Quality of Life, Treatment Satisfaction, and Treatment Preference Associated With Use of a Pen Device Delivering a Premixed 70/30 Insulin Aspart Suspension (Aspart Protamine Suspension /Soluble Aspart) Versus Alternative Treatment Strategies

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Interest in intensified insulin therapy has contributed to the increased popularity of alternative insulin delivery systems, including insulin pen delivery devices. Although there have been several studies of patient-reported outcomes associated with insulin pen use (1–6), there has been no adequate assessment of *1*) the most advanced devices, pens delivering premixed intermediate-acting and rapid-acting analog insulin; *2*) the effects of pens for patients previously naïve to insulin; *3*) the effects of pens on general quality of life; and *4*) what factors contribute to preference for different insulin delivery systems.

RESEARCH DESIGN AND METHODS

— Participants were patients with type 2 diabetes who completed a satisfaction substudy after being enrolled by their physicians in a 3-month clinical experience program of NovoLog Mix 70/30 in a prefilled FlexPen insulin pen device that delivered a 70/30 mixture of intermediate-acting and rapid-acting analog insulin (a suspension of protamine-crystallized insulin aspart and soluble insulin aspart). Of 899 patients who originally signed and returned a card indicating consent to participate in the satisfaction substudy, 372 (41%) returned completed questionnaires, for which they were given US$25. The questions included items from validated measures. Diabetes treatment satisfaction was measured by the Diabetes Treatment Satisfaction Questionnaire (change) (DTSQc) (7) and Quality of Life status and change (QLsc) (8). Quality of life was measured by the QLsc. Table 1 describes the measures, including the questions used for each measure, the reliability of each measure, and the metric by which questions for each measure were scored.

Patients were primarily white (75.5%), female (55.9%), middle aged (52.4% were aged ≥60 years), and of modest socioeconomic status (49.5% with income under $35,000 and 50.3% with no college). They had diabetes of long duration (46.2% with >10 years). Most (85.2%) had used insulin before the study, and 41.4% had used an insulin pen.

Respondents were divided into five prior treatment subgroups: *1*) a group that had never used insulin; *2*) a group that had never used mixed insulin; *3*) a group that had used 70/30 mixed insulin, but not a pen; *4*) a group that had used 70/30 mixed insulin in a pen; and *5*) a group that had used various mixed insulins via pen or syringe and did not fit into one of the other groups. Thus, each group allowed a comparison of the study pen with a different treatment strategy.

The criterion for statistical significance was set at $P < 0.05$, two tailed for all analyses. All analyses were conducted using SPSS 11.5 (SPSS, Chicago, IL).

RESULTS

— Respondents rated the study pen significantly more positively than their prior treatment on all measures in the total sample and in all subgroups (Table 1). The advantage for the study pen ranged from 0.5 to 3.7 SD units (median 1.4).

Key determinants of overall treatment preference were identified by hierarchical multiple regression analyses controlling for age, sex, race/ethnicity, and education. Perceived convenience, flexibility, clinical efficacy, and quality of life were entered into the models together (results not shown). In the total sample, all ratings of the study pen except quality of life had significant independent associations with overall preference. In addition, conve-

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Abbreviations: QLsc, Quality of Life status and change.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

Table 1—*Rating of study pen device in the total sample and prior treatment subgroups*

