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Effect of the rapid-acting insulin analogue insulin aspart on quality of life and treatment satisfaction in patients with Type 1 diabetes

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Abstract

Aims To compare quality of life (QoL) and treatment satisfaction in patients with Type 1 diabetes receiving the rapid-acting insulin analogue, insulin aspart (IAsp), with that in patients receiving soluble human insulin (HI).

Methods In this 6-month, multinational, randomized, open-label trial, 424 patients from German-speaking countries were subjected to psychometric assessment before and after randomization (ratio 2 : 1) to basal-bolus treatment with either IAsp (n = 283) or HI (n = 141). Patients on HI were advised to keep an injection–meal interval of 30 min, whereas patients on IAsp were advised to inject immediately before meals. Treatment satisfaction and diabetes-related QoL were assessed using validated instruments to measure the domains of patients' individual treatment goals, physical complaints, worries about the future, social relations, leisure time flexibility, daily hassles, diet restrictions, burdens and fear of hypoglycaemia, blood glucose fluctuations, self-efficacy, and fear of insulin analogues.

Results After 6 months, IAsp was associated with significantly greater improvement in treatment satisfaction than HI in two different scales ($P < 0.01$), and in QoL with respect to diet restrictions ($P < 0.01$). Improved satisfaction was mainly due to increased dietary and leisure time flexibility ($P < 0.0001$). Twenty-three percent of the IAsp group vs. 14% of the HI group achieved small but important improvements of total QoL (between-group difference, $P < 0.06$). The number needed to treat (NNT) with IAsp for an important increase in QoL was calculated to be 10. Regression analyses of potential predictors of improvement in QoL highlighted patients intensely striving for physical strength ($P < 0.01$; NNT = 7) and patients feeling less protected against hypoglycaemia ($P < 0.005$; NNT = 8) as being the most likely to benefit from IAsp.

Conclusions Under these study conditions, IAsp improved treatment satisfaction and quality of life regarding diet restrictions when compared with human insulin. The 'numbers needed to treat' for important quality of life benefits indicate that the effect of IAsp in this regard is not trivial.

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Keywords quality of life, treatment satisfaction, insulin analogue, insulin aspart, intensified insulin therapy

Abbreviations IAsp, insulin aspart; HI, soluble human insulin; QoL, quality of life; DTSQ, Diabetes Treatment Satisfaction Questionnaire; DSQOLS, Diabetes-Specific Quality of Life Scale; PWTS, preference-weighted treatment satisfaction; NNT, number needed to treat

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Introduction

Diabetes mellitus greatly affects physical, social and psychological well-being. Patients are impacted by the diagnosis of the disease, the demands of daily treatment, the emotional stresses of coping with the disease and by the threat of acute and late complications [1–4]. Quality of life (QoL) should therefore be an important consideration in the treatment of diabetes; interventions should aim for good glycaemic control [5], but enable patients to maintain their preferred lifestyle [2,4]. QoL and treatment satisfaction are supposed to have an important impact on self-management, acceptance of therapy and metabolic treatment success [6–9]. With the number of treatment options rising, assessment of patient perceptions may increasingly determine therapeutic decisions and the allocation of healthcare resources [10,11].

One new treatment option is insulin aspart (IAsp). This novel insulin analogue has shown improved absorption characteristics in comparison with human insulin (HI). Mealtime administration of IAsp limits postprandial blood glucose exposure to a greater extent than HI injected 30 min before meals [12]. Long-term clinical trials have demonstrated small yet statistically significantly greater improvements in HbA_{1c} in association with IAsp vs. HI, achieved without greater risk of hypoglycaemia [13–15].

Initial clinical research involving the first available insulin analogue (insulin lispro) suggested a beneficial impact on treatment satisfaction during multiple-injection as well as continuous subcutaneous insulin infusion therapy [16]—without improvement of well-being [17] or QoL [18]. However, it is important to realize that 'quality of life' and 'treatment satisfaction' are different constructs with different implications. Treatment satisfaction measures may be more sensitive to motivational effects of new treatments in randomized controlled trials than more descriptive measures of specific treatment burdens and restrictions [7]. Bradley (1993) hypothesized that patients who participate in such a randomized trial are likely to have a preference for the new treatment being evaluated [19].

Several studies indicated that generic health-related QoL scales, which are often used to make comparisons between different diseases and populations [20,21], lack sensitivity when comparing treatment regimens in the field of diabetes [7,22,23]. Disease-specific measures are more appropriate because they achieve a greater responsiveness and sensitivity in terms of longitudinal within-subject changes [20,21].

