ORIGINAL ARTICLE

Twice daily biphasic insulin aspart improves postprandial glycaemic control more effectively than twice daily NPH insulin, with low risk of hypoglycaemia, in patients with type 2 diabetes

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Objective: Biphasic insulin aspart 30 (BIAsp30) is a dual release formulation, containing 30% soluble and 70% protamine-crystallized insulin aspart. This study compared the glycaemic control and safety profiles achieved with either twice daily BIAsp30 or NPH insulin in patients with type 2 diabetes not optimally controlled by oral hypoglycaemic agents (OHAs), NPH insulin or a combination of both.

Methods: In this 16-week multinational, parallel-group, double-blind trial, 403 such patients were randomized to receive either BIAsp30 or NPH insulin immediately before breakfast and evening meals. OHAs were discontinued at randomization. Efficacy was assessed by glycosylated haemoglobin (HbA_{1c}) and self-recorded daily 8-point blood glucose (BG) profiles. Hypoglycaemic and other adverse events were the chosen safety parameters.

Results: HbA_{1c} concentration decreased by >0.6% ($p < 0.0001$ vs. baseline) in both groups, with metabolic control continuing to improve throughout the trial without reaching a stable level. Patients who switched from once or twice daily NPH monotherapy to twice daily BIAsp30 achieved a significantly greater reduction in HbA_{1c} (0.78%) than those randomized to twice daily NPH insulin (0.58%; $p = 0.03$). BIAsp30 decreased mean daily postprandial glycaemic exposure to a greater extent than NPH insulin (mean difference = 0.69 mmol/l; $p < 0.0001$), reflecting greater decreases in the postbreakfast and postdinner increments (of 1.26 and 1.33 mmol/l, respectively), although postlunch increment was relatively increased (by 0.56 mmol/l). Despite the greater reduction in overall postprandial glycaemic exposure in the BIAsp30 group, the overall safety profile of BIAsp30 was equivalent to that of NPH insulin with <2% of patients experiencing major hypoglycaemia, and approximately 33% reporting minor hypoglycaemic episodes, in both groups.

Conclusion: Twice daily BIAsp30 reduced postprandial glucose exposure to a significantly greater extent than NPH insulin and was at least as effective at reducing HbA_{1c} in patients with type 2 diabetes. Both insulins were well tolerated. In patients poorly controlled on OHAs or NPH alone, glycaemic control can be improved by switching to twice daily BIAsp30, without increasing hypoglycaemic risk.

Keywords: biphasic insulin aspart, glycosylated haemoglobin, NPH insulin, oral hypoglycaemic agents, postprandial glucose control, type 2 diabetes

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Introduction

Type 2 diabetes is a progressive disease in which insulin secretion, particularly in response to prandial stimuli, diminishes in the setting of insulin resistance. Approximately 20–30% of people with type 2 diabetes require insulin to correct persistent hyperglycaemia [1], and the proportion that need replacement therapy increases with duration of disease [2].

Although the large United Kingdom Prospective Diabetes Study (UKPDS) demonstrated that intensified insulin treatment can reduce the incidence and delay progression of late diabetic complications in type 2 diabetes [3,4], rigorous multi-injection basal-bolus regimens may be unnecessary for most people with type 2 diabetes who retain some capacity for endogenous insulin secretion. For this reason, insulin is usually initiated in type 2 diabetes as simple, once or twice daily NPH insulin injections, a strategy that provides well for basal requirements but controls poorly the postprandial component of glycaemic control.

Biphasic insulin premixes provide the opportunity to address both the prandial and basal aspects of glucose regulation in insulin regimens that are simple to comply with. Currently, the most widely used premix is biphasic human insulin (BHI30), containing 30% soluble human insulin and 70% NPH insulin. Administered twice daily, BHI30 provides sufficient basal insulin to cover between meal requirements, but due to the delayed absorption of subcutaneously injected soluble human insulin, it offers limited control of postprandial hyperglycaemia, even when injected before meals in an attempt to coordinate plasma insulin peaks with peak glucose absorption [5–7]. Furthermore, 25% of patients fail to comply with the recommended injection-meal interval of 30 min [8], intended to optimize postprandial glycaemic control, and even when this advice is heeded, BHI30 can remain deficient in this important respect [9,10].

