Clinical experience with insulin detemir, biphasic insulin aspart and insulin aspart in people with type 2 diabetes: Results from the Yanbu cohort of the A1chieve study

Moody El Harby, Ahmed Saeed
Department of Diabetic Centre, King Fahd Hospital, Madina, 1Department: Internal Medicine, El Amal Polyclinic, Yanbu, Saudi Arabia

ABSTRACT

Background: The A1chieve, a multicentric (28 countries), 24-week, non-interventional study evaluated the safety and effectiveness of insulin detemir, biphasic insulin aspart and insulin aspart in people with T2DM (n = 66,726) in routine clinical care across four continents. Materials and Methods: Data was collected at baseline, at 12 weeks and at 24 weeks. This short communication presents the results for patients enrolled from Yanbu, Saudi Arabia. Results: A total of 499 patients were enrolled in the study. Four different insulin analogue regimens were used in the study. Study patients had started on or were switched to biphasic insulin aspart (n = 256), insulin detemir (n = 146), insulin aspart (n = 3), basal insulin plus insulin aspart (n = 55) and other insulin combinations (n = 37). At baseline glycaemic control was poor for both insulin naïve (mean HbA1c: 9.4%) and insulin user (mean HbA1c: 9.5%) groups. After 24 weeks of treatment, both the study groups showed improvement in HbA1c (insulin naïve: −2.1%, insulin users: −1.8%). SADRs including major hypoglycaemic events did not occur in the study patients. Conclusion: Starting or switching to insulin analogues was associated with improvement in glycaemic control with a low rate of hypoglycaemia.

Key words: A1chieve study, insulin analogues, type 2 diabetes mellitus, Saudi Arabia, Yanbu

INTRODUCTION

Diabetes prevalence in Saudi Arabia is estimated to be 16.2%, affecting 2.7 million people.1 Fear of hypoglycaemia and gain in body weight are barriers for initiation of insulin therapy.1 Modern insulin analogues are a convenient new approach or tool to glycaemic control, associated with low number of hypoglycaemia and favourable weight change.1 A1chieve, a multinational, 24-week, non-interventional study, assessed the safety and effectiveness of insulin analogues in people with T2DM (n = 66,726) in routine clinical care.1 This short communication presents the results for patients enrolled from Yanbu, Saudi Arabia.

MATERIALS AND METHODS

Please refer to editorial titled: The A1chieve study: Mapping the Ibn Battuta trail.

RESULTS

A total of 499 patients were enrolled in the study. The patient characteristics for the entire cohort divided as insulin-naïve and insulin users is shown in the Table 1. Glycaemic control at baseline was poor in this population. The majority of patients (51.3%) started on or were switched to biphasic insulin aspart. Other groups were insulin detemir (n = 146), insulin aspart (n = 3), basal insulin plus insulin aspart (n = 55) and other insulin combinations (n = 37).
After 24 weeks of treatment, overall hypoglycaemia reduced from 16.3 to 7.2 events/patient-year in insulin user group whereas hypoglycaemic events increased from 0.9 to 2.0 events/patient-year in the insulin naïve group. However, this hypoglycaemia incidence in insulin naïve group at 24 weeks was still lower than that observed in insulin users at baseline. SADRs including major hypoglycaemic events did not occur in the study patients. Body weight and blood pressure decreased from baseline, while overall lipid profile improved at week 24 in complete cohort [Tables 2 and 3].

All parameters of glycaemic control improved from baseline to study end in the total cohort [Table 4].

### Biphasic insulin aspart ± OGLD

Of the total cohort, 256 patients started on biphasic insulin aspart ± OGLD, 153 (59.7%) were insulin naïve and 103 (40.3%) were insulin users. After 24 weeks of treatment, hypoglycaemic events or episodes increased for both the groups (insulin naïve: from 0.3 to 2.3 events/patient-year; insulin users: from 6.9 to 7.1 events/patient-year). Body weight decreased in both insulin naïve and user groups after 24 weeks [Tables 5 and 6].

All parameters of glycaemic control improved from baseline to study end in those who started on or were switched to biphasic insulin aspart for both insulin naïve and insulin user groups [Table 7].