The present evaluation of QoL and treatment satisfaction is the first assessing the use of IAsp in patients with Type 1 diabetes. The study has employed validated, diabetes-specific questionnaires [7,24,25]. In addition, preference-weighted measures were applied to identify specific subgroups of patients (aiming at particular treatment goals) for whom a rapid-acting insulin analogue might be especially beneficial. It was expected that this approach would have a high degree of sensitivity in detecting between-treatment differences.

Research design and methods

QoL and treatment satisfaction were evaluated in a subset of German-speaking patients, using standardized and validated questionnaires, within a large-scale, 6-month, multinational, randomized, open-label study of the efficacy and safety of IAsp used as the mealtime component of basal–bolus therapy for Type 1 diabetes. The subset comprised 424 patients recruited from 36 centres in Germany, Austria and Switzerland and randomized (ratio 2 : 1) to treatment with IAsp ($n = 283$) or HI ($n = 141$). The study conformed to the Helsinki declaration and was approved by the ethical committee.

Adult patients with Type 1 diabetes defined by WHO criteria [26] of at least 2 years' duration, a body mass index (BMI) of ≤ 35.0 kg/m^2 and $HbA_{1c} \leq 11\%$ (reference value < 6.0%) were included. Baseline characteristics are shown in Table 1. All patients had previously been receiving treatment with HI for a period of at least 1 year. During a 4-week run-in period, subjects received a s.c. multiple-injection, basal-bolus regimen, with HI as the meal-related, and NPH insulin as basal insulin. In accordance with product label information, patients on HI were advised to keep an injection–meal interval of 30 min, whereas patients on IAsp were advised to inject immediately before meals.

Assessment of treatment satisfaction was made using a German version of the Diabetes Treatment Satisfaction Questionnaire (DTSQ) [25,27,28] and components of the Diabetes-Specific Quality of Life Scale (DSQOLS), while QoL was assessed using other DSQOLS components [7,24]. HbA_{1c}, hypoglycaemia, adverse events and safety data were recorded for the trial, as reported elsewhere [13]. The DTSQ (eight items; seven-point Likert scale) has been shown to be sensitive to changes following modifications in diabetes management. Measures of perceived frequencies of hyperglycaemia and hypoglycaemia are obtained from individual items, while scores

Table 1 Characteristics of the study population at randomization

	Total sample ($n = 424$)	Insulin aspart ($n = 283$)	Human insulin ($n = 141$)	*P*-value (between-group)
Gender (% females)	45.5	49.5	37.6	0.027
Age (years)	36.9 (16.9)	37.0 (18.5)	36.6 (15.3)	0.93
Diabetes duration (years)	12.5 (15.2)	13.0 (14.5)	11.3 (16.2)	0.36
HbA_{1c} (%)	7.6 (1.6)	7.5 (1.7)	7.6 (1.4)	0.81
Body mass index (kg/m^2)	24.2 (4.0)	24.2 (3.5)	24.4 (5.0)	0.81

Data are median (interquartile range).
P-values calculated with Mann–Whitney *U*-test, except for gender ratio calculated with χ^2 test.

Table 2 Quality of life and treatment satisfaction subscales used in the trial and their homogeneity

Subscale α	Example	Cronbach'
Preference-weighted treatment satisfaction (PWTSS) (10 products)	For diabetes treatment it is especially important to me, or it would be my goal that … I can arrange my free time with flexibility How satisfied have you been over the last 4 weeks with the flexibility in arranging your free time?	0.84
Social relations (11 items)	Because of diabetes it is much harder to make friends	0.89
Physical complaints (9 items)	I suffer from thirst or having a dry mouth	0.84
Worries about future (5 items)	I am often worried about the long-term complications of diabetes	0.86
Leisure time flexibility (6 items)	Diabetes prevents me from spontaneous physical activities	0.83
Diet restrictions (9 items)	It bothers me that I cannot eat like other people	0.88
Daily hassles (6 items)	It bothers me that I have to spend so much time on my diabetes treatment	0.84
Fear of hypoglycaemia (11 items)	I am worried about having a severe episode of low blood sugar at night.	0.93
Blood glucose fluctuations (11 items)	I am often frustrated because my blood glucose values vary inexplicably	0.93
Burdens of hypoglycaemic events (7 items)	Because of episodes of low blood sugar I have to interrupt interesting activities occasionally	0.85
Fear of genetically engineered insulin (3 items)	I'm afraid that too little is known about potential side-effects of genetically engineered insulin	0.81
Self-efficacy (4 items)	Even in difficult situations I know exactly how to get my blood glucose under control	0.75
Treatment satisfaction (DTSQ) (6 items + 2 single items)	How satisfied would you be to continue with your present form of treatment?	0.86

from the remaining six items are combined to provide a measure of treatment satisfaction. In the present study, Cronbach's α was 0.86 with item total correlations between 0.49 (item 6) and 0.77 (item 5).