Insulin aspart is a rapid-acting insulin analogue that has been used successfully as the prandial component of basal-bolus regimens and is designed for injection immediately before meals. Used in this way, it can improve glycaemic control compared with human insulin-based regimens and can reduce the concomitant risk of hypoglycaemia [11–13]. Biphasic insulin aspart (BIAsp30), a dual release formulation containing 30% soluble and 70% protamine-crystallized insulin aspart, retains the improved postprandial glucose control characteristic of insulin aspart [10,14,15], as well as sharing the simplicity of other biphasic premixes. The protaminated insulin aspart fraction displays the same protracted absorption profile as NPH insulin [15], while the free fraction enables superior postprandial glycaemic control compared with BHI30 in type 2 diabetes [5,7,10].

Once daily NPH insulin is a widely used treatment in insulin-requiring patients with type 2 diabetes. When metabolic control fails, a second NPH injection is the customary intensification strategy; often no mealtime insulin is added to cover prandial requirements. This study investigated the potential advantages to glycaemic control, both glycosylated haemoglobin (HbA_{1c}) and postprandial glucose, of switching people with type 2 diabetes from NPH insulin to BIAsp30, as well as evaluating the use of BIAsp30 as a starting insulin in previously insulin naïve type 2 diabetes.

Patients and Methods

Patients

The study included 403 men and women aged $\geq$18 years with type 2 diabetes, $HbA_{1c} \leq 11.0\%$ and body mass index (BMI) $\leq 35\,kg/m^2$. Patients taking insulin were included only if their daily dose was <1.8 IU/kg. Participants represented a typical cross-section of people with type 2 diabetes, including insulin naïve patients and those receiving OHA therapy and/or once or twice daily NPH insulin monotherapy. Evidence of serious late diabetic complications or other serious disease excluded participation. All individuals gave informed consent prior to entering the study.

Design

Thirty-four trial sites in nine countries participated in this randomized, controlled, double-blind study, which comprised 11 visits over 18 weeks: a screening visit, nine visits during the 16 weeks of treatment and a follow-up visit 2 weeks after returning to pretrial medication regimen. Patients were randomized in a 1 : 1 ratio to receive subcutaneous BIAsp30 or human NPH insulin, both 100 IU/ml in 3-ml Penfill® cartridges, administered using the NovoPen® 3-ml delivery system (Novo Nordisk A/S, Bagsvaerd, Denmark), immediately before breakfast and evening meals. All OHA therapies were discontinued at randomization.

The starting dose in previously insulin naïve patients was 8–16 U/day, at the discretion of the attending physician; patients taking NPH insulin before the study commenced on a dose that reflected their pretrial requirement. Patients were instructed how to measure 8-point blood glucose (BG) readings using the BG meter supplied and were advised on the target range for fasting/preprandial BG of 5–8 mmol/l. Subsequent dose titration

was based on BG measurements in accordance with accepted diabetes treatment guidelines. After 16 weeks of treatment, patients discontinued the trial drug and reinstituted their pretrial regimen unless advised otherwise by their physician.

The study was conducted in accordance with the Helsinki Declaration and with Good Clinical Practice Guidelines.

Efficacy assessments

HbA_{1c} was measured four times during the 16 weeks of treatment, at monthly intervals. Other efficacy parameters included endpoints derived from 8-point BG profiles including prandial glucose increment at each meal (the mean difference between BG concentration 90 min after and before a meal), mean daily prandial glucose increment, mean daily BG concentration and minimum–maximum range of BG concentration.

Safety assessments

Hypoglycaemic Episodes

Hypoglycaemic episodes were recorded, whether observed or spontaneously reported. Minor episodes were defined as those during which the patient experienced hypoglycaemic symptoms (with or without confirmation by BG measurement), but did not require assistance. Major hypoglycaemia was defined by the requirement for third-party assistance or injection of glucose or glucagon.

Adverse Events

An adverse event was defined as any undesirable medical event occurring during the trial, irrespective of its relation to the trial product. Clinical laboratory abnormalities were considered adverse events only if suggestive of disease and/or organ toxicity and of a severity that necessitated active intervention. Adverse events were considered serious if they endangered life, required hospitalization or caused persistent and significant disability.

