Effects of a Patient Education Support Program on Pramlintide Adherence

Gayle M. Lorenzi, RN, CDE, Susan M. LaRue, RD, CDE, and Susan Enos Collins RD, CHES

INTRODUCTION

Recent scientific discoveries have provided new treatment options for managing diabetes, and resultant glycemic control has improved through the years. However, according to data from the 2003–2004 National Health and Nutrition Examination Survey, only 56% of the population with diabetes has achieved glycemic control defined as having an A1C level of < 7%.1,2 Treatment efficacy and health outcomes are heavily influenced by medication adherence.3–5 Unfortunately, adherence to prescribed medications across multiple chronic diseases, including diabetes, is about 50%.6 A retrospective analysis of patients remaining on oral antidiabetic agents for 6–24 months showed medication adherence rates of 36–93%, and reports of medication adherence for insulin ranged from 60 to 80%.7,8 Adherence to diabetes medications is linked to improved clinical outcomes,9,10 whereas lack of adherence is associated with a significantly higher risk of all-cause hospitalizations and mortality.11

Adherence to diabetes treatments may require patients to make significant lifestyle and behavior changes over time and to adjust to ongoing treatment modifications. Rubin8 identified six factors that influence adherence to diabetes treatment: comprehension of the treatment regimen, perception of benefits, potential side effects, medication costs, regimen complexity, and the patient’s emotional well-being. In addition, it has been demonstrated that as complexity, cost, and duration of treatment increase, adherence decreases.4 However, in a health care system that focuses primarily on acute care, integration of strategies that foster medication adherence in patients coping with chronic disease is limited.12 Efforts to adequately address the challenges that affect medication adherence can often be pre-empted by time and resource limitations. Opportunities exist to bridge the gap between what is prescribed and what is actually taken.

Pramlintide: Bridging a Gap

Pramlintide is a synthetic analog of amylin, a hormone normally co-secreted from pancreatic β-cells with insulin in response to meals.13,14 Pramlintide acetate for injection is approved by the U.S. Food and Drug Administration for the treatment of patients with type 1 or type 2 diabetes who use mealtime insulin.15 Pramlintide has multiple mechanisms of action16–18 that decrease postprandial glycemia, resulting in improved glycemic control with less insulin and the potential for weight loss.18–21

The addition of pramlintide to an established insulin regimen necessitates dynamic adjustments in which the patient and the health care provider rely on self-monitoring of blood glucose (SMBG) and tolerability data to guide pramlintide titration and insulin adjustment. As therapy begins, daily glucose patterns may be altered, and hyperglycemia may result from initial insulin reduction. Subsequently, knowledge of how to manage side effects (e.g., satiety at mealtimes and transient nausea), awareness of realistic glycemic control and weight loss targets, and aid in communicating with family members become important.

Early post-marketing prescription data revealed that ~ 50% of patients prescribed pramlintide discontinued therapy within the first 2 months.22 Despite receipt of product education from their health care providers, patients reported difficulty initiating...
and continuing to use pramlintide. Data collected from early pramlintide users indicated that lack of sufficient weight loss, side effects, complicated dosing, and perceived lack of effectiveness accounted for 57% of the reasons for product discontinuation (Figure 1).

We hypothesized that an ancillary, third-party support program that targeted the educational needs of patients new to pramlintide could facilitate learning and positively affect adherence to therapy. The program used variable communication options (e.g., telephone, print, and Internet) and was designed to complement the education provided by patients’ health care providers. This article provides a discussion of the motivators and barriers associated with initiation of pramlintide therapy; describes the development of a patient support program; and reviews the impact of the program on adherence to pramlintide therapy.

METHODS

Program Overview

The pramlintide support program (Symlin Support Program [SSP]) was developed by Amylin Pharmaceuticals, Inc., to address the treatment expectations and management issues that patients often experience when using pramlintide. The SSP was created primarily to support patients initiating therapy and secondarily to provide education and support to patients on established therapy by augmenting the education provided by their health care providers. Program goals included 1) providing a framework to support safe and effective initiation of therapy, 2) filling a recognized gap in patient education and support, and 3) facilitating continued use of therapy.