The original DSQOLS was validated within a population-based study to assess quality of diabetes care in a representative sample of 684 patients with Type 1 diabetes in the North-Rhine district of Germany [7,29]. The assessment of treatment satisfaction was based on a combination of patients' expressed preferences from 10 specified treatment goals, and their satisfaction with the treatment's success in meeting these goals. The product of these (preferences × satisfaction; summing up 10 pairs) provided a score for preference-weighted treatment satisfaction (PWTS). In addition, the self-administered questionnaire comprised six homogeneous diabetes-related subscales (39 items; six-point Likert scale) to assess QoL in the domains of: social relations, leisure time flexibility, diet restrictions, physical complaints, daily hassles and worries about the future [7].

Based upon semistructured interviews with patients with Type 1 diabetes focusing on rapid-acting insulin analogues, this assessment was expanded by a further five components: fear of hypoglycaemia, blood glucose fluctuation, burden of hypoglycaemia, fear of genetically engineered insulin analogues, and self-efficacy regarding adaptation of insulin dosage. The expanded scale was validated in a sample of 134 patients, as previously described [24].

In the present study, QoL and treatment satisfaction were assessed at baseline and at 3 and 6 months. Table 2 shows the Cronbach's α (indicating internal consistency for each component at baseline) for the QoL subscales and the overall PWTS and DTSQ measures, together with representative items. Based on results from preceding studies involving insulin lispro, four subscales were specified as primary outcome domains: treatment satisfaction, diet restrictions, burden of hypoglycaemia and blood glucose fluctuations. It was hypothesized that IAsp would show the greatest relative benefit within these domains.

Statistical analysis

Statistical analyses were performed with the Statistical Package for the Social Sciences (SPSS) [30,31]. Reliability coefficients (Cronbach's α) were computed for all psychometric subscales. Statistical analyses of QoL and treatment satisfaction scores included between-group differences at baseline, between-group differences in change of score from baseline and within-group change of scores from baseline. Between-group comparisons were performed using analyses of variance (ANOVA) adjusting for baseline scores and gender. These were made for each individual QoL or treatment satisfaction domain as well as for overall scores. Within-group changes from baseline were analysed using both parametric (paired *t*-test) and non-parametric (Wilcoxon) methods. To facilitate the comparability of individual subscales, all crude scores were converted to a 100% scale: (score – minimum score) × 100/(maximum score – minimum score). High scores indicate good QoL or high treatment satisfaction.

Multiple logistic regression analyses were performed to elucidate potential predictors of QoL improvement. The threshold for a small but important QoL improvement was defined as an average improvement of ≥ 0.5 points on every QoL item (≥ 41 points improvement on the total DSQOLS comprising 82 items), according to Guyatt *et al.* [32]. (This is based on Guyatt's finding of a ≥ 0.5 point improvement being the smallest difference regarded as important in patients with respiratory problems.) The number needed to treat (NNT) for a small but important QoL improvement was calculated using the formula of Guyatt *et al.* [32], shown in Table 3. The NNT indicates in this case the number of patients that must be switched from HI to IAsp in order to achieve an important QoL improvement in one patient.

Results

The treatment groups were well matched in terms of age, disease history, glycaemic control and BMI, although there

Table 3 Calculation of number needed to treat for a small but important quality of life improvement

		IAsp treatment		
HI controls		Improved 0.226 (x)	Unchanged 0.711 (y)	Deteriorated 0.063 (z)
Improved	0.136 (a)	0.03 (ax)	0.10 (ay)	0.009 (az)
Unchanged	0.777 (b)	0.18 (bx)	0.55 (by)	0.05 (bz)
Deteriorated	0.087 (c)	0.02 (cx)	0.06 (cy)	0.005 (cz)
		(bx + cx + cy) – (ay + az + bz)		
		(0.18 + 0.02 + 0.06) – (0.10 + 0.01 + 0.05) = 0.10		
		1/0.10 = 10 (number needed to treat)		

The numbers (a, b, c, x, y, z) refer to the proportions of patients experiencing significant change in quality of life as outlined in Statistical analysis. Method of calculation after Guyatt *et al*. 1998 [32].

was a higher proportion of male patients in the HI group (Table 1).