Statistical methods

The intention-to-treat (ITT) population was defined as all subjects who were exposed to trial products and had any efficacy data recorded. To be included within the per-protocol (PP) population, patients had to have discontinued OHAs, maintained compliance with treatment with a lapse of $\leq$5 days and have complied fully with all other aspects of the protocol.

Calculation of sample size was based on estimates of variability of HbA_{1c} in previous large-scale phase III trials in type 2 diabetes. Using a sample of 400 subjects, the size of the ITT population on which efficacy analyses were based, a difference of 0.3% units of HbA_{1c} can be detected with a power of 85%.

Efficacy

Analysis of the primary endpoint (HbA_{1c} during 16 weeks of treatment) was performed for both the ITT and PP populations using a repeated measures analysis of variance (ANOVA) model with postbaseline HbA_{1c} values as the response variables and baseline HbA_{1c} as a covariate. Secondary endpoints (last valid assessment of HbA_{1c}, BG endpoints and insulin dose) were analysed for the ITT population only. 8-point BG profiles were analysed as per the primary endpoint, without adjustment for baseline value. HbA_{1c} at 16 weeks was also analysed using ANOVA models including the prognostic demographic variables of gender, country, baseline BMI, duration of diabetes and previous treatment, and baseline HbA_{1c} was used as a covariate and treatment as a fixed effect.

Safety

Safety analyses were calculated on all subjects exposed to trial products using a significance level of 5%. No formal statistical analysis was performed on major hypoglycaemic events, as these were very few. A log linear Poisson regression model, with treatment and country as the only factors, was used to evaluate minor hypoglycaemic events, which were also analysed as daytime (06:00 until midnight) and nocturnal (midnight to 06:00) events using a Mantel Haenszel test to compare the probability of experiencing one or more hypoglycaemic episodes.

All statistical analyses were performed using SAS version 6.12 and version 8.0 including the StatXact procedure. The mixed procedure was used for the repeated measures ANOVA and the Genmod procedure for the Poisson regression analysis.

Results

Subjects

A total of 403 patients received at least one dose of either BIAsp30 (n = 201) or NPH insulin (n = 202). There were

11 withdrawals from the study, of which two or fewer patients in either group cited adverse effects or ineffective therapy as the cause. Physical examination revealed few abnormal findings, the most common being the neuropathic and cardiovascular complications of diabetes. Demographic data are presented in table 1.

Efficacy

HbA_{1c}

HbA_{1c} concentration decreased linearly and statistically significantly in both treatment groups (reductions of 0.67% and 0.61% in BIAsp30 and NPH groups, respectively; $p < 0.0001$ vs. baseline), and in both ITT and PP populations, during the 16 weeks of treatment (fig. 1). A parallel decline in HbA_{1c} concentration was observed, with reductions of approximately 0.1–0.2% units between each monthly visit ($p < 0.0001$ between visits), and HbA_{1c} had still not reached a stable level at trial completion. Lower baseline BMI was a significant predictor of lower HbA_{1c} at 16 weeks ($p = 0.01$).

When analysed by pretrial therapy, a highly significant predictor of HbA_{1c} at 16 weeks ($p = 0.002$), the most marked reductions in HbA_{1c} were observed in patients previously taking NPH insulin monotherapy and in those who were insulin naïve. Patients previously receiving NPH monotherapy who were switched to twice daily BIAsp30 achieved a significantly greater reduction in HbA_{1c} at 16 weeks than those placed on twice daily NPH insulin (−0.78% vs. −0.58%, respectively; $p = 0.03$) (fig. 2), an improvement due largely to the significant reduction in HbA_{1c} achieved during the first 4 weeks of treatment (−0.42%). This patient subgroup, whose mean baseline HbA_{1c} was 8.7% (lower than that of the insulin naïve and NPH/OHA combination therapy groups) completed the study with an HbA_{1c} of 7.9%.

