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

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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 Andhra Pradesh, India. Results: A total of 3077 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 = 2452), insulin detemir (n = 308), insulin aspart (n = 226), basal insulin plus insulin aspart (n = 21) and other insulin combinations (n = 68). At baseline glycaemic control was poor for both insulin naïve (mean HbA1c: 8.9%) and insulin user (mean HbA1c: 9.2%) groups. After 24 weeks of treatment, both the groups showed improvement in HbA1c (insulin naïve: −1.2%, insulin users: −1.1%). 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, Andhra Pradesh, 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 act as 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.[3] 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.[3] This short communication presents the results for patients enrolled from Andhra Pradesh, India.

MATERIALS AND METHODS

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

RESULTS

A total of 3077 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 (79.7%) started on or switched to biphasic insulin aspart. Other groups were insulin detemir (n = 308), insulin
aspart \((n = 226)\), basal insulin plus insulin aspart \((n = 21)\) and other insulin combinations \((n = 68)\).

After 24 weeks of treatment, overall hypoglycaemic events reduced in both insulin naïve (from 0.9 events/patient-year to 0.0 events/patient-year) and insulin user (from 0.6 events/patient-year to 0.0 events/patient-year) groups. No hypoglycaemic episode in insulin naïve group even at 24 weeks suggests low event rate than insulin users at baseline. A decrease in body weight was also observed at the end of the study. SADRs including major hypoglycaemic events did not occur in any of the study patients. Blood pressure decreased while overall lipid profile and quality of life improved at week 24 in the total cohort [Tables 2 and 3].

All parameters of glycaemic control improved from baseline to study end in those who started on or were

### Table 1: Overall demographic data

| Parameters                  | Insulin naïve | Insulin users | All          |
|-----------------------------|---------------|---------------|--------------|
| Number of patients          | 2366          | 711           | 3077         |
| Male N (%)                  | 1533 (64.8)   | 463 (65.1)    | 1996 (64.9)  |
| Female N (%)                | 833 (35.2)    | 248 (34.9)    | 1081 (35.1)  |
| Age (years)                 | 50.3          | 54.8          | 51.3         |
| Weight (kg)                 | 69.7          | 71.2          | 70.1         |
| BMI (kg/m²)                 | 26.0          | 27.1          | 26.3         |
| Duration of DM (years)      | 4.5           | 10.2          | 5.8          |
| No therapy                  | 18            |               |              |
| >2 OGLD                     | 33            | 8             | 41           |
| HbA₁c                       | 8.9           | 9.2           | 8.9          |
| FPG (mmol/L)                | 9.8           | 10.3          | 9.9          |
| PPPG (mmol/L)               | 14.3          | 15.1          | 14.5         |
| Macrovascular complications, N (%) | 492 (20.8) | 353 (49.7) | 845 (27.5) |
| Microvascular complications, N (%)  | 665 (28.1) | 543 (76.5) | 1208 (39.3) |

