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

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A B S T R A C T

Background: The A1chieve, is a multicentric (28 countries), 24-weeks, non-interventional study to evaluate 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 Manama, kingdom of Bahrain. Results: A total of 115 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 = 67), insulin detemir (n = 16), insulin aspart (n = 4), basal insulin plus insulin aspart (n = 21) and other insulin combinations (n = 7). At baseline, glycaemic control was poor for both insulin naïve (mean HbA1c: 10.2%) and insulin users (mean HbA1c: 9.8%) groups. After 24 weeks of treatment, both the groups showed improvement in HbA1c (insulin naïve: −1.1%, insulin users: −1.3%). 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, Bahrain, insulin analogues, type 2 diabetes mellitus

INTRODUCTION

The prevalence of diabetes in Bahrain is estimated to be 22.4%, affecting 185 thousand and is ranked the 9th in the world.[1] Fear of hypoglycaemia and gain in body weight are barriers for initiation of insulin therapy.[2] Modern insulin analogues are a convenient new approach or tool to glycaemic control, associated with low number of hypoglycaemia and favourable weight change.[3] A1chieve, a multinational, 24-weeks, non-interventional study, assessed the safety and effectiveness of insulin analogues in people with T2DM (n = 66,726) in routine clinical care.[4] This short communication presents the results for patients enrolled from Manama, Kingdom of Bahrain.

MATERIALS AND METHODS

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

RESULTS

A total of 115 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 started on or were switched to biphasic insulin aspart (58.3%). Other groups were on insulin detemir (n = 16), insulin aspart (n = 4), basal insulin plus insulin aspart (n = 21) and other insulin combinations (n = 7).
After 24 weeks of treatment, overall hypoglycaemic events reduced from 4.3 events/patient-year to 1.3 events/patient-year in the insulin users group and increased from 0.0 events/patient-year to 1.9 events/patient-year in the insulin naive group. However, this hypoglycaemia incidence in insulin naive 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 increased while overall lipid profile improved at week 24 in the entire 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, 67 patients started on biphasic insulin aspart ± OGLD, of which 19 (28.3%) were insulin naïve patients and 48 (71.7%) were insulin users. After 24 weeks of starting or switching to biphasic insulin aspart, hypoglycaemic events reduced from 4.6 events/patient-year to 1.6 events/patient-year in the insulin user group and increased from 0.0 events/patient-year to 1.6 events/patient-year in the insulin naive group. Body weight increased after 24 weeks in both insulin naïve and insulin user groups [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 users groups [Table 7].

### Basal + insulin aspart ± OGLD

Of the total cohort, 21 patients were started on basal + insulin aspart ± OGLD, of which 2 (9.5%) were insulin naïve patients and 19 (90.5%) were insulin users. After 24 weeks of starting or switching to basal + insulin aspart, hypoglycaemic events reduced from 1.4 events/patient-year to 0.9 events/patient-year in the insulin users group, whereas

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**Table 1: Overall demographic data**

| Parameters                                      | Insulin naive | Insulin users | All  |
|------------------------------------------------|---------------|---------------|------|
| Number of participants                         | 40            | 75            | 115  |
| Male N (%)                                     | 22 (55.0)     | 39 (52.0)     | 61 (53.0) |
| Female N (%)                                   | 18 (45.0)     | 36 (48.0)     | 54 (47.0) |
| Age (years)                                    | 55.4          | 49.0          | 51.3  |
| Weight (kg)                                    | 76.6          | 75.1          | 75.6  |
| BMI (kg/m²)                                    | 29.1          | 28.9          | 28.9  |
| Duration of DM (years)                         | 9.9           | 10.8          | 10.5  |
| No therapy                                     | 3             |               |      |
| >2 OGLD                                        | 9             | 7             | 16    |
| HbA₁c c                                        | 10.2          | 9.8           | 10.0  |
| FPG (mmol/L)                                   | 13.7          | 9.8           | 10.9  |
| PPPG (mmol/L)                                  | 19.0          | 15.8          | 16.6  |
| Macrovascular complications, N (%)             | 12 (30.0)     | 7 (9.3)       | 19 (16.5) |
| Microvascular complications, N (%)             | 26 (65.0)     | 35 (46.7)     | 61 (53.0) |
| Pre-study therapy, N (%)                       | Insulin users | 75 (65.2)     |      |
| OGLD only                                      | 37 (32.2)     |               |      |
| No therapy                                     | 3 (2.6)       |               |      |
| Baseline therapy, N (%)                        | Insulin detemir±OGLD | 16 (13.9) |      |
| Insulin aspart±OGLD                            | 4 (3.5)       |               |      |
| Basal+ insulin aspart±OGLD                     | 21 (18.3)     |               |      |
| Biphasic insulin aspart±OGLD                   | 67 (58.3)     |               |      |
| Others                                         | 7 (6.1)       |               |      |
| Missing                                        | 0             |               |      |