Blinded prescription data that was compliant with patient privacy principles (Health Insurance Portability and Accountability Act [HIPPA]) was used to quantify adherence to therapy. In this study, adherence was defined as the extent to which the patient continued therapy and was a composite assessment of therapy persistence and compliance. Persistence was defined as timely prescription refills as calculated from the prescribed dose and was measured as the time between the first prescription and end of the last prescription filled. Compliance was defined as the degree of continued and accurate use and was measured by the amount of product dispensed relative to the dose prescribed. Noncompliance was calculated by comparing total days of medication supply to length of therapy. To quantify therapy persistence, pharmacy data were used to identify and compare a test group and non-test group. Test group participants were patients “new-to-product” (pramlintide) who enrolled in the support program during this evaluation period. The non-test group was composed of a randomly selected subset of patients, matched for age and sex, who were in the prescription database and were also “new-to-product” but were not enrolled in the program.

Development of Program Content

To help identify the key motivators and barriers to either starting or maintaining therapy, in-depth telephone interviews were conducted with current and former pramlintide users (n = 15) and diabetes care specialists (physicians or certified diabetes educators, n = 25). Patients were recruited via flyers sent to community-based endocrinologists and diabetes educators. Interested patients were instructed to independently contact the third-party market research firm conducting the interviews to ensure compliance with HIPPA principles. The physicians and diabetes educators were recruited from outreach telephone calls to relevant community-based clinical practices and from an existing advisory panel of corporate thought-leaders.

Program content was developed to address the motivators and barriers identified by the patients described above and from clinical observations from diabetes health care professionals experienced in the use of pramlintide (Table 1). For patients starting therapy, motivators and barriers were influenced by the practicalities of daily care, whereas maintaining therapy was influenced by a desire for improved health and a greater sense of personal control.

Social cognitive theory strategies (e.g., observational learning

<table>
<thead>
<tr>
<th>Reason for Discontinuation</th>
<th>Percent of Patients</th>
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<tbody>
<tr>
<td>Did not lose weight</td>
<td>28%</td>
</tr>
<tr>
<td>Additional injections required</td>
<td>20%</td>
</tr>
<tr>
<td>Side effects (volunteered)</td>
<td>15%</td>
</tr>
<tr>
<td>Too expensive</td>
<td>13%</td>
</tr>
<tr>
<td>Dosing regimen too complicated</td>
<td>9%</td>
</tr>
<tr>
<td>Lack of effectiveness (volunteered)</td>
<td>5%</td>
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Potentially 57% of reasons for discontinuation can be addressed with additional education / realistic expectations.
[learning from the experiences of others], skills training to increase competency, expectation setting, and personal goal setting and reinforcement were incorporated into the program to facilitate knowledge acquisition, comprehension, self-efficacy, and behavioral change. Health literacy principles (e.g., attention to word choice, sentence structure, content flow, amount of new information, and visual layout), commonly considered in the development of education materials, were considered during development of the SSP.

The SSP provided patients with opt-in opportunities for personal communication with program staff (telephone calls), as well as multiple print communications. Registered nurses employed by a third-party call center (Pharmaceutical Product Development [PPD], Raleigh-Durham, N.C.) were responsible for telephone interactions with patients. These nurses received specific product and program implementation training and had prior clinical practice and call center experience. The guidance and coaching provided to patients were nonprescriptive and consistent across the multiple types of patient contact.

Use of proactive telephone contact was based on the premise that timely and relevant education, combined with personal communication, would facilitate a more positive and enduring treatment experience. Frequency of personal contact was based on patient need and duration of therapy, with open access for questions or assistance and reminders to support diabetes self-management efforts. For the patient new to therapy, the proactive telephone calls provided pertinent product information, problem-solving strategies, and guidance regarding early expectations of therapy. Subsequent telephone calls from the SSP staff addressed issues more specific to continued use of the therapy, as well as reminders about general diabetes management principles.