All psychometric subscales achieved good homogeneity coefficients at baseline (Table 2).

At endpoint, there were no significant differences between the two treatment groups with regard to HbA_{1c} (7.5% at baseline and 6-month follow-up in both groups) or incidence of severe/mild hypoglycaemia (clinical data from the entire multicentre study are published [13]).

Raw data for individual and total QoL and treatment satisfaction domains are shown in Table 4. The DTSQ assessment suggested similar baseline treatment satisfaction for each group. In the DSQOL assessment, patients randomized to IAsp had poorer baseline scores with regard to treatment satisfaction (especially regarding blood glucose stability and diet

Table 4 Baseline quality of life and treatment satisfaction scores by domain and treatment group (raw data, with totals also given as percentage scale)

	Insulin aspart	Human insulin
DSQOL QoL components		
1. Social relations	57.34 (0.47)	57.42 (0.74)
2. Leisure time flexibility	29.51 (0.32)	29.36 (0.49)
3. Physical complaints	44.02 (0.44)	44.22 (0.66)
4. Worries about future	18.47 (0.34)	18.54 (0.52)
5. Diet restrictions	34.86 (0.58)	35.28 (0.90)
6. Daily hassles	24.49 (0.39)	25.34 (0.59)
7. Fear of hypoglycaemia	45.31 (0.75)	45.20 (1.07)
8. Blood glucose fluctuations	41.25 (0.71)	*44.84 (1.13)
9. Fear of genetically engineered insulin	13.37 (0.22)	13.04 (0.31)
10. Self-efficacy	19.10 (0.18)	18.94 (0.31)
11. Burdens of hypoglycaemic events	29.73 (0.45)	30.35 (0.65)
Total DSQOL QoL	357.93 (3.70)	363.17 (6.25)
Total DSQOL QoL, 0–100 scale	67.3% (0.9%)	68.6% (1.5%)
DSQOL treatment satisfaction components		
1. Blood glucose level	3.83 (0.07)	3.99 (0.10)
2. Blood glucose stability	3.59 (0.06)	*3.88 (0.10)
3. Flexibility during free time	4.69 (0.06)	4.80 (0.080
4. Frequency of mild hypoglycaemia	4.46 (0.07)	4.59 (0.09)
5. Protection from long-term complications	4.30 (0.07)	4.43 (0.10)
6. Diet flexibility	4.73 (0.06)	*4.96 (0.07)
7. Physical strength	4.65 (0.06)	4.76 (0.09)
8. Protection from severe hypoglycaemia	4.96 (0.06)	5.04 (0.08)
9. Frequency of blood glucose self-monitoring	4.67 (0.06)	4.84 (0.08)
10. Understanding of other people	4.82 (0.06)	4.87 (0.09)
Total DSQOL treatment satisfaction	44.70 (0.40)	46.12 (0.59)
Total DSQOL treatment satisfaction, 0–100 scale	69.4% (0.8%)	*72.2% (1.2%)
DTSQ treatment satisfaction components		
1. Satisfaction with current treatment	4.38 (0.09)	4.65 (0.12)
2. Unacceptably high blood sugar	2.77 (0.09)	2.48 (0.13)
3. Unacceptably low blood sugar	2.00 (0.08)	1.87 (0.12)
4. Convenience of treatment	4.29 (0.09)	4.50 (0.12)
5. Flexibility of treatment	4.51 (0.08)	4.76 (0.10)
6. Understanding of diabetes	4.79 (0.07)	5.01 (0.08)
7. Recommendation of treatment	5.20 (0.06)	5.18 (0.10)
8. Continuation of treatment	4.76 (0.08)	4.90 (0.10)
DTSQ total	27.94 (0.36)	29.02 (0.48)
DTSQ total, 0–100 scale	77.6% (1.0%)	80.6% (1.3%)

Data are means (SEM), with higher total scores representing higher levels of quality of life. Comparisons between treatment groups based on ANOVA adjusted for gender: $*P < 0.05$.