### Basal + insulin aspart ± OGLD

Of the total cohort, 55 patients started on basal + insulin aspart ± OGLD, of which 17 (30.9%) were insulin naïve and 38 (69.1%) were insulin users. After 24 weeks, hypoglycaemic events reduced from 42.1 to 5.5 events/patient-year in insulin user group whereas hypoglycaemia

#### Table 1: Overall demographic data

| Parameters                                      | Insulin naïve | Insulin users | All   |
|------------------------------------------------|---------------|---------------|-------|
| Number of participants                         | 313           | 186           | 499   |
| Male N (%)                                      | 205 (66.6)    | 112 (61.9)    | 317 (64.8) |
| Female N (%)                                    | 103 (33.4)    | 69 (38.1)     | 172 (35.2) |
| Age (years)                                     | 50.3          | 52.3          | 51.0  |
| Weight (kg)                                     | 84.2          | 84.8          | 84.4  |
| BMI (kg/m²)                                     | 30.9          | 30.5          | 30.7  |
| Duration of DM (years)                          | 8.9           | 14.2          | 10.8  |
| No therapy                                     | 6             |               |       |
| >2 OGLD                                        | 20            | 11            | 31    |
| HbA₁c                                          | 9.4           | 9.5           | 9.4   |
| FPG (mmol/L)                                   | 11.2          | 11.2          | 11.2  |
| PPPG (mmol/L)                                  | 14.8          | 13.9          | 14.5  |
| Macrovascular complications, N (%)             | 81 (25.9)     | 90 (48.4)     | 171 (34.3) |
| Microvascular complications, N (%)             | 209 (66.8)    | 166 (89.2)    | 375 (75.2) |
| Pre-study therapy, N (%)                       |               |               |       |
| Insulin users                                   | 186 (37.3)    | 307 (61.5)    | 6 (1.2) |
| OGLD only                                      |               |               |       |
| No therapy                                     |               |               |       |
| Baseline therapy, N (%)                        |               |               |       |
| Insulin detemir±OGLD                           | 146 (29.3)    |               |       |
| Insulin aspart±OGLD                            | 3 (0.6)       |               |       |
| Basal+insulin aspart±OGLD                      | 55 (11.0)     |               |       |
| Biphasic insulin aspart±OGLD                   | 256 (51.3)    |               |       |
| Others                                         | 37 (7.4)      |               |       |
| Missing                                        | 2 (0.4)       |               |       |

BMI: Body mass index, OGLD: Oral glucose-lowering drug, HbA₁c: Glycated hemoglobin A₁c, FPG: Fasting plasma glucose, PPPG: Postprandial plasma glucose, DM: Diabetes mellitus

#### Table 2: Overall safety data

| Parameter                                                                 | N   | Baseline | Week 24 | Change from baseline |
|---------------------------------------------------------------------------|-----|----------|---------|----------------------|
| Hypoglycaemia (insulin naïve), events/patient-year                        |     |          |         |                      |
| All                                                                       | 313 | 0.9      | 2.0     | 1.1                  |
| Nocturnal                                                                 |     | 0.2      | 0.4     | 0.2                  |
| Major                                                                     |     | 0.1      | 0.0     | −0.1                 |
| Hypoglycaemia (insulin users), events/patient-year                        |     |          |         |                      |
| All                                                                       | 186 | 16.3     | 7.2     | −9.1                 |
| Nocturnal                                                                 |     | 5.8      | 3.1     | −2.7                 |
| Major                                                                     |     | 3.4      | 0.0     | −3.4                 |
| Body weight, kg                                                           |     |          |         |                      |
| Insulin naïve                                                             | 313 | 83.7     | 81.7    | −2.0                 |
| Insulin users                                                             | 186 | 84.6     | 82.9    | −1.7                 |
| Lipids and BP (insulin naïve)                                             |     |          |         |                      |
| LDL-C, mean (mmol/L), (N, % <2.5 mmol/L)                                  | 241 | 3.1 (50, 20.7) | 2.4 (140, 58.3) | −0.7 |
| HDL-C, mean (mmol/L), (N, % >1.0 mmol/L)                                  | 239 | 1.0 (142, 59.4) | 1.1 (91, 78.6) | 0.1 |
| TG, mean (mmol/L), (N, % <2.3 mmol/L)                                     | 278 | 2.4 (168, 60.4) | 1.7 (250, 90.6) | −0.6 |
| SBP, mean (mmHg), (N, % <130 mmHg)                                        | 312 | 136.9 (85, 27.2) | 124.9 (171, 58.6) | −12.0 |
| Lipids and BP (insulin users)                                             |     |          |         |                      |
| LDL-C, mean (mmol/L), (N, % <2.5 mmol/L)                                  | 138 | 3.0 (40, 29.0) | 2.7 (69, 43.9) | −0.4 |
| HDL-C, mean (mmol/L), (N, % >1.0 mmol/L)                                  | 139 | 1.0 (79, 56.8) | 1.1 (94, 59.9) | 0 |
| TG, mean (mmol/L), (N, % <2.3 mmol/L)                                     | 160 | 2.2 (94, 58.8) | 1.9 (142, 88.2) | −0.3 |
| SBP, mean (mmHg), (N, % <130 mmHg)                                        | 184 | 142.8 (31, 16.8) | 131.9 (47, 27.2) | −10.9 |

BP: Blood pressure, LDL-C: Low-density lipoprotein cholesterol, HDL-C: High-density lipoprotein cholesterol, TG: Triglycerides, SBP: Systolic blood pressure
increased from 0.0 to 2.4 events/patient-year in insulin naïve group [Tables 8 and 9].