Patients were encouraged to call with questions or concerns that arose between scheduled telephone calls, and ad hoc queries were addressed using uniform and reproducible information. Patients were referred back to their health care providers for issues related to individual treatment management and questions that were beyond the scope of the program. Complementary information was delivered via print and electronic media (e.g., newsletters), starter and welcome kits, and a program Web site. Program content, regardless of delivery method, was consistent with the pramlintide product label.

**Implementation**

Patients learned about the no-cost program from their health care providers or independently via the Symlin Web site (www.symlin.com). Enrollment in the program could be accomplished via the Web site, by calling a toll-free number, or by sending in a business reply card. Once a patient had opted in to the program, contact was initiated by an SSP nurse.

During the initial call, the nurse assessed individual goals for therapy, reviewed treatment benefits, described product actions, and reinforced prescribed dosing. The nurse also reviewed early expectations of therapy, including the potential for transient symptoms (e.g., blood glucose elevations, a sense of fullness, and nausea).

Subsequent telephone calls included information related to dose titration, the influence of concomi-

| Table 1. Barriers and Motivators to Starting and Maintaining Pramlintide Therapy |
|---------------------------------|---------------------------------|
| **Starting Pramlintide Therapy** | **Maintaining Pramlintide Therapy** |
| **Barriers** | **Motivators** |
| • Lack of health care provider support/education | • Additional injections |
| • Frustration: different routine/considerations | • Side effects |
| • Unanticipated hyperglycemia | • Therapy disappointment |
| • Injection burden/treatment complexity | • Impact of changes on family dynamics |
| • Unexpected side effects | • Suboptimal dosing: fewer benefits realized |
| **Motivators** | **Motivators** |
| • Health care provider knowledge | • Improved glucose levels, less flux |
| • Realistic expectations | • Improved A1C |
| • Hope for improvement | • Perceived benefits of therapy |
| • Adjustment period/need for flexibility | • Increased sense of control of diabetes |
| • Insulin/appetite changes | • Weight loss |
| • Weight loss | • Less insulin |
tient medications, care and storage of the medication, and travel tips. Repetition of important information and acknowledgment of small changes made by patients were key strategies used to encourage self-efficacy (confidence in one’s ability to adhere to therapy) and promote assimilation of new information and self-care behaviors. The nurse acknowledged psychosocial concerns and made proactive efforts to reassure patients that feelings and concerns about treatment issues and frustration with disease management or worsening diabetes commonly accompany changes in a treatment or management routine. Telephone interactions continued to reinforce dosing frequency and timing, the importance and use of SMBG results to assess treatment efficacy, and concomitant insulin adjustment under the guidance of a health care provider.

All patients received educational materials and newsletters on a predetermined schedule regardless of their participation in the proactive telephone-based portion of the SSP. Print materials provided reinforcement, emphasized problem-solving strategies, provided reminders about realistic expectations of therapy, and shared motivational strategies that were aligned with the identified motivators and barriers associated with the duration of therapy.

Evaluation
The program’s effectiveness was determined by assessing its impact on patients’ willingness and ability to start and maintain pramlintide therapy. Surveys were used to obtain qualitative feedback from SSP participants and health care providers. The participant surveys were included in the December 2008 (survey 1) and July 2009 (survey 2) program newsletters and assessed satisfaction and self-reported behavior changes over time. Health care provider satisfaction was assessed using an anonymous survey mailed in April 2008 and January 2009 to providers who were diabetes specialists based on their clinical practice.

The initial program evaluation period was from March 2007 through October 2008 and included 162 and 1,157 participants in the test (enrolled in the SSP) and non-test (not enrolled in the SSP) groups, respectively. De-identified prescription data mostly from retail pharmacies for the period March 2007 through July 2009 were obtained from SDI (a health care analytics company; Plymouth Meeting, Pa.) to validate the previous results; 223 and 1,201 participants were included in the test and non-test groups, respectively. The test and non-test groups were compared using a large sample z test for comparing two proportions; one-sided P values were reported and used to test for significant differences at the P = 0.05 level.

RESULTS
Most patients who enrolled in the SSP were referred by their health care providers, had type 2 diabetes, and were using mealtime insulin via injections or continuous infusion. Reasons cited for enrolling included 1) being told by their health care provider that the program would be helpful, 2) a desire to learn more about how the therapy worked, and 3) to learn how to better optimize and integrate the therapy into their diabetes care routine.