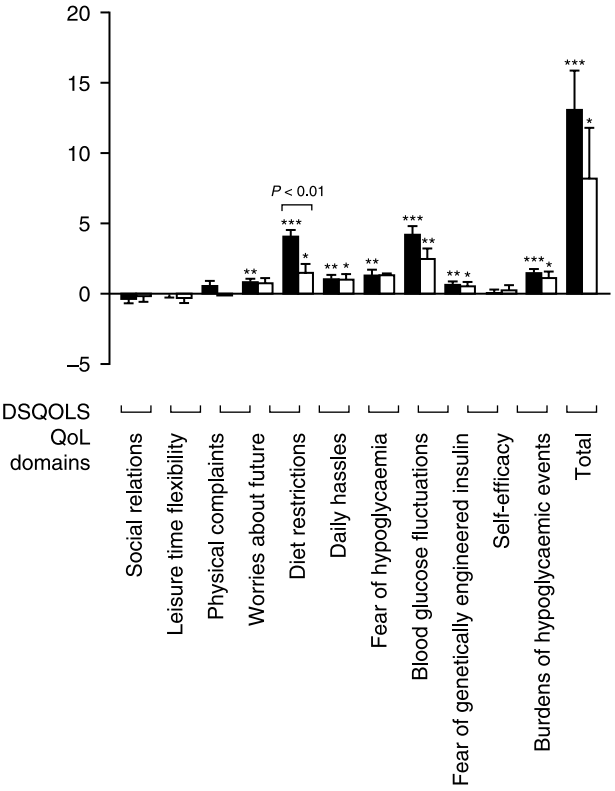

Figure 1 Six-month changes from baseline by treatment group in score for the individual (and total) QoL components of the Diabetes-Specific Quality of Life Scale (DSQOLS). Data are mean changes in raw scores ± SEM. *$P < 0.05$; **$P < 0.01$; ***$P < 0.001$ for within-group change from baseline (paired *t*-test). *P*-values shown correspond to between-group differences in the magnitude of change (anova adjusted for baseline and gender). ■, Insulin aspart; □, human insulin.

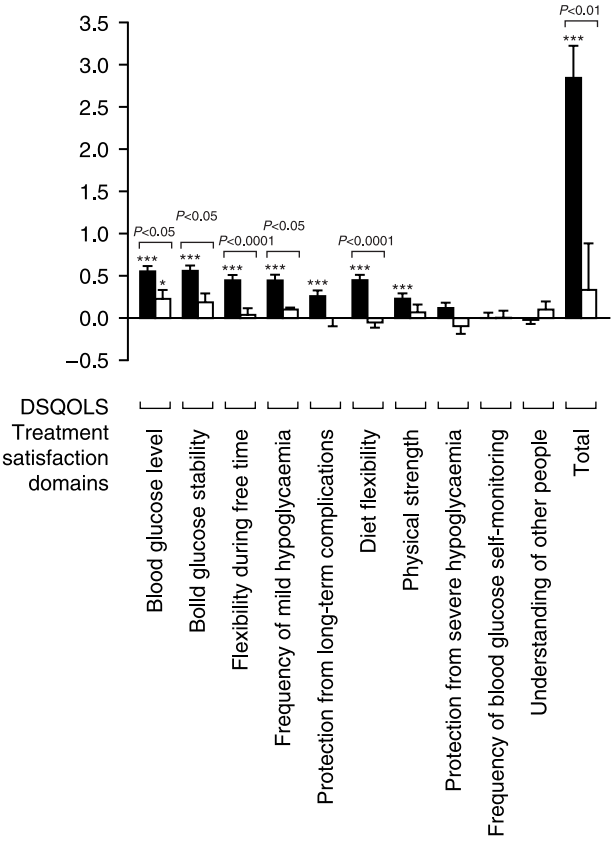

Figure 2 Six-month changes from baseline by treatment group in score for the individual (and total) treatment satisfaction components of the Diabetes-Specific Quality of Life Scale (DSQOLS). Data are mean changes in raw scores ± SEM. *$P < 0.05$; **$P < 0.01$; ***$P < 0.001$ for within-group change from baseline (paired *t*-test). *P*-values shown correspond to between-group differences in the magnitude of change (ANOVA adjusted for baseline and gender). ■, Insulin aspart; □, human insulin.

flexibility, $P < 0.05$) and the QoL domain of blood glucose fluctuations ($P < 0.05$).

The changes in scores from baseline to 6 months are presented graphically for the individual items and totals for the QoL and treatment satisfaction instruments in Figs 1–3. As data were normally distributed, parametric statistics are presented. Significant improvements were seen in most DSQOL QoL domains in both treatment groups. However, in only one of these domains (the perception of diet restriction) was a significant between-group difference in change of score detected ($P < 0.01$), favouring IAsp. The DSQOL treatment satisfaction analysis showed significant improvement overall (and in five individual items) in association with IAsp, but not HI. Consequently, the between-group difference in change of score was statistically significantly in favour of IAsp ($P < 0.01$). An even higher level of significance ($P < 0.0001$) applied to the between-group difference in change of total score in the DTSQ analysis, where four of the eight items and the overall score improved significantly with IAsp. It should be noted that the change scores for the 'negative' domains of 'unacceptably high' and 'unacceptably low blood sugar' (Fig. 3) have been reversed from negative to positive values in order to avoid confusion; these two domains are unique among those assessed in the study in that low, rather than high, scores are desirable. These two domains are excluded from the total DTSQ analysis following Bradley [25].

