Treatment satisfaction and quality of life with insulin glargine plus insulin lispro compared with NPH insulin plus unmodified human insulin in people with Type 1 diabetes

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Running title: Quality of life with insulin analogues

Word count (text): 3966

Number of figures: 1

Number of tables: 2

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Abstract

Objective   To compare quality of life and treatment satisfaction when using insulin glargine + insulin lispro with that on NPH insulin + unmodified human insulin in adults with Type 1 diabetes managed with multiple injection regimens.

Research Design and Methods   As part of a 32-week, five-centre, two-way cross-over study in 56 people with Type 1 diabetes randomized to evening insulin glargine + meal-time insulin lispro or to NPH insulin (once- or twice-daily) + meal-time unmodified human insulin, the Diabetes Treatment Satisfaction Questionnaire (DTSQ) and the Audit of Diabetes Dependent Quality of Life (ADDQoL) questionnaire were completed at baseline, weeks 16 and 32, with additional interim DTSQ measurements.

Results   For all patients combined, mean baseline present quality of life (QoL) score was 1.3, reflecting 'good' QoL. Present QoL improved with glargine+lispro but did not change with NPH+human insulin (1.6±0.1 [±SE] vs 1.3±0.1, difference 0.3 (95 % CI 0.1, 0.6), p=0.014). Baseline mean average weighted impact score (AWI) of diabetes on QoL was –1.8, indicating a negative impact of diabetes on QoL. AWI score at endpoint improved significantly with glargine+lispro but changed little with NPH+human insulin (-1.4±0.1 vs -1.7±0.1, 0.3 (0.0, 0.6), p=0.033). Treatment satisfaction (DTSQ 36-0 scale score) at endpoint was markedly greater with glargine+lispro compared with NPH+human insulin (32.2±3.4 vs 23.9±7.2, 8.6 (6.5, 10.6), p<0.001).

Conclusions   Insulin glargine + insulin lispro improves treatment satisfaction, reduces the negative impact of diabetes on QoL and improves QoL, in comparison with NPH insulin + unmodified human insulin in Type 1 diabetes.

Keywords   Insulin glargine, Insulin lispro, Type 1 diabetes, Quality of life, Treatment satisfaction, Insulin analogues.

The primary aim for most physicians advising on the management of Type 1 diabetes is to help the individual to achieve good blood glucose control without excessive hypoglycaemia. One of the management strategies that can be employed to achieve this is the use of analogue insulin preparations in a multiple daily injection regimen. However, many physicians are concerned that the increased number of injections might have a negative impact on individual quality of life (QoL) [1], although others have anticipated the QoL benefits that may follow from a regimen that allows flexible eating and insulin dosing [2] [3]. The maintenance, or indeed improvement, in psychological outcomes such as quality of life and treatment satisfaction should thus be an additional but related goal in the management of people with Type 1 diabetes [4]. Rapid- and extended-acting insulin analogues have been shown to improve blood glucose control in people with Type 1 diabetes [5-10]. However, it cannot be assumed that these therapies concurrently improve psychological outcomes. The evaluation of quality of life and, more specifically, treatment satisfaction is thus an important part of the assessment of new insulin preparations.

Insulin glargine combined with a rapid-acting insulin analogue such as insulin lispro provide a more physiological replacement of meal-time and basal insulin, compared with previous insulin regimens. It was previously shown, in the same study participants involved in the present report, that insulin glargine in combination with insulin lispro improves overall glycaemic control as assessed by HbA$_{1c}$ and 24-h plasma glucose monitoring to a clinically significant degree, together with a reduction in nocturnal hypoglycaemia [8]. Whilst psychological outcomes have been evaluated in studies comparing insulin glargine with NPH insulin [4], and rapid-acting insulin analogues with unmodified human insulin [11-14], there are no comprehensive reports of psychological outcomes comparing a combined rapid-acting and long-acting analogue regimen with NPH insulin plus unmodified human insulin.

Here we report treatment satisfaction, overall quality of life and the impact of diabetes on quality of life in a randomized clinical trial comparing once-daily insulin glargine + insulin lispro with once- or twice-daily NPH insulin + unmodified human insulin in adults with Type 1 diabetes.

Research Design and Methods

A 32-week, open, randomized, two-way cross-over clinical trial in people with Type 1 diabetes was conducted in five UK sites. The study was approved by local ethics committees, and written informed consent was obtained from all participants before the study began. The study design and metabolic outcome measures have previously been reported in detail [8]. Here we present the psychological outcome measures recorded during the study.