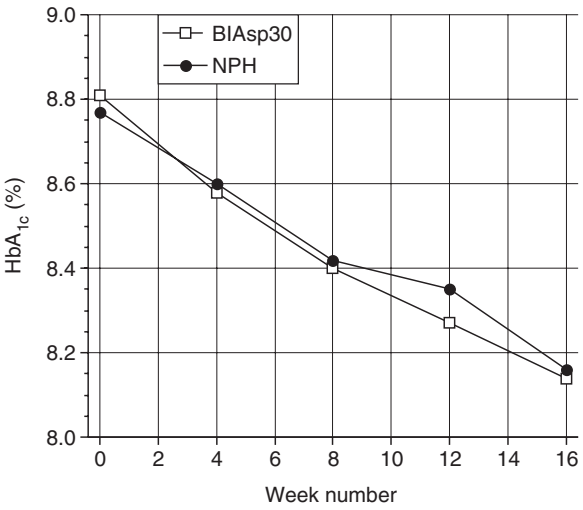

Fig. 1 Both biphasic insulin aspart 30 (BIAsp30) and NPH insulin reduced glycosylated haemoglobin (HbA_{1c}) significantly during 16 weeks of twice daily treatment (intention-to-treat (ITT) population; $p < 0.0001$ vs. baseline and between monthly visits).

Although twice daily BIAsp30 and NPH insulin also resulted in significant reductions in HbA_{1c} in insulin naïve and NPH/OHA combination therapy patients (table 2), there were no significant differences between study treatments in either group. Differences between participants taking NPH/OHA combination therapy and those who were insulin naïve prior to the trial failed to reach statistical significance.

Table 1 Patients' baseline demographic characteristics

Variable	Biphasic insulin aspart 30	NPH
Patients exposed (n)	201	202
Age (years)	59.3 ± 9.7	59.6 ± 9.1
Gender (% men)	47	50
Body mass index (kg/m^2)	28.0 ± 3.7	28.4 ± 3.7
Duration of diabetes (years)	9.2 ± 5.6	10.5 ± 6.8
Baseline glycosylated haemoglobin (%)	8.8 ± 1.3	8.8 ± 1.2
Previous treatment n (%)		
Insulin-treated		
NPH monotherapy	66 (33%)	66 (33%)
NPH + Oral hypoglycaemic agents	55 (27%)	59 (29%)
Insulin-naïve		
Oral hypoglycaemic agents only	78 (39%)	75 (37%)
None	2 (1%)	2 (1%)

Data are means ± SD.

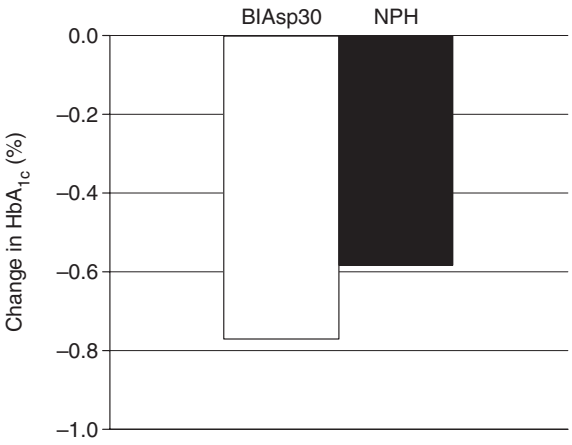

Fig. 2 Individuals taking NPH insulin monotherapy prior to the trial achieved a significantly greater reduction in glycosylated haemoglobin (HbA_{1c}) when switched to biphasic insulin aspart 30 (BIAsp30) twice daily compared to those who were treated with twice daily NPH insulin ($p = 0.03$).

Daily Blood Glucose Control

Mean daily BG concentration decreased significantly in both groups between baseline (11.2 and 11.3 mmol/l in BIAsp30 and NPH insulin groups, respectively) and study completion (9.4 mmol/l in both groups; $p < 0.0001$ vs. baseline), as did BG range (reductions of −1.55 and −1.57 mmol/l from baseline in BIAsp30 and NPH groups, respectively), both with no significant difference between treatments. Patients previously treated with NPH monotherapy achieved a significantly lower mean daily BG level when treated with BIAsp30 compared to NPH insulin (0.57 mmol/l lower when analysed from week 1 onwards; $p = 0.03$).