Most of the within- and between-group differences were apparent at 3 months (data not shown), but there was evidence that the magnitude of the within- and between-group changes in treatment satisfaction scores increased between 3 and 6 months (Fig. 4). Figure 5 indicates that patients randomized to IAsp started with a somewhat lower QoL score (summing up all 82 QoL items, Cronbach's $\alpha = 0.97$), but experienced a greater increase of total score compared with patients on HI.

Small but important improvements in total QoL occurred in 23% of IAsp- and 14% of HI-treated patients ($P = 0.057$). The NNT with IAsp to achieve a small but important improvement in total QoL in one case was calculated to be 10 (Table 3). Logistic regression analyses were performed to identify potential predictors of such QoL improvements. The only significant predictor in the first analysis considering the 10 different treatment goals of the DSQOLS at baseline was the extent to

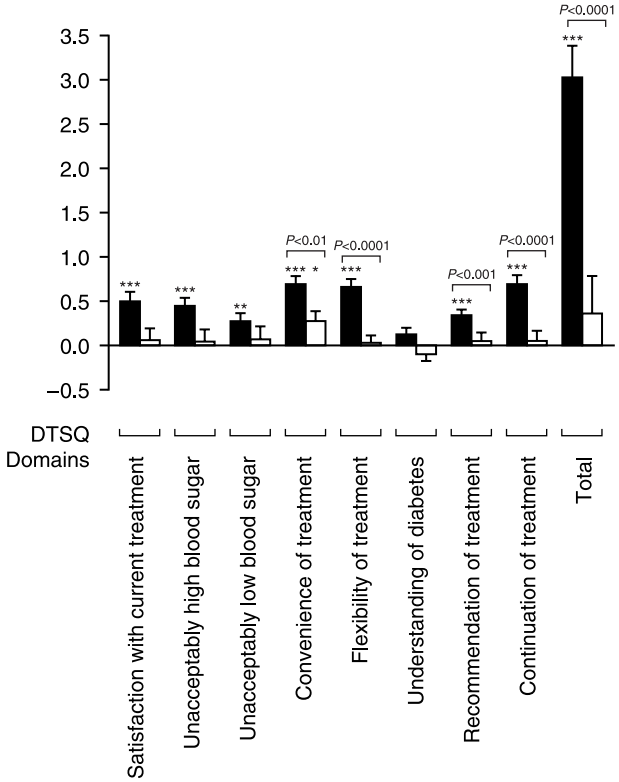

Figure 3 Six-month changes from baseline by treatment group in score for the individual (and total) treatment satisfaction components of the Diabetes Treatment Satisfaction Questionnaire (DTSQ). Data are mean changes in raw scores ± SEM. $*P < 0.05$; $**P < 0.01$; $***P < 0.001$ for within-group change from baseline (paired *t*-test). *P*-values shown correspond to between-group differences in the magnitude of change (ANOVA adjusted for baseline and gender). ■, Insulin aspart; □, human insulin. Changes for domains 2 and 3 are shown as positive values although the scores reduced. This is because these domains, uniquely, have negative valuation, hence reduced score is desirable.

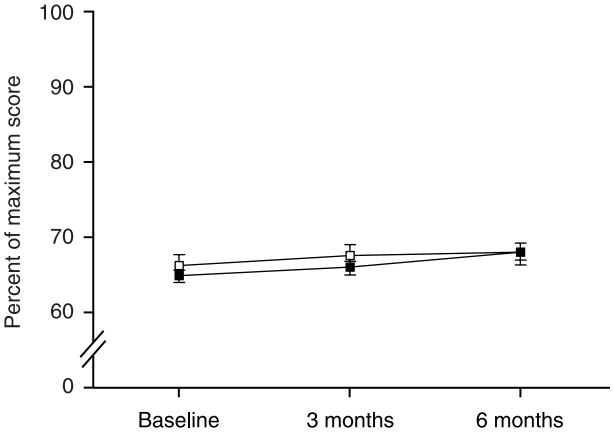

Figure 5 Total quality of life scores at baseline and at the two follow-up examinations. Data are means, adjusted to 0–100 scale, ± SEM. □, Human insulin; ■, insulin aspart.

