2925

Improved Treatment Satisfaction and Perceived Metabolic Control with Insulin Glargine, Regardless of Whether Injected Before Breakfast, Dinner or Bedtime, in Patients with Type 1 Diabetes

Clare Bradley[1], Louise Silvestre[2], Elke Witthaus[3]

[1]Royal Holloway, University of London, Egham, Surrey, UK; [2]Aventis, Romainville, France; [3]Covidence GmbH, Eschborn, Germany

Abstract

Background and Aims: Insulin glargine (LANTUS®) is a once-daily basal insulin analogue that facilitates HbA_{1c} targets <7%. A recent study showed that insulin glargine, plus prandial insulin, is effective when injected either before breakfast, before dinner or at bedtime in patients with Type 1 diabetes. The effect of these administration times on treatment satisfaction and perceived metabolic control is presented. **Materials and Methods:** This was an open-label, randomized, parallel group, multicentre, 24-week study, in which patients treated with insulin glargine plus prandial insulin before breakfast, before dinner or at bedtime completed the Diabetes Treatment Satisfaction Questionnaire status (DTSQs) at baseline and study endpoint. **Results:** A total of 332/378 treated patients completed the DTSQs. At baseline, 275 (72.8%) patients in the clinically evaluated population had an injection time preference (118 [42.9%]: breakfast, 28 [10.2%]: dinner, 105 [38.2%]: bedtime); 24 (8.7%) preferred a combination. Mean (±SD) baseline treatment satisfaction scores, when most patients were using NPH insulin, were 27.8 ± 5.0, 27.4 ± 5.5 and 28.1 ± 5.3 in the breakfast, dinner and bedtime groups, respectively, and increased in all groups from baseline to endpoint (1.4, p=0.079; 2.5, p=0.0002; 1.8, p=0.009, respectively; paired t-test). The largest increases came from a change in the DTSQ convenience score (breakfast: 0.5, p=0.005; dinner: 0.8, p=0.0001; bedtime: 0.7, p=0.0001) and 'wish to continue' (breakfast: 0.4, p=0.054; dinner: 0.8, p=0.0001; bedtime: 0.6, p=0.0007). In terms of perceived metabolic control, the perceived frequency of hyperglycaemia decreased significantly at endpoint in the breakfast (–0.4, p=0.02) and bedtime groups (–0.5, p=0.0005) but not in the dinner group (–0.3, p=0.07). Perceived frequency of hypoglycaemia decreased significantly in the three groups combined (–0.18, p=0.04), but not in separate groups. **Conclusions:** These data complement the clinical study results and, in addition, show treatment satisfaction improved with insulin glargine, regardless of injection time. Thus, insulin glargine can be used effectively according to individual patients' needs or preference, before breakfast, before dinner or at bedtime.

Introduction

- New treatments for diabetes are increasingly being evaluated for their impact on individual-orientated outcomes
- The attainment and improvement of psychological outcomes needs to be monitored in conjunction with diabetes control to ensure that improved metabolic control is not achieved to the detriment of psychological factors
- Insulin glargine (LANTUS®), a long-acting human insulin analogue, has a smooth activity profile with no pronounced peaks[1]. Previous studies with insulin glargine have shown improved satisfaction with treatment in people with Type 1 diabetes switching from NPH insulin to insulin glargine[2–3]
- A recent study showed that the administration of insulin glargine, plus prandial insulin, to people with Type 1 diabetes, was equally effective in reducing mean HbA_{1c} from baseline to endpoint, when administered at three different times during the day: the percentage of people achieving target HbA_{1c} <7.0% at endpoint was similar between all groups (breakfast: 29.5%, dinner: 29.8%, bedtime: 25.8%)[4]
- Therefore, it is likely that insulin glargine, administered any time of day, at the same time every day, plus prandial insulin, would be expected to enhance patient convenience by allowing them to choose the time of dosing that best suits their usual schedule. In people with Type 1 diabetes, this would be expected to lead to increased compliance and satisfaction
- The data here describe additional findings from this study[4] with regard to patient reported outcomes