Participants

Seventy-one people were recruited (by examination of their medical records with regard to inclusion criteria followed by invitation to enter the study). Two withdrew before randomization and 13 did not fulfil study inclusion criteria. Fifty-six people were randomized. Two people withdrew after randomization but before receiving study treatment, one in each group. Neither knew the treatment they had been randomized to receive; 54 people were thus randomized and treated. Three people withdrew during the study (two randomized to glargine plus lispro, and one to NPH plus unmodified human insulin, all during the first treatment period) and 51 completed the study. One person withdrew due to an adverse event, one felt unable to continue with the demands of the study protocol, and one was unable to complete the 24-h in-patient studies.

A modified intention-to-treat (ITT) sample was used for all psychological analyses, consisting of all randomized participants who received at least one dose of the study medication and had at least one post-baseline efficacy measurement of treatment satisfaction or QoL in each treatment period. This sample consisted of 48 people, 22 randomized to insulin glargine plus insulin lispro (glargine + lispro) for the first treatment period, and 26 to NPH insulin + unmodified human insulin (NPH + human) (Table 1). Insufficient questionnaire data were collected for the remaining three participants to allow inclusion. There were no clinically significant differences between the recorded characteristics of the modified ITT sample for the QoL analysis and those of the main efficacy study sample. The modified ITT sample for the QoL analysis consisted of 18 men and 30 women, age 18–65 yr with Type 1 diabetes and no previous experience of insulin glargine, who had been using a multiple insulin injection regimen for at least 1 year (mean 10.5 ± 8.4 yr [±SD]) prior to randomization. Participants had

4

a random C-peptide ≤0.10 nmol/l and HbA1c 7.0 – 9.5 % (non-diabetic <5.9 %). Two of the study centres, and thus some of the participants recruited at these sites, had previously taken part in the DAFNE (Dose Adjustment For Normal Eating) study and had thus been trained in insulin dose adjustment to allow considerable dietary freedom. It has been shown that DAFNE training resulted in significant improvements in treatment satisfaction using the DTSQ and both present quality of life and the impact of diabetes on quality of life measured by the ADDQoL [15]. There were no statistically significant differences in baseline characteristics between the two randomized groups.

Methods

After a 4-week screening period during which previous insulin therapy was continued, people were randomized to bed-time insulin glargine (Lantus®; Sanofi-Aventis, Paris) in combination with pre-meal insulin lispro (Humalog®; Lilly, Indianapolis, USA) (glargine + lispro), or to NPH insulin (HOE 36HPR; Aventis) in combination with pre-meal unmodified human insulin (HOE 31HPR; Aventis) (NPH + human). Randomization was by telephone using a central computer randomization program.

The first 4 weeks of the 16-week treatment period consisted of a dose titration period during which study visits occurred weekly. In the subsequent 12 weeks, visits were fortnightly, or more frequently if necessary. At each consultation self-monitored blood glucose levels and insulin doses were reviewed, and insulin doses titrated according to a target-driven algorithm that was identical for all study sites and both insulin regimens. Target blood glucose levels were identical for each regimen: pre-prandial and post-prandial targets were 4.0–6.5 mmol/l, in the absence of hypoglycaemia. The blood glucose target for 03:00 h was ≥5.0 mmol/l.

Insulin glargine was initially given at bed-time, but could be injected earlier in the evening if blood glucose levels were frequently high or rising at bedtime or 03:00 h. All people randomized to the human insulin regimen received NPH insulin, once-daily at bed-time or twice-daily, at bed-time and breakfast, the frequency of injection being determined by the person's prior dosing frequency. Insulin lispro was recommended to be given immediately before meals, while participants were recommended to inject unmodified human insulin 30

minutes before eating. The OptiPen® Pro 1 injection device (Aventis) was used to give all insulin injections except insulin lispro (HumaPen® Ergo; Lilly).

At the end of the 16-week treatment period, participants were admitted for a 24-h in-patient plasma glucose assessment. At the end of the first 24-h study, participants commenced the alternative insulin regimen and the study sequence was repeated.

Questionnaires

The Diabetes Treatment Satisfaction Questionnaire (DTSQ), and Audit of Diabetes Dependent Quality of Life (ADDQoL) questionnaire, are self-administered instruments that have demonstrated validity and reliability in diabetes patient populations [4, 14, 16-19].