which patients were striving for physical strength (Wald χ^2 6.66; $P = 0.0099$). Altogether, 289 patients (69%) perceived physical strength as a very important treatment goal, indicating the highest level on the six-point Likert scale. In this subgroup, who particularly valued physical strength, 28% of those randomized to IAsp achieved a small but important improvement of QoL compared with 13% of those randomized to HI. Thus, the NNT to achieve a small but important improvement in QoL with IAsp was 7 in this patient category. The only significant predictor in the second analysis, using the 10 baseline satisfaction items of the DSQOLS as potential predictors of QoL improvement during the follow-up period, was the extent to which patients felt protected from severe hypoglycaemia (Wald χ^2 10.72; $P = 0.0011$). Altogether, 27% of patients expressed some level of dissatisfaction with their protection from severe hypoglycaemia. Within this patient category, IAsp was associated with a small but important improvement in QoL in 35%, while HI was associated with such improvement in 24%. Thus, the NNT with IAsp to achieve a small but important QoL improvement in these patients was 8.

Discussion

The present study has shown that treatment with IAsp, under these study conditions, is able to improve patients' treatment satisfaction and reduce their perception of diet restriction when compared with HI. To avoid complex adjustments for

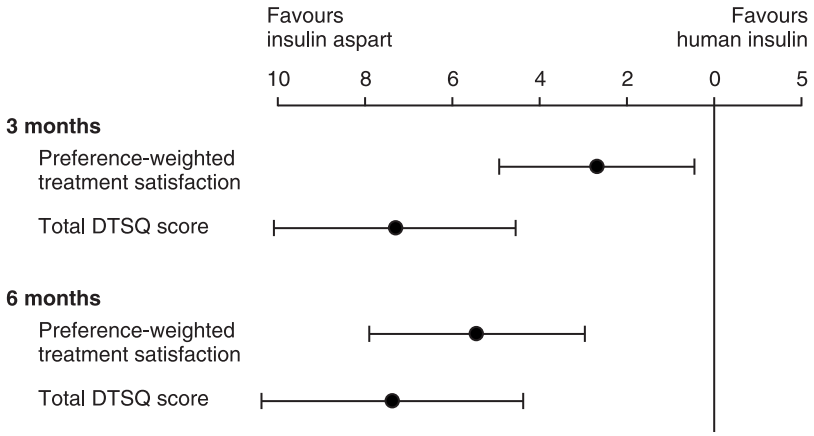

Figure 4 Difference between groups in change of score from baseline at 3 and 6 months, for total treatment satisfaction scores. Data are mean differences in unadjusted Δ scores (0–100 scale) with 95% confidence intervals. [Between-group difference in preference-weighted treatment satisfaction (PWTS) is not significant at 3 months when adjusted for gender or baseline.]

multiple testing, *a priori* hypotheses regarding the main outcome variables were defined [33,34]. It was predicted that IAsp would have the strongest positive effect in the domains of treatment satisfaction, diet restriction, burden of hypoglycaemia and blood glucose fluctuation. The level of significance for the differences in both treatment satisfaction scales and the diet restriction scale ($P \leq 0.003$) obtained at 6-month follow-up would also withstand the rather conservative method of Bonferroni adjustment [33,34].

Although the between-group differences were numerically small, they should be viewed in the context of baseline glycaemic control. The fact that most patients were in good metabolic control (HbA_{1c} of 7.5%) suggests that there would be little room for further improvement of QoL aspects associated with hyperglycaemic symptoms. In the present study, only diabetes-specific scales that had been previously validated were applied [7,24,25,27,28]. Of the 12 subscales, five were based on patient interviews specifically designed to elucidate the potential benefits and disadvantages of rapid-acting insulin analogues. It is therefore likely that the questionnaire comprehensively covered the crucial diabetes-specific QoL domains that might be affected by new insulin analogues.

Diet restriction represented the only QoL component that was significantly improved by IAsp in comparison with HI. This improvement appeared to be largely attributable to the shorter injection–meal interval recommended for insulin aspart compared with HI. In Germany, most patients employ rather short injection–meal intervals for HI, of 0–15 min, despite the rather heterogeneous recommendations of diabetologists for a longer interval [35,36]. In the current trial, compliance with injection–meal interval was not assessed, but patients were instructed in accordance with the product labels. Compliance in this trial is likely to have reflected that in everyday clinical practice. A previous comparative study of insulin lispro and HI within multiple-injection regimens, in which both insulins were injected shortly before meals, showed no significant patient preference for either treatment [37]. This finding is concordant with the hypothesis that the injection–meal interval is an important factor in treatment satisfaction.