Study objectives

- To assess the effect of breakfast, dinner or bedtime administration of insulin glargine, in combination with prandial insulin, on treatment satisfaction and perceived metabolic control in people with Type 1 diabetes

Study design and methods

Study design

- Multicentre, 24-week, open-label, randomized (1:1:1), parallel study

Study population

- People with Type 1 diabetes with at least 1 year of intensified, basal–bolus insulin treatment, and at least 6 months' treatment with basal insulin plus fast-acting insulin, were randomly assigned into three treatment groups:
  - Insulin glargine injected before breakfast (n=121)
  - Insulin glargine injected before dinner (n=128)
  - Insulin glargine injected before bedtime (n=129)
- The majority of people (71%) had been using NPH insulin as the only basal insulin prior to the study. The remaining people used Lente insulin (7%), other insulins (1%) or a combination of the above mentioned insulins (15%). For 6% of people, the prior basal insulin used is unknown
- More than 90% of people had been using a fast-acting analogue as their mealtime insulin prior to the study
- The dose of insulin glargine was individually titrated to each person according to a predefined titration algorithm towards a target pre-breakfast blood glucose level of 4.4–6.7 mmol/L
- Prandial insulin was individually titrated as necessary, after preprandial glucose values reached the target defined by the insulin glargine titration algorithm, and injected subcutaneously before or immediately after a meal
- The Diabetes Treatment Satisfaction Questionnaire (DTSQ), the items from which are shown in Table 1, was completed by the study population at study baseline, weeks 8, 18 and 24, and endpoint
- The DTSQ was developed as a status measure of satisfaction with treatment and perceptions of glycaemic control in people with diabetes[5–6] and is recommended by the World Health Organization and the International Diabetes Federation to measure psychological outcomes of diabetes care[7]

Outcome measures

- The change from baseline to endpoint in the DTSQ in the intent-to-treat population for:
  - Treatment satisfaction (sum of items 1, 4, 5, 6, 7 and 8)
  - Perceived frequency of hyperglycaemia (item 2)
  - Perceived frequency of hypoglycaemia (item 3)

Statistical analysis

- The analysis of change from baseline scores on the DTSQ was an analysis of covariance (ANCOVA) using a model with treatment and pooled centre as fixed effects and with the baseline DTSQ score as covariate

Table 1. Diabetes Treatment Satisfaction Questionnaire items

1	**How satisfied are you with your current treatment?**								
	Very satisfied	6	5	4	3	2	1	0	Very dissatisfied
2	**How often have you felt that your blood sugars have been unacceptably high recently?**								
	Most of the time	6	5	4	3	2	1	0	None of the time
3	**How often have you felt that your blood sugars have been unacceptably low recently?**								
	Most of the time	6	5	4	3	2	1	0	None of the time
4	**How convenient have you been finding your treatment recently?**								
	Very convenient	6	5	4	3	2	1	0	Very inconvenient
5	**How flexible have you been finding your treatment recently?**								
	Very flexible	6	5	4	3	2	1	0	Very inflexible
6	**How satisfied are you with your understanding of your diabetes?**								
	Very satisfied	6	5	4	3	2	1	0	Very dissatisfied
7	**Would you recommend this form of treatment to someone else with your kind of diabetes?**								
	Yes, I would definitely recommend the treatment	6	5	4	3	2	1	0	No I would definitely not recommend the treatment
8	**How satisfied would you be to continue with your present form of treatment?**								
	Very satisfied	6	5	4	3	2	1	0	Very dissatisfied

Results

- Baseline demographics and characteristics of people enrolled in the study are summarized in Table 2
- A total of 332/378 (87.8%) of the study population completed the DTSQ (Table 2)