Treatment satisfaction was assessed using the DTSQ [18, 19]). This is an eight–item questionnaire in which each item is scored on a 7-point scale. The Treatment Satisfaction score is the sum of six of the items of the DTSQ for each respondent. The additional two items measure perceived frequency of hyperglycaemia and hypoglycaemia, and are considered separately.

The DTSQ status version (DTSQs) assesses treatment satisfaction over the few weeks prior to its completion. Each item is scored from 6-0 with a higher score indicating greater satisfaction. The Treatment Satisfaction score can thus range from 36 (very satisfied) to 0 (very dissatisfied). The two additional items measuring perceived frequency of hypo- and hyperglycaemia are scored from 0 ('none of the time') to 6 ('most of the time'). The DTSQs can be limited by a ceiling effect when treatment satisfaction is high at baseline [20]. The DTSQ change version (DTSQc), uses the same eight item stems as the DTSQs but has different response options and asks respondents to assess changes in treatment satisfaction with their current, compared with their previous treatment and thus overcomes any ceiling effect that may occur with the DTSQs [14]. Each of the 6 items of the DTSQc is scored from +3 (e.g. 'much more satisfied now') to -3 (e.g. 'much less satisfied now'), The DTSQc Treatment Satisfaction change score can thus range from +18 to -18. The items measuring perceived frequency of hypo- and hyperglycaemia were scored from -3 ('much less of the time now') to +3 ('much more of the time now') such that a higher score indicates more hyper- or hypoglycaemia.

The DTSQs was completed at baseline, and at weeks 8 and 16 of each 16-week treatment period. The DTSQc was completed once at the end of the study.

The impact of diabetes on quality of life was assessed using the ADDQoL questionnaire. Eighteen of the 20 items of the ADDQoL concern specific life domains such as social life and working life, and are scored on a seven-point impact scale, accompanied by a related importance rating scale for each domain used to assess the importance of each aspect of life for the individual's QoL. The impact of diabetes on each of these life domains is then weighted by the domain's importance for the respondent's quality of life and the resulting weighted impact scores are averaged across all applicable domains to provide an average weighted impact (AWI) score. Weighted impact scores for single domains and the AWI score can range from +9 (maximum positive impact of diabetes) to –9 (maximum negative impact of diabetes). The two remaining overview items are scored separately and include a single Diabetes-specific QoL item measuring the impact of diabetes on quality of life that is scored from +3 (maximum positive impact of diabetes) to -3 (maximum negative impact of diabetes), and a single item, Present Quality of Life, that is scored from +3 (excellent) to –3 (extremely bad) to measure overall QoL.

The ADDQoL was completed at baseline and at the endpoint of each treatment period (weeks 16 and 32).

In order to achieve a high response rate, participants were asked to complete the questionnaires during trial visits and to return them to the investigators in a sealed envelope. The completed questionnaires were not inspected by the investigators but were analysed by a statistician blinded to the randomized group.

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Statistical analysis

Sample size was calculated using HbA_{1c}, the primary endpoint of the main study [8]. Participant-reported outcomes from the ADDQoL and DTSQ were analyzed by an analysis of variance (ANOVA) model including period and sequence effects. All statistical tests were performed at a two-sided significance level of α=5 %. Data are provided as mean ± SE and

mean difference (95 % CI) unless otherwise stated. Analysis was performed using SAS software. The model included fixed effects for treatment, sequence, and period, as well as a random effect to account for subjects within sequence.

Results

ADDQoL

The mean Present QoL score for the whole study sample at baseline was 1.3 ±1.1 (±SD), reflecting 'good', rather than 'very good' or 'excellent' QoL. The average weighted impact (AWI) score at baseline was -1.8 ± 1.2 (±SD), indicating an overall negative impact of diabetes on quality of life.

The Present QoL score increased by 0.3 points during treatment with glargine + lispro but did not change with NPH + human (endpoint scores 1.6 ± 0.1 (± SE) vs 1.3 ± 0.1, difference 0.3 (95 % CI 0.1, 0.6), p=0.014) (Figure 1A). Diabetes-specific QoL at endpoint did not differ between treatment groups [-1.4 ± 0.1 vs -1.5 ± 0.1, 0.2 (-0.1, 0.5), NS].