All parameters of glycaemic control improved from baseline to study end in those who started on or were basal + insulin aspart ± OGLDs for both insulin naïve and insulin user groups [Table 10].

**Insulin detemir ± OGLD**

Of the total cohort, 146 patients started on insulin detemir ± OGLD, of which 133 (91.1%) were insulin naïve and 13 (8.9%) were insulin users. After 24 weeks of starting or switching to insulin detemir, hypoglycaemic events reduced from 4.0 to 0.0 events/patient-year in insulin users whereas no change in hypoglycaemia was noted in insulin naïve group compared to baseline. Body weight also decreased at the end of the study [Tables 11 and 12].

**Table 3: Insulin dose**

| Parameter | N Pre-study | N Baseline | N Week 24 |
|-----------|-------------|------------|-----------|
| Insulin, U/day | | | |
| Insulin naïve | 0 | 0.0 | 312 | 35.5 | 293 | 42.8 |
| Insulin users | 186 | 54.5 | 84 | 59.6 | 173 | 69.8 |

**Table 4: Overall efficacy data**

| Parameter | N Baseline | Week 24 | Change from baseline |
|-----------|------------|---------|----------------------|
| Glycaemic control (insulin naïve) | HbA1c, mean (%) | 287 | 9.4 | 7.4 | −2.1 |
| FPG, mean (mmol/L) | 263 | 11.2 | 6.8 | −4.3 |
| PPGG, mean (mmol/L) | 220 | 14.8 | 8.9 | −6.2 |

**Table 5: Biphasic insulin aspart±oral glucose-lowering drug safety data**

| Parameter | N Baseline | Week 24 | Change from baseline |
|-----------|------------|---------|----------------------|
| Hypoglycaemia, events/patient-year | Insulin naïve | 153 | 0.3 | 2.3 | 2.0 |
| Insulin users | 103 | 6.9 | 7.1 | 0.2 |
| Body weight, kg | Insulin naïve | 148 | 86.3 | 84.4 | −1.9 |
| Insulin users | 97 | 87.4 | 84.7 | −2.7 |

**Table 6: Insulin dose**

| Parameter | N Pre-study | N Baseline | N Week 24 |
|-----------|-------------|------------|-----------|
| Insulin dose, U/day | | | |
| Insulin naïve | 0 | 0.0 | 153 | 46.2 | 150 | 49.5 |
| Insulin users | 103 | 53.1 | 103 | 60.9 | 101 | 66.6 |

**Table 7: Biphasic insulin aspart±oral glucose-lowering drug efficacy data**

| Parameter | N Baseline | Week 24 | Change from baseline |
|-----------|------------|---------|----------------------|
| Glycaemic control (insulin naïve) | HbA1c, mean (%) | 148 | 9.3 | 7.1 | −2.2 |
| FPG, mean (mmol/L) | 141 | 11.1 | 6.4 | −4.7 |
| PPGG, mean (mmol/L) | 126 | 15.6 | 8.4 | −7.2 |

**Table 8: Basal+insulin aspart±oral glucose-lowering drug safety data**

| Parameter | N Baseline | Week 24 | Change from baseline |
|-----------|------------|---------|----------------------|
| Hypoglycaemia, events/patient-year | Insulin naïve | 17 | 0.0 | 2.4 | 2.4 |
| Insulin users | 38 | 42.1 | 5.3 | −36.6 |
| Body weight, kg | Insulin naïve | 16 | 80.7 | 79.7 | −1.0 |
| Insulin users | 31 | 81.8 | 82.2 | 0.3 |

**Table 9: Insulin dose**

| Parameter | N Pre-study | N Baseline | N Week 24 |
|-----------|-------------|------------|-----------|
| Insulin, U/day | | | |
| Insulin naïve | 0 | 0.0 | 17 | 54.9 | 16 | 74.1 |
| Insulin users | 38 | 66.9 | 37 | 59.0 | 33 | 79.4 |

**Table 10: Basal+insulin aspart±oral glucose-lowering drug efficacy data**

| Parameter | N Baseline | Week 24 | Change from baseline |
|-----------|------------|---------|----------------------|
| Glycaemic control (insulin naïve) | HbA1c, mean (%) | 16 | 10.1 | 8.0 | −2.2 |
| FPG, mean (mmol/L) | 16 | 12.4 | 7.6 | −4.8 |
| PPGG, mean (mmol/L) | 16 | 14.2 | 9.5 | −4.7 |

HbA1c: Glycated haemoglobin A1c, FPG: Fasting plasma glucose, PPGG: Postprandial plasma glucose
All parameters of glycaemic control improved from baseline to study end in those who started on or were switched to insulin detemir ± OGLDs for both insulin-naïve and insulin user groups [Table 13].