Table 2. Study population demographics and baseline characteristics

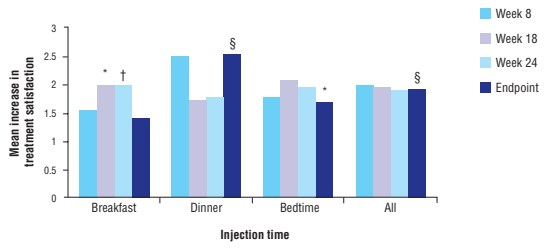
	Insulin glargine breakfast injection (n=103)	Insulin glargine dinner injection (n=113)	Insulin glargine bedtime injection (n=116)	Overall (n=332)
Age (years)	41.6 ± 12.6	40.0 ± 11.1	40.4 ± 12.2	40.6 ± 12.0
BMI (kg/m²)	25.5 ± 3.9	25.5 ± 3.3	25.0 ± 3.5	25.3 ± 3.6
Sex				
Male, n (%*)	55 (53.4)	68 (60.2)	53 (45.7)	176 (53.0)
Female, n (%*)	48 (46.6)	45 (39.8)	63 (54.3)	156 (47.0)
Duration of diabetes (years)	17.0 ± 10.9	17.1 ± 10.6	17.5 ± 12.6	17.2 ± 11.4
Age at onset of diabetes (years)	24.9 ± 11.9	23.3 ± 12.7	23.3 ± 13.3	23.8 ± 12.6

Data are mean ± standard deviation unless otherwise stated*; BMI = body mass index

Diabetes Treatment Satisfaction Questionnaire scores

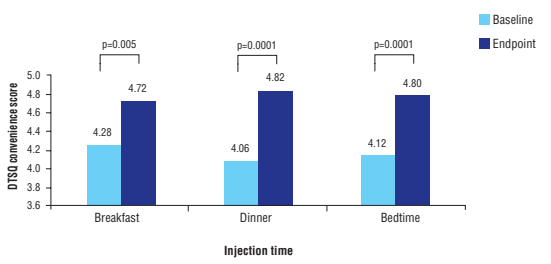
- Overall mean (± standard deviation [SD]) baseline treatment satisfaction scores, with most people using NPH insulin at baseline, were 27.8 ± 5.0, 27.4 ± 5.5 and 28.1 ± 5.3 in the breakfast, dinner and bedtime groups, respectively, and increased in all groups from baseline after switching to insulin glargine (Figure 1)
  - These improvements were statistically significant at endpoint in the pooled population and dinner and bedtime groups, but not in the breakfast group (Figure 1)
  - This reflects a higher rate of dropouts in the first few weeks in the breakfast group (10 people) than was observed in the other two groups (1 person for each group); those people who remained in the study were then as satisfied as those in the other treatment groups
- The largest increases came from changes in DTSQ convenience (Figure 2) and the 'wish to continue' (DTSQ scores: 4.61 vs 5.02, p=0.054; 4.44 vs 5.21, p=0.0001; 4.71 vs 5.28, p=0.0007, in the breakfast, dinner and bedtime groups at baseline versus endpoint, respectively)

Figure 1. Overall mean increase from baseline in Diabetes Treatment Satisfaction Questionnaire treatment satisfaction at weeks 8, 18, 24 and at endpoint (last available measurement)



*p <0.01, †p <0.05, §p <0.001, significance of increase from baseline; All=pooled population

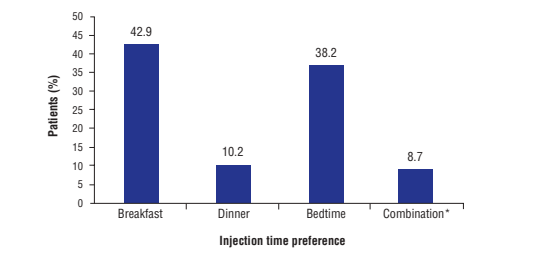
Figure 2. Change in Diabetes Treatment Satisfaction Questionnaire (DTSQ) score: convenience of treatment