The AWI score improved by 0.4 points with glargine + lispro but changed little with NPH + human (endpoint scores -1.4 ± 0.1 vs -1.7 ± 0.1, 0.3 (0.0, 0.6), p=0.033). The AWI score followed a similar pattern during the study as Present QoL (Figure 1A). The negative impact of diabetes on quality of life in the following domains was improved with glargine + lispro, compared with NPH + human: social life [-0.8 ± 0.2 vs -1.8 ± 0.2, 1.0 (0.3, 1.7), p=0.007]; sex life [-0.8 ± 0.2 vs -1.5 ± 0.2, 0.6 (0.1, 1.2), p=0.023]; society's reaction [-0.7 ± 0.1 vs -1.1 ± 0.1, 0.4 (0.0, 0.7), p=0.048]; and enjoyment of food [-1.6 ± 0.1 vs -2.1 ± 0.1, 0.5 (0.1, 0.9), p=0.014].

DTSQ

Treatment Satisfaction at baseline was high in this population, with a mean DTSQ Treatment Satisfaction score of 28.8 ± 5.7. Nineteen people (39.6 %) had a baseline DTSQ summary score between 31 and the maximum of 36.

Treatment Satisfaction increased by 3.2 points with glargine + lispro but decreased by 4.9 points with NPH + human [32.3 ± 0.7 vs 23.7 ± 0.7, 8.6 (6.5, 10.6), p<0.001]. The Treatment Satisfaction score showed a progressive increase from baseline to endpoint during treatment

with glargine + lispro. Conversely, with NPH + human, there was a progressive decrease in Treatment Satisfaction through the course of the treatment period (Figure 1B).

Significant differences favouring glargine + lispro were found for five of the six items of the Treatment Satisfaction scale: current satisfaction with treatment (5.4 ± 0.2 vs 3.8 ± 0.2, $p<0.001$); convenience of treatment (5.3 ± 0.1 vs 4.1 ± 0.1, $p<0.001$); flexibility of treatment (5.2 ± 0.1 vs 3.9 ± 0.2, $p<0.001$); recommend to others (5.5 ± 0.2 vs 3.7 ± 0.2, $p<0.001$); and satisfaction to continue current treatment (5.7 ± 0.2 vs 3.2 ± 0.2, $p<0.001$).

Results from the DTSQc were similar to those obtained with the DTSQs: predominantly negative scores for items 1 and 4-8 with NPH + human indicated worsened treatment satisfaction when compared to previous treatment with glargine + lispro. (Table 2 – online appendix)

Perceptions of blood glucose control

Perceived frequency of hyperglycaemia at endpoint (DTSQs) was lower with glargine + lispro compared with NPH + human (2.7 ± 0.2 vs 4.0 ± 0.2, $p<0.001$). The DTSQc showed a decrease in perceived frequency of hyperglycaemia with insulin glargine + lispro and an increase with NPH + human at endpoint when respondents compared their experience of treatment in treatment period 2 with that in period 1 (-0.8 ± 0.5 vs 0.5 ± 0.5, $p=0.043$). (Table 2 – online appendix)

Perceived frequency of hypoglycaemia at endpoint (DTSQs and DTSQc) did not differ between glargine + lispro and NPH + human. (Table 2 – online appendix)

Conclusions

This study compared treatment satisfaction and quality of life in people with Type 1 diabetes randomized to insulin glargine plus insulin lispro or to NPH insulin plus unmodified human insulin, using a 32-week, open, multicentre, two-way cross-over design. Together with observed improvements in blood glucose control with insulin glargine plus insulin lispro [8], quality of life and treatment satisfaction also improved compared with NPH insulin plus unmodified human insulin. Present Quality of Life increased with the analogue, compared with the human insulin regimen, and the negative impact of diabetes on quality of life, particularly

9

on social life, sex life, society's reaction and enjoyment of food, was reduced. Treatment satisfaction improved progressively through the study with insulin glargine plus insulin lispro, with notable improvements in flexibility and convenience.

Participants using glargine plus lispro reported a significantly reduced perception of the frequency of hyperglycemia, but there was no difference between treatment groups in perceived frequency of hypoglycemia on the DTSQs. However, self-monitored and in-patient-assessed hyperglycemia as well as symptomatic nocturnal hypoglycemia were reduced with the analogue compared with the human insulin regimen [8], Episodes of all recalled/ diary-monitored symptomatic hypoglycaemia did not differ between treatment groups. The DTSQ does not assess severity of hypoglycaemia. It is thus possible that, when completing the DTSQ, respondents would be influenced more by frequent minor symptoms of daytime hypoglycaemia than by less frequent but more troublesome instances of more severe (eg nocturnal) hypoglycaemia to the extent that participants did not indicate any difference in overall hypoglycaemia between treatments.

