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

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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 Haryana, India. Results: A total of 345 patients were enrolled in the study. Four different insulin analogue regimens were used in the study. Patients had started on or were switched to biphasic insulin aspart (n = 236), insulin detemir (n = 66), insulin aspart (n = 28), basal insulin plus insulin aspart (n = 1) and other insulin combinations (n = 14). At baseline glycaemic control was poor for both insulin naïve (mean HbA1c: 10.7%) and insulin user (mean HbA1c: 10.5%) groups. After 24 weeks of treatment, both the groups showed improvement in HbA1c (insulin naïve: −3.9%, insulin users: −3.3%). SADRs including major hypoglycaemic events or episodes did not occur in any of 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, Haryana, insulin analogues, type 2 diabetes mellitus

INTRODUCTION

62.4 million Indians were reported to have type 2 diabetes mellitus (T2DM) putting India on the forefront of diabetic epidemic across globe.[1,2] Fear of hypoglycaemia and gain in body weight are barriers for initiation of insulin therapy.[3] Modern insulin analogues are a convenient new approach or tool to glycaemic control, associated with low number of hypoglycaemia and favourable weight change.[4] 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.[5] This short communication presents the results for patients enrolled from Haryana, India.

MATERIALS AND METHODS

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

RESULTS

A total of 345 patients were enrolled in the study. The patient characteristics for the entire cohort divided as insulin-naïve and insulin users is shown in Table 1. Glycaemic control at baseline was poor in this population. The majority of patients (68.41%) started on or switched to biphasic insulin aspart. Other groups were insulin detemir (n = 66), insulin aspart (n = 28), basal insulin plus insulin aspart (n = 1) and other insulin combinations (n = 14).
After 24 weeks of treatment, overall hypoglycaemic events reduced from 1.1 events/patient-year to 0.1 events/patient-year in insulin naive group and from 2.6 events/patient-year to 0.0 events/patient-year in insulin user group. The hypoglycaemia incidence in insulin naive group at 24 weeks was lower than that observed in insulin users at baseline. SADRs including major hypoglycaemic events or episodes did not occur in any of the study patients. Blood pressure decreased in the total cohort, but the finding was limited by number of observations. Quality of life improved at 24 weeks [Table 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, 236 patients started on biphasic insulin aspart ± OGLD, of which 197 (83.5%) were insulin naive and 39 (16.5%) were insulin users. After 24 weeks of starting or switching to biphasic insulin aspart, hypoglycaemic events reduced from 0.6 events/patient-year to 0.0 events/patient-year in insulin naïve group and from 3.0 events/patient-year to 0.0 events/patient-year in insulin users group. Quality of life improved at the end of the study [Table 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 ± OGLD for both insulin naïve and insulin user groups [Table 7].

**Basal + insulin aspart ± OGLD**
Of the total cohort, only one patient was started on basal + insulin aspart ± OGLD.

**Insulin detemir ± OGLD**
Of the total cohort, 66 patients started on insulin detemir ± OGLD, of which 58 (87.9%) were insulin naive and 08 (12.1%) were insulin users. After 24 weeks of starting or switching to biphasic insulin aspart, hypoglycaemic events reduced from 2.7 events/patient-year to 0.0 events/patient-year in insulin naïve group and from 1.6 events/patient-year to 0.0 events/patient-year in insulin users group. Quality of life improved at the end of the study [Table 5 and 6].

### Table 1: Overall demographic data

| Parameters                          | Insulin naïve | Insulin users | All       |
|-------------------------------------|---------------|---------------|-----------|
| Number of participants              | 295           | 50            | 345       |
| Male (%)                            | 199 (67.5)    | 38 (76.0)     | 237 (68.7)|
| Female (%)                          | 96 (32.5)     | 12 (24.0)     | 108 (31.3)|
| Age (years)                         | 45.1          | 49.9          | 45.8      |
| Weight (kg)                         | 67.1          | 69.7          | 67.5      |
| BMI (kg/m²)                         | 26.7          | 25.6          | 26.6      |
| Duration of DM (years)              | 4.0           | 5.1           | 4.2       |
| No therapy                          | 20            |               |           |
| >2 OGLD                             | 3             |               | 3         |
| HbA₁c                               | 10.7          | 10.5          | 10.7      |
| FPG (mmol/L)                        | 13.3          | 11.9          | 13.1      |
| PPPG (mmol/L)                       | 18.6          | 17.8          | 18.5      |
| Macrovascular complications, N (%)  | 17 (5.8)      | 8 (16.0)      | 25 (7.2)  |
| Microvascular complications, N (%)  | 65 (22.0)     | 20 (40.0)     | 85 (24.6) |