Measures (no. of items)	Source of items	α	Insulin naïve	Pen naïve (no mixed insulin)	Pen naïve (70/30 mixed)	Pen (70/30 mixed)	Various mixed	Total sample
n	—	—	55	59	91	81	86	372
Convenience (1)	DTSQc no. 4	NA	1.70 ± 1.59 (1.07)	2.42 ± 0.75 (3.22)	2.19 ± 1.15 (1.90)	2.03 ± 1.30 (1.56)	1.91 ± 1.44 (1.33)	2.06 ± 1.29 (1.60)
Flexibility (1)	DTSQc no. 5	NA	1.62 ± 1.38 (1.17)	2.17 ± 0.90 (2.41)	1.96 ± 1.22 (1.61)	1.82 ± 1.19 (1.53)	1.76 ± 1.28 (1.38)	1.87 ± 1.21 (1.54)
Clinical efficacy (6)	DTSQc nos. 2 and 3; QLcs nos. 1–4	0.75	1.28 ± 0.98 (1.30)	1.16 ± 0.81 (1.43)	1.12 ± 0.97 (1.15)	0.87 ± 0.84 (0.73)	0.81 ± 1.00 (0.81)	1.03 ± 0.94 (1.09)
Quality of life (8)	QLcs nos. 5–12	0.94	0.94 ± 1.13 (0.83)	1.17 ± 0.94 (1.24)	1.06 ± 1.04 (1.02)	0.64 ± 0.89 (0.72)	0.59 ± 1.08 (0.55)	0.86 ± 1.03 (0.83)
Overall preference (4)	DTSQc nos. 1, 7, and 8*	0.82	2.21 ± 0.95 (2.32)	2.42 ± 0.66 (3.66)	2.06 ± 1.18 (1.75)	2.16 ± 0.80 (2.70)	2.01 ± 1.01 (1.99)	2.15 ± 0.96 (2.24)

Data are means ± SD (number of SD units >0). Possible range of means is −3 to 3. Means greater than zero indicate that the pen device was rated higher than the previous treatment system. All means are significantly greater than zero at $P < 0.001$ by one sample *t* test. For questions that were not diabetes specific (quality of life), respondents were asked to assess how they felt at the time they filled out the questionnaire compared with just before they started to use the study pen. For the remaining questions that were diabetes specific, respondents were asked to compare their experience with the study pen with their experience with the treatment they were using prior to using the study pen. *The overall preference measure contains an item developed for this study: "What is your overall view of taking insulin now compared with just before you started [the study]".

nience was significant in all subgroups, and perceived clinical efficacy, flexibility, and quality of life were each significant independent predictors of preference in at least one subgroup.

CONCLUSIONS — Patients overwhelmingly preferred the study pen to their prior treatment strategies, and using the study pen was associated with enhanced convenience, flexibility, perceived clinical efficacy, and quality of life for all subgroups of patients. These advantages were all >0.5 SD units (corresponding to a "moderate" effect size [9]), which was identified in a recent review of patient-reported outcomes (10) as the criterion for the minimum difference that a person would be able to detect. So the differences observed in this study were meaningful as well as statistically significant.

The current study is the first to assess differences in outcomes for patients with different prior treatment strategies. We found differences of the sort one might expect. Patients previously naïve to insulin tended to report the greatest improvements in clinical efficacy and the smallest benefits in convenience and flexibility. Among patients who had used insulin previously, those who had only used syringes to deliver unmixed insulin reported the greatest benefits on all outcomes. As patients' prior treatment strategy more closely approximated the study intervention (from pen naïve with unmixed insulin, to pen naïve with mixed insulin, to pen experienced with mixed insulin) there was a decrease in the advantage of the study system in convenience, flexibility, perceived clinical efficacy, and quality of life.

Our study is the first to systematically assess factors contributing to patients' reported preference for pen devices over syringes (1–6). Our results indicated that convenience, flexibility, perceived clinical efficacy, and quality of life each made independent contributions to preference for treatment strategies among selected patient subgroups, and the contributing factors differed for different subgroups.

The major limitation of this study is the result of various sources of sampling bias. Therefore, it is prudent to assume that the results are most likely to be representative of patients willing to change to an insulin pen, including those not satisfied with their current form of treatment. In addition, the data did not allow us to

definitively confirm the treatment used immediately before the study pen. When patients reported more than one prior treatment, we assumed that the most intensive treatment was the most recent one, which could have led to underestimating the perceived advantages of the study pen. Despite these limitations, the present study has demonstrated the usefulness of performing subgroup analyses.

Patients new to insulin in this study reported improved quality of life and better glucose control and said their treatment had become more convenient and flexible, suggesting that pen use could counter some of the common reasons that patients raise for resisting insulin therapy (11–12). For patients already using insulin, an insulin delivery system that improves treatment satisfaction could help facilitate intensified treatment and result in improved clinical outcomes (13). The advantages of delivery systems like the pen device used in this study should be considered by health care providers when they counsel patients regarding treatment options.

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