During enrollment, patients were asked two questions about whether they had received previous education about the product: 1) “Did you receive patient education materials either from your health care provider or from the product Web site?” and 2) “When you were at your health care provider’s office, did anyone explain to you the importance of using the product exactly as prescribed and working closely with your health care team to carefully add the product to your mealtime insulin therapy?” Approximately 88% of the patients indicated receipt of some training about pramlintide before contacting the SSP, and 80% indicated that they had received product-specific education materials from their health care provider or via the product Web site. Despite previous receipt of product-specific education, health care providers recommended and patients sought the SSP to obtain additional education support.

Participants reported satisfaction with program content, as well as with the method and frequency of contacts. Respondents to participant Survey 1 (n = 358) generally wanted the same or more frequent contact and information from the SSP in addition to the same or longer duration of each contact. These findings were consistent with Survey 2 (n = 238), in which responses were the same or slightly greater than those recorded in Survey 1 (Figure 2).

Self-reports of diabetes care practices indicated that a high percentage of patients persisted with therapy through the first 3 months and continued to use pramlintide. Frequency of dosing, use of standard dose amounts, and prescription refill data, as reported by the participants, were similar across both participant surveys (Figure 3). In addition, ~70% of respondents indicated that the SSP assisted them in taking pramlintide, ~30% indicated that the SSP contributed to their using pramlintide for a longer period, and ~50% indicated that the SSP helped them when talking with their health care provider about pramlintide.

Respondents to the health care provider survey (n = 488) were primarily physicians; approximately one-third were endocrinologists and
two-thirds were internists or primary care providers. Approximately half of the respondents had certified diabetes educators on staff, and most reported seeing >50 patients with diabetes per month. The SSP was perceived as valuable by provider respondents who referred patients to it. However, general awareness of the SSP was low (21%) among health care provider respondents.

Participants in the test group (those who were “new-to-product” and enrolled in the SSP, n = 223) were 74% female, with a mean age of 50.3 years. Participants in the non-test group (those who were “new-to-product” and not enrolled in the SSP, n = 1,201) were sex- and age-matched to the test group (Table 2).

Comparison of the test and non-test groups demonstrated that participation in the SSP improved adherence to therapy. Product discontinuation (a measure of persistence) had decreased by 19.4% (P = 0.01) at 3 months, by 16.7% (P < 0.01) at 6 months, and by 10.6% (P = 0.02) at 8 months, indicating a decreasing trend but an overall increase in continued product use among those enrolled in the support program. When the test group was compared to the non-test group, compliance had increased by 6% at 3 months and by 7% at 6 and 8 months. Noncompliance in the test group had decreased by 37.5% (P = 0.02), 23.3% (P = 0.03), and 21.2% (P = 0.04) at months 3, 6, and 8, respectively, compared to the non-test group (Figure 4).

Product persistence in the test and non-test groups also was evaluated by age and sex. Patients ≥35 years of age in the test group (n = 203) tended to have higher gains in persistency when compared to equivalent age-groups in the non-test group (n = 1,095). Of note, data from patients <35 years of age did not demonstrate the tendency toward improved persistency in the test group (n = 20) compared to the non-test group (n = 106). No differences between sexes were seen between the test and non-test group results at months 3, 6, or 8.

**DISCUSSION**

Adherence to prescribed medication regimens is relevant to clinical practice and remains problematic across disease states. The impact of nonadherence transcends patient out-
Chronic diseases, especially those for which treatment requires lifestyle adaptation and daily decision-making, result in a higher patient burden that can interfere with adherence to the prescribed therapy. In addition, factors associated with a treatment, such as the frequency and complexity of the treatment, side effects, and monitoring requirements, can influence patient behaviors and treatment choices. The SSP was developed to assist patients new to pramlintide in integrating this therapy into their established diabetes regimen. The goal was to provide information appropriate to patients’ specific stage of therapy. Initially, program information addressed potential issues associated with therapy initiation. As therapy continued, information was more reflective of the duration of therapy and potential associated issues.