The study was not blinded due to differences in the appearance of the basal insulin preparations. It is thus possible that some of the observed improvements in treatment satisfaction and quality of life might have simply reflected participant expectations of a new insulin regimen. Whilst this possibility cannot be entirely discounted, the improvements in treatment satisfaction with insulin glargine plus insulin lispro increased progressively through the study. This indicates that any expectations of the perceived benefits of the analogue insulin regimen held by participants are likely to have been met and that such benefits were not transient but maintained, and indeed improved further through the course of the study. Whilst it would have been technically possible, though difficult, to blind the study, it was felt that this would not have been acceptable to participants. Additionally, blinded study designs have major limitations in studying psychological outcomes relating to insulin therapy. For example, convenience and flexibility were improved with the analogue insulin regimen, reflecting differences between analogue and human insulin regimens in the frequency of insulin injections and their timing in relation to meals. A blinded design would have been unable to detect such differences in treatment satisfaction between regimens as such a

design would require the necessity for placebo injections, which create an artificial experience of treatment that is more demanding than either treatment in clinical reality.

Three of the 51 patients randomized to the main study did not complete any quality of life or treatment satisfaction questionnaires. Whilst there were no clinically significant differences between the recorded characteristics of this sample of 48 used for the QoL and treatment satisfaction analysis and the sample of 51 used for the main efficacy study sample, subtle differences cannot be excluded. As in all such studies, ascertainment bias as a result of the recruitment of patients motivated to enter this clinical trial, can also not be excluded.

Rapid-acting insulin analogues have been shown to improve treatment satisfaction compared with unmodified human insulin in people with Type 1 diabetes, with reported between-group differences in the DTSQs Treatment Satisfaction score of 1.6-2.3 [11-14]. Similar studies have reported improvements in the DTSQs Treatment Satisfaction score with insulin glargine compared with NPH insulin of 0.9-1.8 [4, 21]. In the current study however, the between-group difference in the DTSQs Treatment Satisfaction score was much greater, at 8.6. The between-group differences in each of the items of the DTSQs in the current study were also much greater than those reported in previous studies comparing insulin glargine with NPH insulin or rapid-acting insulin analogues with unmodified human insulin [4, 13, 22]. This suggests that the combination of insulin glargine and a rapid-acting insulin analogue might have a synergistic benefit on treatment satisfaction. However, the use of carbohydrate counting skills and prandial insulin dose adjustment by some of the participants of the present study might have contributed to these improved QoL results.

The DAFNE study provided people with Type 1 diabetes with an educational package at the heart of which was the acquisition of skills to count carbohydrate and adjust rapid-acting insulin doses accordingly, thus allowing dietary flexibility [15]. The improvements in measures of QoL in people who undertook this course compared to the control group who were yet to do so are similar to those recorded in the present study comparing analogue and human insulin regimens: DTSQs Treatment Satisfaction improved by 8.8 and perceived frequency of hyperglycaemia by 1.1 in the DAFNE study. The AWI score improved by 0.4 and Present QoL by 0.3. The only difference between DAFNE and the present study is the improvement in the item 'freedom to eat as I wish' that was much greater in DAFNE. Two of the five centres

involved in the present study (that together contributed 39 % of the total study sample) had previously taken part in the DAFNE study. Some of the investigators and participants enrolled in the present study at these sites had thus undergone DAFNE training. Whilst carbohydrate counting and rapid-acting dose adjustment skills were not an inclusion criterion of the present study and were not taught during the study, a high proportion of participants recruited from these two study sites would be likely to have previously acquired these skills. Some of the improved QoL and treatment satisfaction benefits observed in the present study (which were markedly greater that those seen in previous studies comparing insulin glargine with NPH insulin or rapid-acting insulin analogues with unmodified human insulin) might thus relate to the combined benefits of an insulin analogue regimen and dietary freedom in the participants who were DAFNE-trained. A post-hoc analysis comparing QoL and treatment satisfaction in DAFNE compared with non-DAFNE centres is problematic due to the small number of centres (2 vs 3) but ADDQoL AWI score, freedom to eat and Present QoL did not differ between sites (data not shown).