Impact of injection time preference

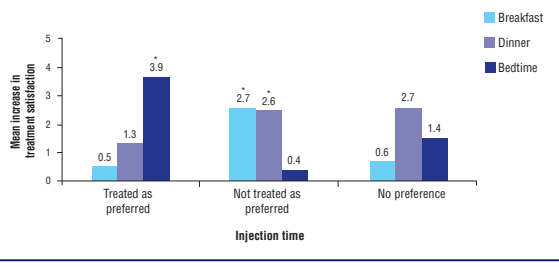
- At baseline, 275 (72.8%) people in the clinically evaluated population had an injection time preference (Figure 3)
- Of those who expressed an injection time preference, 81 people were treated as they preferred, whereas 157 people were not treated as they preferred
- Overall, allocation or non-allocation to the preferred choice of treatment group did not affect treatment satisfaction during the study
- In terms of individual treatment groups within the preference categories, subgroups with significant changes from baseline were the bedtime group if treated as preferred, and the breakfast and dinner groups if not treated as preferred (Figure 4)

Figure 3. Injection time preference at baseline



*Preference for a combination of timings

Figure 4. Effect of pre-study injection time preference on change in Diabetes Treatment Satisfaction Questionnaire scores: treatment satisfaction



*p <0.05 significance of increase from baseline

Perceived metabolic control

- The perceived frequency of hyperglycaemia decreased significantly at endpoint in the study population as a whole (–0.4, p=0.0001) and in the breakfast (–0.4, p=0.02) and bedtime (–0.5, p=0.005) groups, but not in the dinner group (–0.3, p=0.07)
- Perceived frequency of hypoglycaemia decreased significantly in the three groups combined (–0.18, p=0.04) but not in separate groups

Conclusions

- The psychological measures used in this study show significant improvement in treatment satisfaction with insulin glargine in all treatment groups, regardless of whether it was injected before breakfast, before dinner or at bedtime
- Insulin glargine had a favourable effect on treatment satisfaction means in all subgroups, irrespective of prior preference
- The most significant benefits were observed regarding convenience of treatment and 'wish to continue' with treatment
- There was an improvement in perceived metabolic control regarding both perceived frequency of hyperglycaemia and hypoglycaemia
- These data complement the clinical results and support the recommendation that insulin glargine can be used effectively according to an individual's needs or preference for any one of the three times of day

References

1. Lepore M, Pampanelli S, Fanelli C, Porcellati F, Bartocci L, Di Vincenzo A, et al. Pharmacokinetics and pharmacodynamics of subcutaneous injection of long-acting human insulin analog glargine, NPH insulin, and ultralente human insulin and continuous subcutaneous infusion of insulin lispro. *Diabetes* 2000; **49**(12): 2142–2148.
2. Witthaus E, Stewart J, Bradley C. Treatment satisfaction and psychological well-being with insulin glargine compared with NPH in patients with Type 1 diabetes. *Diabet Med* 2001; **18**(8): 619–625.
3. Fulcher G, Yue D, Gilbert R. Insulin glargine vs NPH insulin in patients with Type 1 diabetes: the effects of intensive insulin therapy on glycaemic control, hypoglycaemia and quality of life. *Diabetologia* 2002; **45**(Suppl 2): A258 (Abstract 801).
4. Hamann A, Matthaei S, Rosak C, Silvestre L, HOE901/4007 Study Group. A randomized clinical trial comparing breakfast, dinner or bedtime administration of insulin glargine in patients with type 1 diabetes. *Diabetes Care* 2003; **26**(6): 1738–1744.
5. Bradley C, Lewis KS. Measures of psychological well-being and treatment satisfaction developed from the responses of people with tablet-treated diabetes. *Diabetic Med* 1990; **7**(5): 445–451.
6. Bradley C. The Diabetes Treatment Satisfaction Questionnaire: DTSQ. In: Bradley C, ed. *Handbook of Psychology and Diabetes: a Guide to Psychological Measurement in Diabetes Research and Practice*. Switzerland: Harwood Academic Publishers, 1994.
7. Bradley C, Gamsu DS. Guidelines for encouraging psychological well-being: Report of a Working Group of the World Health Organization Regional Office for Europe and International Diabetes Federation European Region St. Vincent Declaration Action Programme for Diabetes. *Diabet Med* 1994; **11**(5): 510–516.

E-mail: c.bradley@rhul.ac.uk