Postprandial Glucose Control

Postprandial BG control improved in both groups during the 16-week treatment phase. Postbreakfast values decreased by −2.3 and −2.2 mmol/l in the BIAsp30 and NPH groups, respectively; postlunch values by −1.9 and −2.1 mmol/l, respectively and postdinner values by −2.3 and −2.1 mmol/l, respectively. Mean prandial glucose increment over the three main meals was significantly lower in the BIAsp30 group (0.69 mmol/l lower; $p < 0.0001$, between groups) reflecting lower prandial glucose increments after breakfast (1.26 mmol/l lower; $p < 0.0001$) and dinner (1.33 mmol/l lower; $p < 0.0001$), although postlunch increment was 0.56 mmol/l higher ($p = 0.003$) (fig. 3).

Previously NPH monotherapy-treated patients showed trends similar to the whole group: postbreakfast and postdinner BG increments were significantly lower in the BIAsp30 group (by 1.85 and 1.56 mmol/l, respectively; $p < 0.0001$ between treatments from week 1 onwards in both cases). In this subgroup, however, the lunchtime prandial glycaemic increment was similar in both treatment groups. The mean prandial glucose increment in previously NPH monotherapy-treated patients was significantly lower in the BIAsp30 group than the NPH group (by 1.05 mmol/l; $p < 0.0001$ from week 1 onwards).

Fasting and Nocturnal Blood Glucose Control

BG levels recorded at bedtime or 23:00, whichever came earlier, were 0.72 mmol/l lower in the BIAsp30 group ($p < 0.004$), but by 02:00 no difference was apparent. Fasting BG levels decreased by similar amounts in both groups (1.4 and 1.5 mmol/l in BIAsp30 and NPH groups, respectively), but final values were 0.95 mmol/l higher in the BIAsp30 group ($p < 0.0001$). In the subgroup of previously NPH monotherapy-treated patients, the fasting BG level was 0.96 mmol/l higher in the BIAsp group compared to the NPH group ($p = 0.0009$ when analysed from week 1 onwards). Nocturnal glycaemic control was similar in both groups, 10.9 and 11.4% of patients taking BIAsp30 and NPH insulin, respectively, experienced one or more minor nocturnal hypoglycaemic episode ($p = NS$).

Insulin Dose

Mean daily insulin dose increased in both groups throughout the treatment period, without stabilizing at

Table 2 Reduction in glycosylated haemoglobin in patients who were insulin naïve or receiving NPH/oral hypoglycaemic agents combination therapy prior to treatment with twice daily biphasic insulin aspart 30 or NPH insulin. There was no significant difference between treatments in either patient subgroup

	Insulin naïve		NPH/Oral hypoglycaemic agents combination therapy	
	Biphasic insulin aspart 30	NPH insulin	Biphasic insulin aspart 30	NPH insulin
Glycosylated haemoglobin at baseline (%)	9.00	9.10	8.80	8.80
Glycosylated haemoglobin at 16 weeks (%)	8.24*	8.24*	8.36*	8.54*
Reduction in glycosylated haemoglobin (%)	−0.76	−0.86	−0.26	−0.44

*$p < 0.0001$ vs. baseline.

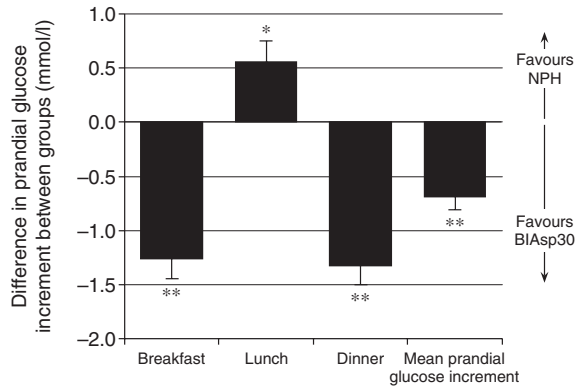

Fig. 3 Treatment with biphasic insulin aspart 30 (BIAsp30) resulted in lower prandial glucose increments at breakfast and dinner than NPH insulin, and a higher increment after lunch. The resulting mean daily prandial glucose increment was 0.69 mmol/l lower in the BIAsp30 group. Data are whole-group analyses. *$p < 0.005$; **$p < 0.0001$.

completion of the study (fig. 4). A greater mean dose increase was required in the BIAsp group (0.23 IU/kg) than the NPH group (0.15 IU/kg; $p = 0.004$).