It may be noted that people in the present study tended to show worsened satisfaction with the conventional insulin regimen during the study. This is most marked after exposure to the combined analogue regimen (Figure 1B), and reflects the commonly observed disappointment with the previously satisfactory control treatment after experiencing a treatment that participants preferred [23].

In conclusion, insulin glargine in combination with a rapid-acting insulin analogue improves both biomedical and psychosocial outcomes compared with NPH insulin plus unmodified human insulin. These data reinforce the suggestion that the use of combined insulin analogue therapy should be considered as an option for all people with Type 1 diabetes.

Acknowledgements and Duality of Interest

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Table 1 Characteristics of the modified intention-to-treat population with Type 1 diabetes randomized and treated (all randomized participants who received at least one dose of the study medication and had at least one post-baseline efficacy measurement of treatment satisfaction or QoL in each treatment period)

|	Glargine + lispro in first treatment period	NPH + human in first treatment period
N	22	26
Sex (M:F)	7:15	11:15
Age (yr)	41.7 ± 13.9	42.2 ± 9.1
BMI (kg m^{-2})	26.3 ± 2.8	25.8 ± 3.0
Weight	72.9 ± 11.1	73.5 ± 9.6
Duration of diabetes (yr)	22.3 ± 15.5	21.5 ± 10.7
HbA$_{1c}$	8.1 ± 0.8	8.0 ± 0.8
Pre-study insulin therapy (n [%])		
Basal insulin		
Once-daily NPH insulin	12 (55)	17 (65)
Twice-daily NPH insulin	5 (23)	6 (23)
Insulin zinc suspension	3 (14)	2 (8)
Unknown/ other	2 (9)	1 (4)
Meal-time insulin		
Unmodified human insulin	14 (64)	16 (62)
Rapid-acting insulin analogue	8 (36)	9 (35)
Unknown	0	1 (4)
ADDQoL scores		
Present Qol	1.4 ± 0.8	1.2 ± 1.3
Diabetes-specific QoL	-1.7 ± 1.1	-1.8 ± 1.0
Average weighted impact of diabetes on QoL	-0.7 ± 0.5	-0.9 ± 0.5
DTSQ scores		
Treatment satisfaction	29.4 ± 5.0	28.2 ± 6.3
Perceived frequency of hyperglycaemia	3.9 ± 1.0	3.6 ± 1.4
Perceived frequency of hypoglycaemia	2.9 ± 1.5	2.3 ± 1.2

Mean ± SD or n (%)
No statistically significant differences between groups

Table 2 Individual item analysis of endpoint DTSQs and DTSQc scores (mean ± SE) with insulin glargine + insulin lispro or NPH insulin + unmodified human insulin

Item	DTSQs			DTSQc		
	Glargine+lispro	NPH+human	p	Glargine+lispro	NPH+human	p
1. Current satisfaction with treatment *	5.4 ± 0.2	3.8 ± 0.2	<0.001	2.1 ± 0.4	-0.5 ± 0.4	<0.001
2. Perceived frequency of hyperglycaemia **	2.7 ± 0.2	4.0 ± 0.2	<0.001	-0.8 ± 0.5	0.5 ± 0.5	0.043
3. Perceived frequency of hypoglycaemia **	2.6 ± 0.2	3.0 ± 0.2	0.078	-0.5 ± 0.4	-0.1 ± 0.5	NS
4. Convenience of treatment *	5.3 ± 0.1	4.1 ± 0.1	<0.001	2.4 ± 0.2	-0.3 ± 0.3	<0.001
5. Flexibility of treatment *	5.2 ± 0.1	3.9 ± 0.2	<0.001	2.2 ± 0.3	-0.3 ± 0.3	<0.001
6. Satisfaction with understanding of own diabetes *	5.2 ± 0.1	5.1 ± 0.1	NS	2.2 ± 0.2	2.0 ± 0.3	NS
7. Recommend to others *	5.5 ± 0.2	3.7 ± 0.2	<0.001	2.0 ± 0.4	-0.5 ± 0.5	<0.001
8. Satisfaction to continue with current treatment *	5.7 ± 0.2	3.2 ± 0.2	<0.001	2.5 ± 0.5	-0.7 ± 0.5	<0.001
Treatment Satisfaction (items 1,4-8 summed) *	32.3 ± 0.7	23.7 ± 0.7	<0.001	13.5 ± 1.7	-0.4 ± 1.8	<0.001