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                                            | 40 | 0.0      | 1.9     | 1.9                  |
| Nocturnal                                      | 0.0| 0.4      | 0.4     |                      |
| Major                                          | 0.0| 0.0      | 0.0     |                      |
| Hypoglycaemia (insulin users), events/patient-year |    |          |         |                      |
| All                                            | 75 | 4.3      | 1.3     | -3.0                 |
| Nocturnal                                      | 0.4| 0.2      | 0.2     |                      |
| Major                                          | 0.4| 0.0      | 0.0     |                      |
| Body weight, kg                                |    |          |         |                      |
| Insulin naïve                                  | 40 | 77.2     | 78.6    | 1.4                  |
| Insulin users                                  | 75 | 73.4     | 74.5    | 1.1                  |
| Lipids and BP (insulin naïve)                  |    |          |         |                      |
| LDL-C, mean (mmol/L), (N, % <2.5 mmol/L)       | 15 | 5.2 (5, 33.3) | 3.0 (5, 45.5) | -2.2 |
| HDL-C, mean (mmol/L), (N, % >1.0 mmol/L)       | 14 | 1.2 (8, 57.1) | 1.0 (6, 60.0) | -0.2 |
| TG, mean (mmol/L), (N, % <2.3 mmol/L)          | 18 | 1.7 (13, 72.2) | 1.5 (11, 100) | -0.2 |
| SBP, mean (mmHg), (N, % <130 mmHg)             | 40 | 131.5 (17, 42.5) | 127.1 (17, 50.0) | -4.4 |
| Lipids and BP (insulin users)                  |    |          |         |                      |
| LDL-C, mean (mmol/L), (N, % <2.5 mmol/L)       | 16 | 2.3 (9, 56.3) | 1.9 (29, 78.4) | -0.4 |
| HDL-C, mean (mmol/L), (N, % >1.0 mmol/L)       | 16 | 1.2 (14, 87.5) | 1.3 (35, 89.7) | 0     |
| TG, mean (mmol/L), (N, % <2.3 mmol/L)          | 48 | 1.5 (41, 85.4) | 1.4 (36, 94.7) | -0.1 |
| SBP, mean (mmHg), (N, % <130 mmHg)             | 72 | 125.6 (38, 52.8) | 120.2 (36, 66.7) | -5.4 |

BP: Blood pressure, LDL-C: Low-density lipoprotein cholesterol, HDL-C: High-density lipoprotein cholesterol, TG: Triglycerides, SBP: Systolic blood pressure
insulin hypoglycaemic events remained nil similar to that of baseline in insulin naive group. Body weight increased for insulin users at the end of the study [Tables 8 and 9].

All parameters of glycaemic control improved from baseline to study end in those who started on or were switched to basal + insulin aspart ± OGLDs in the insulin users [Table 10].

**Insulin detemir ± OGLD**

Of the total cohort, 16 patients were started on insulin detemir ± OGLD, of which 14 (87.5%) were insulin naïve patients and 2 (12.5%) were insulin users. After 24 weeks of starting or switching to insulin detemir, hypoglycaemic events reduced from 13.0 events/patient-year to 0.0 events/patient-year in the insulin users group, whereas hypoglycaemia increased from 0.0 events/patient-year to 3.6 events/patient-year in insulin naive group. A small decrease in body weight was observed in the insulin naive group [Tables 11 and 12].

All parameters of glycaemic control improved from baseline to study end in those who started on or were switched to insulin detemir ± OGLDs in the insulin naive group, whereas mean HbA1c values deteriorated in the insulin users [Table 13].