BM: 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                                    | 295 | 1.1      | 0.1     | −1.0                 |
| Nocturnal                              | 50  | 0.6      | 0.0     | −0.6                 |
| Major                                  | 50  | 0.0      | 0.0     | 0.0                  |
| Hypoglycaemia (insulin users), events/patient-year |      |          |         |                      |
| All                                    | 50  | 2.6      | 0.0     | −2.6                 |
| Nocturnal                              | 50  | 1.0      | 0.0     | −1.0                 |
| Major                                  | 50  | 0.8      | 0.0     | −0.8                 |
| Body weight, kg                       |     | 206      | 66.5    | 66.8                 |
| Insulin naïve                          | 41  | 69.2     | 70.5    | 1.3                  |
| BP (insulin naïve)                     |     | 48       | 128.8 (18, 37.5) | 126.1 (5, 62.5) | −2.6 |
| SBP, mean (mmHg), (N, %<130 mmHg)     | 19  | 132.9 (6, 31.6) | 126.3 (4, 57.1) | −6.6 |
| Quality of life, VAS scale (0-100)    |     | 207      | 52.8    | 83.6                 |
| Insulin naïve                          | 41  | 53.2     | 79.8    | 26.6                 |

BP: Blood pressure, SBP: Systolic blood pressure, VAS: Visual analogue scale
patient-year to 0.0 events/patient-year in insulin users group. Body weight decreased and quality of life improved at 24 weeks [Table 8 and 9].

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 10].

### Table 3: Insulin dose

| Parameter          | N  | Pre-study | N  | Baseline | N  | Week 24 |
|--------------------|----|-----------|----|----------|----|---------|
| Insulin naïve      | 0  | 0.0       | 295| 32.4     | 210| 29.9    |
| Insulin users      | 50 | 24.8      | 50 | 32.5     | 42 | 29.8    |

### Table 4: Overall efficacy data

| Glycaemic control (insulin naïve) | N  | Baseline | Week 24 | Change from baseline |
|----------------------------------|----|----------|---------|----------------------|
| HbA1c, mean (%)                  | 206| 10.7     | 6.8     | −3.9                 |
| FPG, mean (mmol/L)               | 207| 13.3     | 7.7     | −5.7                 |
| PPPG, mean (mmol/L)              | 188| 18.6     | 11.2    | −7.5                 |

Glycaemic control (insulin users)

| Parameter          | N  | Baseline | Week 24 | Change from baseline |
|--------------------|----|----------|---------|----------------------|
| HbA1c, mean (%)    | 40 | 10.5     | 7.2     | −3.3                 |
| FPG, mean (mmol/L) | 42 | 11.9     | 7.4     | −4.4                 |
| PPPG, mean (mmol/L)| 28 | 17.8     | 13.2    | −4.5                 |

Achievement of HbA1c <7.0% at week 24

| Parameter          | N  | Baseline | Week 24 | Change from baseline |
|--------------------|----|----------|---------|----------------------|
| Insulin naïve      | 207| 45.9%    |         |                      |
| Insulin users      | 42 | 40.5%    |         |                      |

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

| Parameter          | N  | Baseline | Week 24 | Change from baseline |
|--------------------|----|----------|---------|----------------------|
| Hypoglycaemia, events/patient-year | | | | |
| Insulin naïve      | 197| 0.6      | 0.0     | −0.6                 |
| Insulin users      | 39 | 3.0      | 0.0     | −3.0                 |
| Body weight, kg    | 130| 66.5     | 66.9    | 0.3                  |
| Insulin naïve      | 30 | 69.7     | 72.1    | 2.3                  |
| Insulin users      | 129| 52.4     | 83.9    | 31.5                 |
| Quality of life, VAS scale (0-100) | | | | |
| Insulin naïve      | 30 | 53.9     | 78.6    | 24.7                 |
| Insulin users      | 47 | 10.9     | 6.6     | −4.3                 |
| FPG, mean (mmol/L) | 47 | 14.2     | 7.8     | −6.4                 |
| PPPG, mean (mmol/L)| 47 | 18.8     | 10.3    | −8.5                 |

### Table 6: Insulin dose

| Parameter          | N  | Pre-study | N  | Baseline | N  | Week 24 |
|--------------------|----|-----------|----|----------|----|---------|
| Insulin naïve      | 0  | 0.0       | 197| 30.8     | 131| 30.3    |
| Insulin users      | 39 | 25.8      | 39 | 33.3     | 31 | 30.8    |