* Higher score indicates greater satisfaction

** Higher score indicates greater perceived hyper- or hypoglycaemia

A
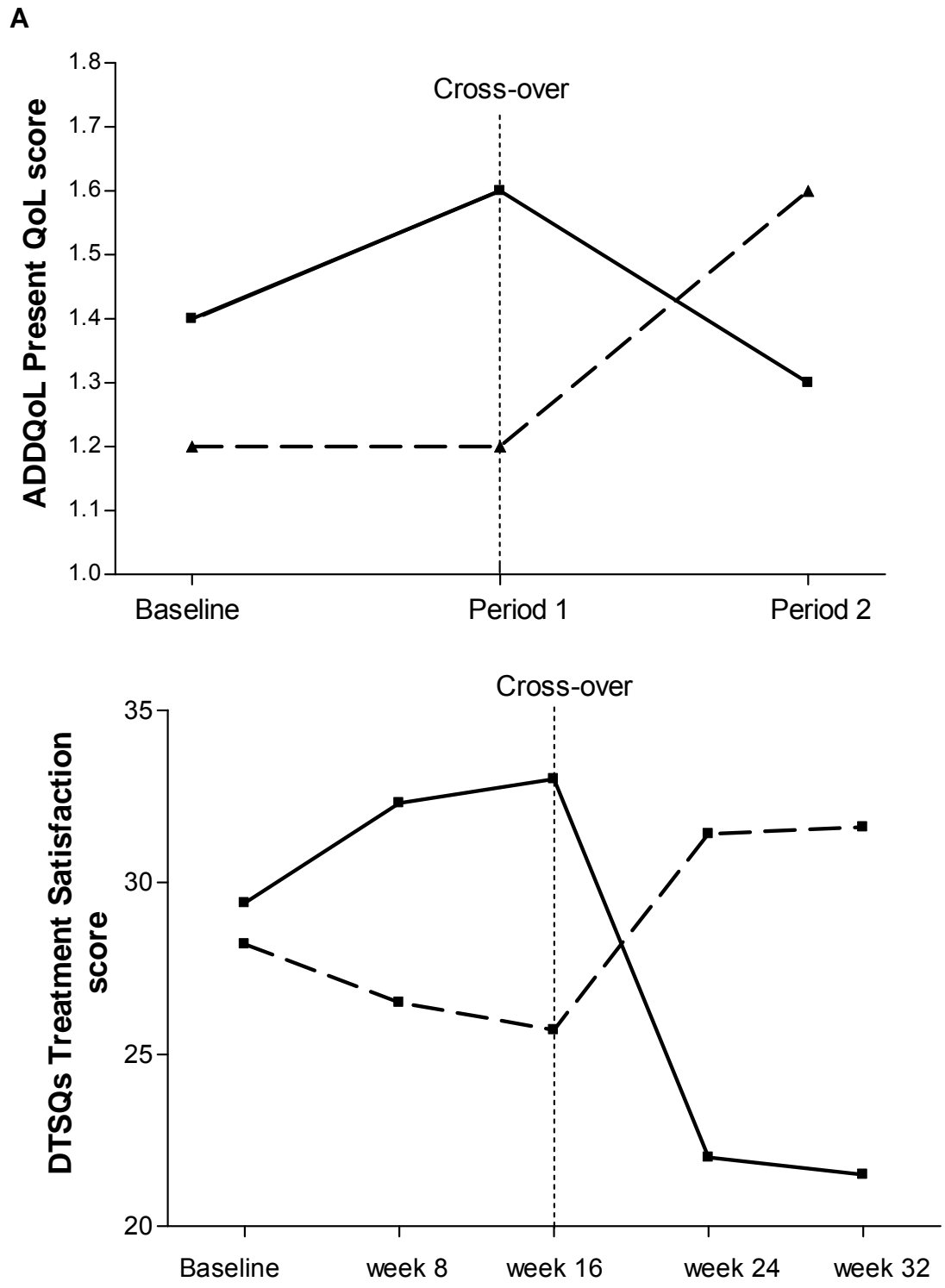
B

Figure 1 ADDQoL Present QoL score (A) and DTSQs Treatment Satisfaction score (B) in those who used glargine + lispro (——) and in those who used NPH + human (----) in period 1 of the study, switching to the alternative insulin regimen in Period 2

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