Consistent with preceding studies involving insulin lispro [17,18], the rapid-acting analogue IAsp had a greater impact on treatment satisfaction than on QoL relative to HI. This may be attributable to the different concepts underlying the perceptions of 'satisfaction', and 'burdens and restrictions'. It seems that 'treatment satisfaction' reflects a patient's personal assessment within a certain frame of reference. It is characterized by the individual's treatment goals and any disparities between their present situation and what they perceive as realistic and achievable [38,39]. In contrast, QoL—as measured by the DSQOLS—represents a temporary description of extant burdens and restrictions [7]. Therefore, the statistical correlation between 'treatment satisfaction' and 'quality of life' or between 'treatment satisfaction' and 'quality of treatment' is sometimes poor [7,40].

The DTSQ scores showed that patients perceived treatment with IAsp as more convenient and flexible, and they were more enthusiastic about continuing it themselves and recommending it to others than was the case for HI, an insulin therapy with which they had become familiar over many years. The only areas in which IAsp was not associated with positive changes, as detected by the DSQOL treatment satisfaction analysis, were in the domains of feeling protected from severe hypoglycaemia, self-monitoring of blood glucose and exchanging views with relatives or friends on treatment demands and decisions. The unblinded nature of the present trial is expected to have influenced patient preferences and expectations. In the IAsp group, treatment satisfaction tended to improve with time (Fig. 4). It seems that patients need a certain amount of time to become acquainted with a new therapy, but this requires confirmation in follow-up assessments.

The advantages of IAsp on treatment satisfaction and diet-related QoL did not appear to be mediated by glycaemic control, as HbA_{1c} values and the frequency of mild or severe hypoglycaemic events did not differ significantly between groups in this German substudy. At the end of the study, HbA_{1c} correlated only slightly with aspects of treatment satisfaction and QoL. Blood glucose fluctuations ($r = -0.19$), worries about the future ($r = -0.18$), and PWTS ($r = -0.17$) revealed the highest correlations, indicating improved treatment satisfaction and QoL with lower HbA_{1c}.

Guyatt *et al.* emphasized that 'even if the mean difference between a treatment and a control is appreciably less than the smallest change that is important, treatment may still have an important impact on many patients' [32]. They therefore suggested that clinical trials should report the difference in the proportion of patients who experience important improvement of QoL and the associated NNT. In the present study, NNT with IAsp for a small but important improvement of QoL was 10, reducing to 7 and 8 in specified patient subgroups. In diabetology in general, there are almost no data on QoL to provide reference data for NNT. For comparison, however, DCCT data suggest that the NNT to prevent one case of neuropathy within 5 years via intensified insulin therapy is 15 [41]. This example indicates that the effect of IAsp on QoL may not be trivial.

The validity of satisfaction or QoL scores can potentially be optimized when patients are able to select dimensions of most concern and their preferences, as is possible with the PWTS [7,42]. However, both treatment satisfaction scales revealed similar results and the calculation of preference weightings did not improve the sensitivity to change in this study. Further studies are required to evaluate if preference-weighted measures provide additional information of clinical relevance.

One possible use of preference-weighted measures of treatment satisfaction may be found in the opportunity to investigate individual preferences and treatment goals, revealing motivational structures that have to be considered while treating, educating or counselling patients. Two subgroups were identified in which IAsp appeared to be particularly beneficial.

Patients striving for physical strength achieved the greatest benefit with IAsp, possibly because such patients perceived postprandial hyperglycaemia (which is more pronounced when using regular HI [12]) as physically disturbing. Indeed, interviews conducted during the validation of the DSQOLS indicated that some patients feel physically and cognitively less efficient during periods of postprandial hyperglycaemia, even when these periods have little impact on HbA_{1c}. Patients who felt less protected from severe hypoglycaemia also derived a relatively greater benefit from IAsp. This is predictable, in that the short duration of action of IAsp should facilitate anticipation of insulin action and therefore adaptation of the dose to balance postprandial control with avoidance of hypoglycaemia [43].

In conclusion, the present study demonstrated that IAsp, used as the mealtime component of basal-bolus insulin therapy, was associated with greater treatment satisfaction than HI using two different diabetes satisfaction instruments. Further, insulin aspart resulted in more favourable scores than human insulin for the quality of life domain of diet restriction. The use of preference-weighted treatment satisfaction scores highlighted individual patients gaining particular benefit from insulin aspart, while the 'number needed to treat' calculations suggested that the quality of life impact of insulin aspart was not trivial.

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