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

| Parameter          | N  | Baseline | Week 24 | Change from baseline |
|--------------------|----|----------|---------|----------------------|
| Glycaemic control (insulin naive) | | | | |
| HbA1c, mean (%)    | 130| 10.6     | 6.8     | −3.8                 |
| FPG, mean (mmol/L) | 129| 13.2     | 7.6     | −5.6                 |
| PPPG, mean (mmol/L)| 114| 18.6     | 11.0    | −7.7                 |

### Table 8: Insulin detemir±oral glucose-lowering drug safety data

| Parameter          | N  | Baseline | Week 24 | Change from baseline |
|--------------------|----|----------|---------|----------------------|
| Hypoglycaemia, events/patient-year | | | | |
| Insulin naïve      | 58 | 2.7      | 0.0     | −2.7                 |
| Insulin users      | 8  | 1.6      | 0.0     | −1.6                 |
| Body weight, kg    | 47 | 66.4     | 65.5    | 0.8                  |
| Insulin naïve      | 8  | 64.9     | 63.7    | −1.2                 |
| Insulin users      | 18 | 75.0     | 70.3    | −4.7                 |
| Quality of life, VAS scale (0-100) | | | | |
| Insulin naïve      | 47 | 50.1     | 85.5    | 35.4                 |
| Insulin users      | 8  | 53.0     | 84.5    | 31.5                 |

### Table 9: Insulin dose

| Parameter          | N  | Pre-study | N  | Baseline | N  | Week 24 |
|--------------------|----|-----------|----|----------|----|---------|
| Insulin naïve      | 0  | 0.0       | 58 | 32.4     | 47 | 30.5    |
| Insulin users      | 8  | 18.8      | 8  | 26.8     | 8  | 26.3    |

### Table 10: Insulin detemir±oral glucose-lowering drug efficacy data

| Parameter          | N  | Baseline | Week 24 | Change from baseline |
|--------------------|----|----------|---------|----------------------|
| Glycaemic control (insulin naive) | | | | |
| HbA1c, mean (%)    | 47 | 10.9     | 6.6     | −4.3                 |
| FPG, mean (mmol/L) | 47 | 14.2     | 7.8     | −6.4                 |
| PPPG, mean (mmol/L)| 47 | 18.8     | 10.3    | −8.5                 |

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

| Parameter          | N  | Baseline | Week 24 | Change from baseline |
|--------------------|----|----------|---------|----------------------|
| Glycaemic control (insulin naive) | | | | |
| HbA1c, mean (%)    | 31 | 10.4     | 7.2     | −3.2                 |
| FPG, mean (mmol/L) | 31 | 11.6     | 7.3     | −4.3                 |
| PPPG, mean (mmol/L)| 18 | 17.5     | 13.9    | −3.6                 |
and 2 (7.1%) were insulin users. After 24 weeks of starting or switching to biphasic insulin aspart, hypoglycaemic events reduced from 1.0 events/patient-year to 0.0 events/patient-year in insulin naïve group whereas hypoglycaemia was nil in insulin users group similar to that of baseline. Quality of life improved at 24 weeks [Table 11 and 12].

All parameters of glycaemic control improved from baseline to study end in those who started on or were switched to insulin aspart ± OGLDs for insulin naïve group [Table 13].

**CONCLUSION**

Our study reports improved glycaemic control and quality of life following 24 weeks of treatment with any of the insulin analogues (Biphasic insulin aspart; insulin detemir; insulin aspart) with or without OGLD. A decrease in FPG and PPPG was noted for biphasic insulin aspart; insulin detemir; insulin aspart groups; this improvement was higher in insulin naïve compared to insulin users. A small weight reduction was noted for insulin detemir group only. SADRs including major hypoglycaemic events or episodes did not occur in any of 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 Haryana, India.

**REFERENCES**

1. Wild S, Roglic G, Green A, Sicree R, King H. Global prevalence of diabetes: Estimates for the year 2000 and projections for 2030. Diabetes Care 2004;27:1047-53.
2. Shetty P. Public health: India’s diabetes time bomb. Nature 2012;485:S14-6.
3. Korytkowski M. When oral agents fail: Practical barriers to starting insulin. Int J Obes Relat Metab Disord 2002;26 Suppl 3:S18-24.
4. Hirsch IB. Insulin analogues. N Engl J Med 2005;352:174-83.
5. Shah SN, Litwak L, Haddad J, Chakkarwar PN, Hajiaji 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.

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