Table 3: Insulin dose

| Insulin dose, U/day | Pre-study N | Baseline N | Week 24 N |
|--------------------|-------------|------------|-----------|
| Insulin naïve      | 0           | 40         | 39.0      |
| Insulin users      | 75          | 74         | 51.9      |

Table 4: Overall efficacy data

| Glycaemic control (insulin naïve) | N | Baseline | Week 24 | Change from baseline |
|----------------------------------|---|----------|---------|---------------------|
| HbA1c, mean (%)                  | 30 | 10.2     | 9.1     | −1.1                |
| FPG, mean (mmol/L)               | 14 | 13.7     | 8.8     | −4.9                |
| PPPG, mean (mmol/L)              | 13 | 19.0     | 15.9    | −3.1                |
| Glycaemic control (insulin users) | N | Baseline | Week 24 | Change from baseline |
| HbA1c, mean (%)                  | 56 | 9.8      | 8.5     | −1.3                |
| FPG, mean (mmol/L)               | 38 | 9.8      | 8.2     | −1.7                |
| PPPG, mean (mmol/L)              | 37 | 15.8     | 13.3    | −2.5                |

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

| Parameter                              | N | Baseline | Week 24 | Change from baseline |
|----------------------------------------|---|----------|---------|---------------------|
| Hypoglycaemia, events/patient-year     | 19 | 1.4      | 0.9     | −0.5                |
| Body weight, kg                        | 14 | 76.8     | 78.7    | 2.0                 |

Table 6: Insulin dose

| Insulin dose, U/day | Pre-study N | Baseline N | Week 24 N |
|--------------------|-------------|------------|-----------|
| Insulin naïve      | 0           | 19         | 43.7      |
| Insulin users      | 48          | 48         | 46.8      |

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

| Parameter                              | N | Baseline | Week 24 | Change from baseline |
|----------------------------------------|---|----------|---------|---------------------|
| Glycaemic control (insulin naïve)      | 15 | 10.6     | 9.5     | −1.1                |
| HbA1c, mean (%)                        | 9  | 12.6     | 9.2     | −3.4                |
| FPG, mean (mmol/L)                     | 7  | 18.1     | 16.2    | −1.9                |
| Glycaemic control (insulin users)      | 40 | 10.1     | 8.6     | −1.5                |
| HbA1c, mean (%)                        | 34 | 9.9      | 8.4     | −1.5                |
| FPG, mean (mmol/L)                     | 32 | 16.0     | 13.7    | −2.3                |

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

| Parameter                              | N | Baseline | Week 24 | Change from baseline |
|----------------------------------------|---|----------|---------|---------------------|
| Hypoglycaemia, events/patient-year     | 19 | 1.4      | 0.9     | −0.5                |
| Bodyweight, kg                         | 14 | 76.8     | 78.7    | 2.0                 |

Table 9: Insulin dose

| Insulin dose, U/day | Pre-study N | Baseline N | Week 24 N |
|--------------------|-------------|------------|-----------|
| Insulin users      | 19          | 58.3       | 18        |

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

| Parameter                              | N | Baseline | Week 24 | Change from baseline |
|----------------------------------------|---|----------|---------|---------------------|
| Glycaemic control (insulin users)      | 14 | 9.4      | 8.2     | −1.2                |
| HbA1c, mean (%)                        | 4  | 9.4      | 6.3     | −3.1                |
| FPG, mean (mmol/L)                     | 4  | 13.9     | 10.1    | −3.8                |
| PPPG, mean (mmol/L)                    | 4  | 13.9     | 10.1    | −3.8                |
Of the total cohort, 4 patients started on insulin aspart ± OGLD, of which 2 (50%) were insulin naïve patients and 2 (50%) were insulin users. After 24 weeks of starting treatment or switching to insulin aspart, hypoglycaemia remained nil, similar to that of baseline for both insulin naïve and insulin users groups. An increase in body weight was also observed in both the groups. Mean HbA1c and PPPG values improved in the insulin naïve group while mean PPPG values improved in insulin users.

**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. SADRs including major hypoglycaemic events did not occur in the study patients. Body weight increased in the overall cohort. Though the findings are limited by the number of patients, still the trend indicates that insulin analogues can be considered effective and possesses a safe profile for treating type 2 diabetes in Manama, Kingdom of Bahrain.