Safety

Hypoglycaemia

Less than 2% of patients in either group experienced a major hypoglycaemic event. Minor hypoglycaemic episodes were numerically more frequent in the BIAsp30 group (341 events in 77 patients vs. 285 events in 68 patients, respectively), but the relative risk was not statistically significantly different between treatments (RR = 1.21 [95% CI: 0.77; 1.90]; $p = 0.40$).

Hypoglycaemic episodes were more frequent during the first week of treatment in both the groups and declined in frequency with continued treatment. There was no statistical difference in diurnal distribution of hypoglycaemic episodes between treatments.

Other Adverse Events

A similar number of adverse events occurred in both groups (141 events in 72 patients in the BIAsp group vs. 141 events in 76 patients in the NPH insulin group), most of which were mild or moderate in severity and considered unrelated to study medication. Symptoms reported most frequently were headaches and influenza-like symptoms. Three subjects were withdrawn due to adverse events; the only event related to medication was one case of protamine allergy in the NPH group. Only one patient in each group experienced change in weight (5% and 8% weight gain in the BIAsp30 and NPH patient, respectively).

Less than 5% of patients in either group experienced serious adverse events, although a slightly greater number were observed in the NPH group (eight events in seven patients) than in the BIAsp30 group (five events in five patients); all were considered unrelated to the study medication. There was no clinically relevant alteration in biochemical or haematological parameters.

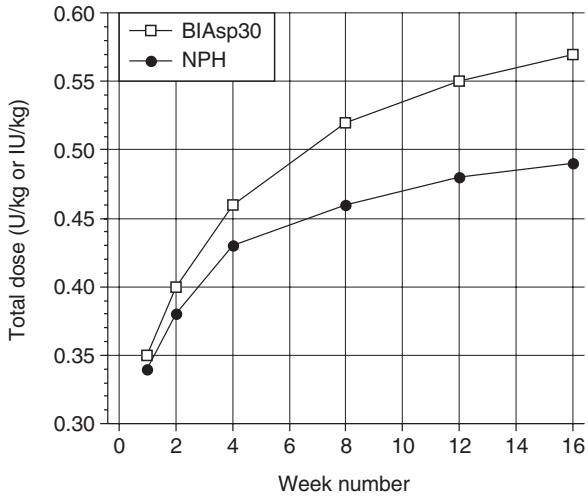

Fig. 4 Mean daily insulin dose increased in both BIAsp and NPH insulin groups, without stabilizing, although a greater dose increase was necessary in the biphasic insulin aspart 30 (BIAsp30) group ($p = 0.004$).

Discussion

The epidemiological evidence for a correlation between postprandial glycaemia and poor macrovascular outcomes has created the expectation that controlling postprandial glucose could be protective against some diabetic complications. Much of the excess protein glycation, characteristic of poorly controlled diabetes, takes place during postprandial peaks of hyperglycaemia [16–20], an important consideration as HbA_{1c} correlates with the risk of late microvascular and macrovascular complications and poor outcomes [21–24]. Furthermore, although prospective studies that intervene to reduce postprandial glucose levels are still awaited, several large epidemiological studies have proven that levels of BG following oral glucose challenge correlate more closely with adverse cardiovascular outcomes and death than do fasting BG levels [25–29].

The ideal treatment in type 2 diabetes would recreate the 'physiological insulin profile', in which plasma

insulin increases rapidly in the prandial setting, but basal insulin level is not unnecessarily high between meals, thereby reducing the risk of hypoglycaemia and weight gain. Although BHI30 was once the only premixed insulin available, the advent of analogue premixes, including BIAsp30, now allows patients the combined advantages of prandial and basal insulin supplementation, in a single injection that is given immediately before meals. The lifestyle flexibility afforded by these novel agents may have advantages for compliance, itself an important step towards better diabetes outcomes.

In this study, injections were given twice daily, immediately before breakfast and dinner, in accordance with recommendations for BIAsp30. While it could be argued that the design favoured BIAsp30, because NPH injections are not usually meal-related in timing, this regimen was chosen in order to enable a double-blind trial to be performed; it was the authors' belief that such a design would create less bias than using an open label design, which would have been the alternative.