The SSP was designed to augment, rather than replace, the education provided by the prescribing health care provider. The program was developed and funded by Amylin Pharmaceuticals, Inc., and implemented by a third-party call center that provided education and support to enrollees. As such, the SSP offered health care providers a no-cost resource for their patients that was independent of and unencumbered by the time or resource constraints that often challenge routine clinical practice.

Social cognitive strategies were incorporated to encourage learning and support self-care behavior change. Proactive education and coaching assisted participants with problem recognition and solution, and attention to daily care issues, such as frequency of dosing, method of administration, and lifestyle challenges, supported patients’ efforts to integrate the therapy into their diabetes routine. Clinical decision-making or issues beyond the scope of the program were referred back to participants’ health care providers, thus reinforcing the importance of close collaboration between participants and their providers.

Not surprisingly, participation in the SSP did not affect persistency in patients < 35 years of age. Although the number of participants in this age-group was inadequate to determine a causal relationship, it is important to recognize generational differences in how information is obtained and used. This age-group generally seeks information using more immediate means (e.g., the Internet) to access knowledge that is specific to their current questions or concerns.

Prescription data provided an objective measure of adherence to therapy. Participation in the SSP resulted in increased persistency (as measured by product discontinuation), increased compliance, and decreased noncompliance to therapy when the test group was compared to the non-test group. However, there are limitations to the use of these data. First, prescriptions filled elsewhere (e.g., via mail order) were

### Table 2. Patient Characteristics

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<thead>
<tr>
<th></th>
<th>Test Group</th>
<th>Non-Test Group</th>
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<tbody>
<tr>
<td>Sex Male (%)</td>
<td>26</td>
<td>25</td>
</tr>
<tr>
<td>Sex Female (%)</td>
<td>74</td>
<td>75</td>
</tr>
<tr>
<td>Average age (years)</td>
<td>50.3</td>
<td>50.4</td>
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Figure 4. Comparison of the test and non-test groups shows that the SSP improved adherence to therapy.
not included in the prescription data used for this analysis. Second, estimates of dose amount and frequency were based on the patients’ type of diabetes and may have differed from the prescribed amount and frequency of dosing. And finally, this analysis assumed that if the product was dispensed, it was taken, and this assumption may not have been completely accurate.

Frequent evaluation of patient education and intervention programs is necessary to meet changing needs and ensure relevance over time. Health care provider and participant feedback, along with prescription data assessments, guided modifications in the program content, frequency, and type of contact to better meet expressed needs and desires. In addition, implementation processes were continually enhanced to increase call efficiency for callers and program staff, and efforts were made to increase program awareness among health care professionals.

CONCLUSION
Adherence to prescribed therapies is a global problem that jeopardizes patient health and health outcomes. The addition of a new therapy to an established medication regimen requires patient education that addresses routine use, side effects, and realistic expectations of the treatment. The SSP was developed to improve adherence for patients using pramlintide therapy by acknowledging and addressing motivators and barriers unique to their stage of therapy.

The pramlintide support program provided timely instruction, supported self-monitoring and self-care efforts, promoted communication between patients and providers, and reinforced behavioral changes to positively affect medication adherence. Further study of patient support programs such as the SSP is needed to better understand the enduring impact of these programs on medication adherence.

REFERENCES
22. Data on file. San Diego, Calif., Amylin Pharmaceuticals

SUGGESTED READINGS


Gayle M. Lorenzi, RN, CDE, is a community health project manager at the University of California at San Diego. Susan M. LaRue, RD, CDE, is a clinical education specialist at Amylin Pharmaceuticals, Inc. Susan Eno Collins, RD, CHES, is a senior vice president at The HealthEd Group.

Notes of disclosure: Ms. Lorenzi is a former employee of and stock shareholder in Amylin Pharmaceuticals, Inc., and has received consulting fees from that company. Ms. LaRue is an employee of and stock shareholder in Amylin Pharmaceuticals, Inc. Ms. Collins is employed by The HealthEd Group, which provides professional services to Amylin Pharmaceuticals, Inc.