**REFERENCES**

1. IDF Diabetes Atlas. 5th ed. 2012. Update. Available from: http://www.idf.org/diabetesatlas/5e/update2012.
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.

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

| Parameter                        | N | Baseline | Week 24 | Change from baseline |
|----------------------------------|---|----------|---------|----------------------|
| Hypoglycaemia, events/patient-year |   |          |         |                      |
| Insulin naïve                    | 14| 0.0      | 3.6     | 3.6                  |
| Body weight, kg                  | 10| 80.3     | 80.1    | -0.2                 |

**Table 12: Insulin dose**

| Insulin dose, U/day | N | Pre-study | N | Baseline | N | Week 24 | N | Week 24 |
|---------------------|---|-----------|---|----------|---|---------|---|---------|
| Insulin naïve       | 0 | 0.0       | 14| 16.9     | 10| 29.3    |   |         |

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

| Parameter                        | N | Baseline | Week 24 | Change from baseline |
|----------------------------------|---|----------|---------|----------------------|
| Glycaemic control (insulin naïve)|   |          |         |                      |
| HbA1c, mean (%)                  | 8 | 10.1     | 8.4     | -1.7                 |
| FPG, mean (mmol/L)               | 5 | 15.6     | 8.0     | -7.6                 |
| PPPG, mean (mmol/L)              | 3 | 17.3     | 15.7    | -1.6                 |

HbA1c: Glycated haemoglobin A1c, FPG: Fasting plasma glucose, PPPG: Postprandial plasma glucose, OGLD: Oral glucose-lowering drug

**Insulin aspart ± OGLD**

Of the total cohort, 4 patients started on insulin aspart ± OGLD, of which 2 (50%) were insulin naïve patients and 2 (50%) were insulin users. After 24 weeks of starting treatment or switching to insulin aspart, hypoglycaemia remained nil, similar to that of baseline for both insulin naïve and insulin users groups. An increase in body weight was also observed in both the groups. Mean HbA1c and PPPG values improved in the insulin naïve group while mean PPPG values improved in insulin users.

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

| Parameter                        | N | Baseline | Week 24 | Change from baseline |
|----------------------------------|---|----------|---------|----------------------|
| Hypoglycaemia, events/patient-year |   |          |         |                      |
| Insulin naïve                    | 14| 0.0      | 3.6     | 3.6                  |
| Body weight, kg                  | 10| 80.3     | 80.1    | -0.2                 |

**Table 12: Insulin dose**

| Insulin dose, U/day | N | Pre-study | N | Baseline | N | Week 24 | N | Week 24 |
|---------------------|---|-----------|---|----------|---|---------|---|---------|
| Insulin naïve       | 0 | 0.0       | 14| 16.9     | 10| 29.3    |   |         |

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

| Parameter                        | N | Baseline | Week 24 | Change from baseline |
|----------------------------------|---|----------|---------|----------------------|
| Glycaemic control (insulin naïve)|   |          |         |                      |
| HbA1c, mean (%)                  | 8 | 10.1     | 8.4     | -1.7                 |
| FPG, mean (mmol/L)               | 5 | 15.6     | 8.0     | -7.6                 |
| PPPG, mean (mmol/L)              | 3 | 17.3     | 15.7    | -1.6                 |

HbA1c: Glycated haemoglobin A1c, FPG: Fasting plasma glucose, PPPG: Postprandial plasma glucose, OGLD: Oral glucose-lowering drug

**Insulin aspart ± OGLD**

Of the total cohort, 4 patients started on insulin aspart ± OGLD, of which 2 (50%) were insulin naïve patients and 2 (50%) were insulin users. After 24 weeks of starting treatment or switching to insulin aspart, hypoglycaemia remained nil, similar to that of baseline for both insulin naïve and insulin users groups. An increase in body weight was also observed in both the groups. Mean HbA1c and PPPG values improved in the insulin naïve group while mean PPPG values improved in insulin users.

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**REFERENCES**

1. IDF Diabetes Atlas. 5th ed. 2012. Update. Available from: http://www.idf.org/diabetesatlas/5e/update2012.
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:** Hussein WI, Taha N. Clinical experience with insulin detemir, biphasic insulin aspart and insulin aspart in people with type 2 diabetes: Results from the Bahraini cohort of the A1chieve study. Indian J Endocr Metab 2013;17:S461-4.

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