**Table 2: Overall safety data**

| Parameter                                      | \(N\) | Baseline | Week 24 | Change from baseline |
|-----------------------------------------------|-------|---------|---------|----------------------|
| Hypoglycaemia (insulin naïve), events/patient-year |       |         |         |                      |
| All                                           | 2366  | 0.9     | 0.0     | −0.9                 |
| Nocturnal                                     |       | 0.3     | 0.0     | −0.3                 |
| Major                                         |       | 0.0     | 0.0     | 0.0                  |
| Hypoglycaemia (insulin users), events/patient-year |       |         |         |                      |
| All                                           | 711   | 0.6     | 0.0     | −0.6                 |
| Nocturnal                                     |       | 0.2     | 0.0     | −0.2                 |
| Major                                         |       | 0.1     | 0.0     | −0.1                 |
| Body weight, kg                               |       |         |         |                      |
| Insulin naïve                                 | 1972  | 69.6    | 68.1    | −1.5                 |
| Insulin users                                 | 673   | 71.2    | 69.6    | −1.6                 |
| Lipids and BP (insulin naïve)                 |       |         |         |                      |
| LDL-C, mean (mmol/L), \(N, <2.5 \text{ mmol/L}\) | 938   | 3.0 (3.17, 3.38) | 2.8 (2.51, 3.99) | −0.3 |
| HDL-C, mean (mmol/L), \(N, >1.0 \text{ mmol/L}\) | 938   | 1.0 (1.49, 5.21) | 0.9 (2.58, 40.48) | −0.1 |
| TG, mean (mmol/L), \(N, <2.3 \text{ mmol/L}\) | 1005  | 2.2 (6.64, 6.91) | 2.0 (549, 81.7) | −0.2 |
| SBP, mean (mmHg), \(N, <130 \text{ mmHg}\)   | 1571  | 126.9 (108, 57.8) | 122.6 (1131, 77.1) | −4.2 |
| Lipids and BP (insulin users)                 |       |         |         |                      |
| LDL-C, mean (mmol/L), \(N, <2.5 \text{ mmol/L}\) | 611   | 3.2 (142, 23.2) | 2.9 (115, 25.0) | −0.3 |
| HDL-C, mean (mmol/L), \(N, >1.0 \text{ mmol/L}\) | 612   | 1.0 (350, 57.2) | 0.9 (189, 40.5) | −0.1 |
| TG, mean (mmol/L), \(N, <2.3 \text{ mmol/L}\) | 630   | 2.2 (441, 70.0) | 2.0 (412, 84.6) | −0.2 |
| SBP, mean (mmHg), \(N, <130 \text{ mmHg}\)   | 667   | 134.2 (239, 35.8) | 135.8 (352, 56.7) | −8.4 |
| Quality of life, VAS scale (0-100)            |       |         |         |                      |
| Insulin naïve                                 | 2188  | 56.6    | 66.7    | 10.1                 |
| Insulin users                                 | 686   | 54.1    | 63.9    | 9.8                  |

BP: Blood pressure, LDL-C: Low-density lipoprotein cholesterol, HDL-C: High-density lipoprotein cholesterol, TG: Triglycerides, SBP: Systolic blood pressure, VAS: Visual analogue scale
switched to biphasic insulin aspart for both insulin naïve and insulin user groups [Table 7].

**Basal + insulin aspart ± OGLD**

Of the total cohort, 21 patients started on basal + insulin aspart ± OGLD, of which 11 (52.4%) were insulin naïve and 10 (47.6%) were insulin users. After 24 weeks of starting or switching to insulin aspart, hypoglycaemic events reduced from 1.2 events/patient-year to zero events in insulin naïve group, whereas hypoglycaemia was nil in insulin user group similar to baseline. A decrease in body weight and improvement in quality of life was also observed at 24 weeks [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 for both insulin naïve and insulin user groups [Table 10].

**Insulin detemir ± OGLD**

Of the total cohort, 308 patients who started on insulin detemir ± OGLD, of which 250 (81.2%) were insulin naïve and 58 (18.8%) were insulin users. After 24 weeks of starting or switching to insulin detemir, hypoglycaemic events reduced to nil for both insulin naïve (0.8 events/patient-year at baseline) and insulin user

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**Table 3: Insulin dose**

| Insulin dose, U/day | N  | Pre-study | N  | Baseline | N  | Week 24 |
|---------------------|----|-----------|----|----------|----|---------|
| Insulin naïve       | 0  | 0.0       | 2366| 25.4     | 2198| 26.8    |
| Insulin users       | 711| 35.3      | 709 | 31.2     | 687 | 32.7    |

**Table 4: Overall efficacy data**

| Parameter | N | Baseline | Week 24 | Change from baseline |
|-----------|---|----------|---------|----------------------|
| Glycaemic control (insulin naïve) | | | | |
| HbA1c, mean (%) | 2168 | 8.9 | 7.6 | −1.2 |
| FPG, mean (mmol/L) | 2191 | 9.8 | 7.1 | −2.7 |
| PPGP, mean (mmol/L) | 2185 | 14.3 | 10.1 | −4.2 |
| Glycaemic control (insulin users) | | | | |
| HbA1c, mean (%) | 679 | 9.2 | 8.1 | −1.1 |
| FPG, mean (mmol/L) | 683 | 10.3 | 8.3 | −2.0 |
| PPGP, mean (mmol/L) | 684 | 15.1 | 12.3 | −2.8 |

