful” or “very useful” by 20/20 participants (Fig. 1). Participants found the audible and visible signals (19/20) and the skin sensor (18/20) to be “useful” or “very useful” (Fig. 1).

Day 60: after 60 days of using the device, all available participants had a “good” (9/18) or “very good” (9/18) general impression of the device and 17/17 participants answered “yes” when asked whether they would like to continue using it, including those who had been using the needle-free Cool.click™ device (4/4).

The most highly rated features at day 60 were the preprogrammed dose, automatic-needle attachment, audible and visible signals, onscreen instructions and dose setting by milligram input, which were all rated as “useful” or “very useful” by 18/18 participants. Other features receiving high “useful” or “very useful” ratings were customisable needle-insertion speed (17/18), the confirmation of injected dose, customisable drug-insertion speed, customisable insertion depth and skin sensor (16/18), dose history (15/18) and the display of the last injection date and time (14/18). Participants’ positive comments on the device at day 60 focused on its ease of set-up and preparation. A small number of negative comments were received on technical aspects of the device, namely high-battery usage (3/18) and the ergonomics of the device (1/18).

4.3. Safety assessments

No adverse events were reported during the treatment or post-treatment phases.

5. Discussion

The current trial tested the use of the Easypod™ device in common practice, through collection of participants’, nurses’ and physicians’ opinions. The results show that the device works
well and is easy to use and patients or their parents considered most features to be useful.

The primary endpoint was the results recorded on the questionnaire after 15 days of use. At this time, each participant rated the device as either “good” or “very good”. All participants rated the display of the remaining drug in the cartridge, the preprogrammed dosing, the onscreen instructions and the automatic needle attachment as “useful” or “very useful”. The “customisable name and picture” feature was considered the least useful by participants, followed by the “teach me” menu. The low rating for the name and picture feature was expected as this was not primarily intended to be useful, but to be appealing to children. The relatively-low ratings for the “teach me” menu were surprising, but could be due to the ease of use of the device.

After 60 days of use, all available participants (18/18) had a good or very good overall impression of the device and 17/18 expressed a preference for the Easypod™ device over their previous device. The negative comments, regarding battery usage of the device have since led to further development of the device to extend its battery life.

Nurses and physicians reported that training participants and parents on how to use the device was “easy” or “very easy”. After training, most participants found the handling of the device and its features easy to use. The most difficulty was experienced with the needle-detachment process, with 7/20 participants finding this “difficult”. One potential explanation for this is that this process is controlled by a needle-release button, in contrast to the Click.easy™ device in which the needle must be unscrewed. Participants already accustomed to unscrewing the needle may have found it harder to adapt to the new device than other patients.

Collection of growth data was outside the scope of the study. Further work, including direct monitoring of patient-growth rates, would be needed to validate assumptions that ease of use and high-patient acceptance of a device lead to better treatment compliance. In addition, this study did not explore all of the features of the Easypod™ device, for example, allowing alteration of the preprogrammed dose.

These results show that the Easypod™ device works well in common practice. Patient acceptance of the device was high and the majority of participants who completed the study expressed a desire to continue therapy using the device.

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References