In this study, twice daily NPH insulin and BIAsp30 significantly improved metabolic control over 16 weeks with significant month-by-month reductions in HbA_{1c} in both groups. HbA_{1c} continued to fall without reaching a stable level, indicating that a longer study is necessary to clarify the maximum potential of, and any differences between, the treatments. Reductions in HbA_{1c} were mirrored by decreasing mean daily BG concentrations and range and reduced postprandial glucose increment after injection in both groups. BIAsp30 demonstrated marked superiority in controlling postprandial glucose, supported by the fact that HbA_{1c} levels in this group paralleled those in the NPH group despite significantly higher fasting glucose levels. It can be speculated that had BIAsp30 been titrated more aggressively to achieve parity in fasting BG with NPH insulin, it might have been possible to demonstrate an HbA_{1c} advantage.

As anticipated, lower BMI improved the likelihood of achieving lower HbA_{1c} concentrations in this study. Body weight was not accounted for during statistical evaluation due to the low number of patients who gained weight in either group.

These results support the value of using BIAsp30 as a 'next step' in the management of patients poorly controlled on OHAs or once daily NPH insulin. Traditionally, the commonest step for patients failing OHAs is to start once daily NPH insulin, and for those on once daily NPH to add a second NPH injection when metabolic control becomes inadequate. This study highlights the potentially greater therapeutic success rate made possible when treatment is intensified by switching to BIAsp30 rather than by increasing daily NPH insulin dose. Furthermore, the benefits gained from using BIAsp30 are not achieved at the cost of increased hypoglycaemic risk because major hypoglycaemic events in this study were few (<2% of patients in each group), and the minor event rate was not significantly different to that of NPH insulin.

The relatively greater number of hypoglycaemic events during the first week in both groups suggests that patients learned quickly how to adjust the timing and dosing of insulin to reduce unwanted effects.

Insulin dose increased in both groups throughout the study, indicative of the higher dose required to provide sufficient basal insulin with a product composed of 70% basal insulin compared with that of a drug with 100% basal activity (NPH insulin). The dose increase was significantly greater in the BIAsp30 group, which probably reflects the fact that patients were titrating insulin to achieve a fasting glucose target, and so were effectively equalizing their overnight basal dose to achieve this target. Because the greater dose increase required for BIAsp30 did not incur any hypoglycaemic penalty or cause loss of postprandial glucose control, the finding poses no clinical concerns. The continued dose increases observed in this trial suggest that a further trial is required to investigate whether greater HbA_{1c} reduction is possible in the setting of dose-optimization.

The subgroup analyses performed should be interpreted with caution because there was no subgroup treatment protocol to ensure consistent management. Nonetheless, the trends revealed may be of clinical relevance and are therefore included. As expected, insulin naïve patients, and those taking NPH insulin monotherapy before the trial, achieved greater improvements in metabolic control when started on more intensive treatment than those previously treated with combination NPH/OHA therapy. A marked and significantly greater reduction in HbA_{1c} was observed in patients taking once daily NPH monotherapy who were switched to twice daily BIAsp30 compared with those who added a second NPH injection. Furthermore, and in common with whole group trends, this subgroup achieved significantly lower postbreakfast and postdinner BG values despite greater fasting BG levels. An additional advantage not observed in the whole group, but seen in patients previously treated with once daily NPH insulin monotherapy, was the small but significantly greater reduction in mean daily BG exposure achieved by switching to BIAsp30 rather than twice daily NPH insulin. These benefits suggest that patients inadequately controlled on once daily NPH monotherapy would do well to switch to BIAsp30 rather than adding a second NPH injection.

Patients starting BIAsp30 for the first time benefited from similar advantages to patients switching from NPH insulin, achieving significantly greater reductions in postprandial BG concentration after breakfast and dinner and significantly lower mean postprandial glycaemic exposure, compared to those started on twice daily NPH insulin.

BIAsp30 aims to combine the benefits of good overall metabolic and postprandial BG control, a low risk of hypoglycaemia and a simple treatment regimen. This study shows it to be effective in improving both aspects of glycaemic control, and well tolerated, in patients who require insulin to treat their type 2 diabetes, with particular advantages for those inadequately controlled on OHAs or once daily NPH insulin alone.

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