**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 | 1939 | 0.9 | 0.0 | −0.9 |
| Insulin users | 513 | 0.7 | 0.0 | −0.7 |
| Body weight, kg | | | | |
| Insulin naïve | 1616 | 69.1 | 67.6 | −1.4 |
| Insulin users | 486 | 71.3 | 69.8 | −1.6 |
| Quality of life, VAS scale (0-100) | | | | |
| Insulin naïve | 1796 | 56.7 | 66.8 | 10.1 |
| Insulin users | 495 | 54.4 | 64.0 | 9.6 |

**Table 6: Insulin dose**

| Insulin dose, U/day | N | Pre-study | N | Baseline | N | Week 24 |
|---------------------|---|-----------|---|----------|---|---------|
| Insulin naïve       | 0 | 0.0       | 1939| 25.9     | 1804| 27.5    |
| Insulin users       | 513| 35.6      | 513 | 30.8     | 496 | 31.9    |

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**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 (%) | 1777 | 8.8 | 7.6 | −1.3 |
| FPG, mean (mmol/L) | 1798 | 9.8 | 7.0 | −2.8 |
| PPGP, mean (mmol/L) | 1795 | 14.2 | 9.9 | −4.2 |
| Glycaemic control (insulin users) | | | | |
| HbA1c, mean (%) | 490 | 9.1 | 8.1 | −1.1 |
| FPG, mean (mmol/L) | 494 | 10.1 | 8.1 | −2.0 |
| PPGP, mean (mmol/L) | 494 | 14.9 | 12.2 | −2.7 |

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**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 | 11 | 1.2 | 0.0 | −1.2 |
| Insulin users | 10 | 0.0 | 0.0 | 0.0 |
| Body weight, kg | | | | |
| Insulin naïve | 8 | 67.4 | 65.8 | −1.6 |
| Insulin users | 10 | 65.0 | 64.2 | −0.8 |
| Quality of life, VAS scale (0-100) | | | | |
| Insulin naïve | 8 | 55.3 | 65.8 | 10.5 |
| Insulin users | 10 | 54.5 | 63.4 | 8.9 |

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**Table 9: Insulin dose**

| Insulin dose, U/day | N | Pre-study | N | Baseline | N | Week 24 |
|---------------------|---|-----------|---|----------|---|---------|
| Insulin naïve       | 0 | 0.0       | 11 | 64.5     | 8 | 47.1    |
| Insulin users       | 10 | 32.2      | 10 | 45.9     | 10 | 36.2    |
(0.2 events/patient-year at baseline) groups. Body weight decreased and quality of life improved after 24 weeks of treatment [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 for both insulin-naïve and insulin user groups [Table 13].

**Insulin aspart ± OGLD**

Of the total cohort, 226 patients started on insulin aspart ± OGLD, of which 129 (57.1%) were insulin naïve and 97 (42.9%) were insulin users. After 24 weeks of treatment starting or switching to insulin aspart hypoglycaemia reduced to zero for both insulin naïve (1.1 events/patient-year at baseline) and insulin user (insulin users: 0.4 events/patient-year at baseline) groups. A decrease in body weight and improvement in quality of life was observed at 24 weeks [Tables 14 and 15].

All parameters of glycaemic control improved from baseline to study end in those who started on or were
switched to insulin aspart ± OGLDs for both insulin naïve and insulin user groups [Table 16].

**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; basal + insulin aspart; insulin detemir; insulin aspart) with or without OGLD. SADRs including major hypoglycaemic events or episodes did not occur in any of the study patients after 24 week of treatment. A decrease in body weight was observed for all the four regimens. 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 Andhra Pradesh, 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, Hajjaji I. The A,chieve 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.