### Table 11: Insulin detemir±oral glucose-lowering drug safety data

| Parameter                  | N     | Baseline | Week 24 | Change from baseline |
|----------------------------|-------|----------|---------|----------------------|
| Hypoglycaemia, events/patient-year |       |          |         |                      |
| Insulin naïve              | 133   | 1.4      | 1.4     | 0.0                  |
| Insulin users              | 13    | 4.0      | 0.0     | −0.4                 |
| Body weight, kg            |       |          |         |                      |
| Insulin naïve              | 112   | 80.7     | 78.3    | −2.4                 |
| Insulin users              | 12    | 80.6     | 79.5    | −1.1                 |

### Table 12: Insulin dose

| Insulin dose, U/day | N | Pre-study | N | Baseline | N | Week 24 |
|---------------------|---|-----------|---|----------|---|---------|
| Insulin naïve       | 0 | 0.0       | 133| 18.9     | 120| 29.0    |
| Insulin users       | 13| 33.2      | 13 | 26.5     | 12 | 44.6    |

### Table 13: Insulin detemir±oral glucose-lowering drug efficacy data

| Parameter                  | N     | Baseline | Week 24 | Change from baseline |
|----------------------------|-------|----------|---------|----------------------|
| Glycaemic control (insulin naïve) |       |          |         |                      |
| HbA1c, mean (%)            | 117   | 9.5      | 7.6     | −1.9                 |
| FPG, mean (mmol/L)         | 101   | 10.9     | 7.2     | −3.8                 |
| PPGG, mean (mmol/L)        | 75    | 13.8     | 8.9     | −4.9                 |
| Glycaemic control (insulin users) |       |          |         |                      |
| HbA1c, mean (%)            | 12    | 8.8      | 7.2     | −1.6                 |
| FPG, mean (mmol/L)         | 11    | 11.3     | 7.7     | −3.6                 |
| PPGG, mean (mmol/L)        | 9     | 13.8     | 9.7     | −4.1                 |

HbA1c: Glycated haemoglobin A1c, FPG: Fasting plasma glucose, PPGG: Postprandial plasma glucose

**Insulin aspart ± OGLD**

Of the total cohort, 3 patients started on insulin aspart ± OGLD and all of them were insulin users. After 24 weeks of treatment, hypoglycaemic events reduced from 30.3 to 0.0 events/patient-year. All parameters of glycaemic control improved from baseline to study end in those who started on or were switched insulin aspart ± OGLDs.

**CONCLUSION**

Our study reports improved glycaemic control following 24 weeks of treatment with any of the insulin analogues (biphasic insulin aspart; basal + insulin aspart; insulin detemir; insulin aspart) with or without OGLD. Their administration even caused a small weight reduction. SADRs including major hypoglycaemic events did not occur in the study patients. Though the findings are limited by number of patients, still the trend indicates that insulin analogues can be considered effective and possess a safe profile for treating type 2 diabetes in Yanbu, Saudi Arabia.

**REFERENCES**

1. IDF Diabetes Atlas. 5th ed. Available from: http://www.idf.org/atlasmap/atlasmap [Last accessed on 2013 Jun 10].
2. Korytkowski M. When oral agents fail: Practical barriers to starting insulin. Int J Obes Relat Metab Disord 2002;26 Suppl 3:S18-24.
3. Hirsch IB. Insulin analogues. N Engl J Med 2005;352:174-83.
4. Shah SN, Litwak L, Haddad J, Chakkarwar PN, Hajjaji I. The A1chieve study: A 60 000-person, global, prospective, observational study of basal, meal-time, and biphasic insulin analogs in daily clinical practice. Diabetes Res Clin Pract 2010;88 Suppl 1:S11-6.

Cite this article as: El Harby M, Saeed A. Clinical experience with insulin detemir, biphasic insulin aspart and insulin aspart in people with type 2 diabetes: Results from the Yanbu cohort of the A1chieve study. Indian J Endocrinol Metab 2013;17:S441-4.

Source of Support: Nil, Conflict of Interest: None declared.