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

Akhil Joshi, Anand Meenawat1, Rajeev Patni2, D. C. Sharma3, Shashi Panicker4

Diabetes Thyroid and Hormone Centre, Kota, 1Satyam Hospital and Research Centre, Jodhpur, 2SDMH and Research Centre, Jaipur, 3Department of Endocrinology, RNT Medical College, Udaipur, 4Sanjeevani Hospital and Diabetes Centre, Jaipur, Rajasthan, India

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 Rajasthan, India. Results: A total of 477 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 = 340), insulin detemir (n = 90), insulin aspart (n = 37), basal insulin plus insulin aspart (n = 7) and other insulin combinations (n = 2). At baseline glycaemic control was poor for both insulin naïve (mean HbA1c: 8.3%) and insulin user (mean HbA1c: 8.4%) groups. After 24 weeks of treatment, both the groups showed improvement in HbA1c (insulin naïve: −0.9%, insulin users: −1.2%). Major hypoglycaemic events decreased from 0.5 events/patient-year to 0.0 events/patient-year in insulin naïve group while no change from baseline (1.3 events/patients-year) was observed for insulin users. SADRs were not reported 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, insulin analogues, Rajasthan, 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 hypos 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.[4] This short communication presents the results for patients enrolled from Rajasthan, India.

MATERIALS AND METHODS

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

RESULTS

A total of 477 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 (71.28%) started on or switched to biphasic insulin...
aspart. Other groups were insulin detemir (n = 28), insulin aspart (n = 24), basal insulin plus insulin aspart (n = 13) and other insulin combinations (n = 3).

After 24 weeks of treatment, overall hypoglycaemic events reduced from 2.1 events/patient-year to 0.0 events/patient-year in insulin naïve group and from 6.8 events/patient-year to 0.0 events/patient-year in insulin users group. The hypoglycaemia incidence in insulin naïve group at 24 weeks was lower than that observed in insulin users at baseline. Major hypoglycaemic events decreased from 0.5 events/patient-year to 0.0 events/patient-year in insulin naïve group while no change from baseline (1.3 events/patients-year) was observed for insulin user group. SADRs were not reported in any of the study patients. Quality of life improved after 24 weeks [Table 2 and 3].

Mean HbA1c and FPG values improved from baseline to study end in the insulin naïve group [Table 4].

**Biphasic insulin aspart ± OGLD**

Of the total cohort, 340 patients started on biphasic insulin aspart ± OGLD, of which 153 (45%) were insulin naïve and 187 (55%) were insulin users. After 24 weeks of starting or switching to biphasic insulin aspart, hypoglycaemic events reduced from 2.3 events/patient-year to 0.0 events/patient-year in insulin naïve group and from 6.3 events/patient-year to 0.0 events/patient-year in insulin users. Body weight decreased in the insulin naïve group. Quality of life improved at the end of the study [Table 5 and 6].

Mean HbA1c and FPG values improved from baseline to study end in those who started on or were switched to biphasic insulin aspart for insulin naïve group [Table 7].

**Basal + insulin aspart ± OGLD**

Of the total cohort, 7 patients started on basal + insulin aspart ± OGLD, of which 2 (28.6%) were insulin naïve and 5 (71.4%) were insulin users. After 24 weeks of treatment, hypoglycaemic events reduced from 10.4 events/patient-year to 0.0 events/patient-year in insulin users whereas hypoglycaemia remained nil in insulin naïve group.

### Table 1: Overall demographic data

| Parameters | Insulin naïve | Insulin users | All |
|-----------|--------------|---------------|-----|
| Number of patients | 239 | 238 | 477 |
| Male (%) | 152 (63.6) | 170 (71.4) | 322 (67.5) |
| Female (%) | 87 (36.4) | 68 (28.6) | 155 (32.5) |
| Age (years) | 45.0 | 49.6 | 46.9 |
| Weight (kg) | 70.0 | 74.6 | 72.2 |
| BMI (kg/m²) | 26.0 | 31.2 | 27.2 |
| Duration of DM (years) | 3.9 | 8.4 | 6.2 |
| >2 OGLD | 3 | 21 | 24 |
| HbA1c (mmol/L) | 8.3 | 8.4 | 8.3 |
| FPG (mmol/L) | 8.6 | 8.9 | 8.6 |
| Microvascular complications, N (%) | - | 19 (8.0) | 19 (4.0) |
| complications, N (%) | 5 (2.1) | 8 (3.4) | 13 (2.7) |
| Pre-study therapy, N (%) | Insulin users | 238 (49.90) | 239 (50.11) |
| OGLD only | | |
| Baseline therapy, N (%) | Insulin detemir±OGLD | 90 (18.87) | 90 (18.76) |
| Insulin aspart±OGLD | 37 (7.76) | 37 (7.76) |
| Basal+insulin aspart±OGLD | 7 (1.47) | 7 (1.47) |
| Biphasic insulin aspart±OGLD | 340 (71.28) | 340 (71.28) |
| Others | 2 (0.42) | 2 (0.42) |
| Missing | 1 (0.21) | 1 (0.21) |

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 | 239 | 2.1 | 0.0 | -2.1 |
| Nocturnal | 0.0 | 0.0 | 0.0 |
| Major | 0.5 | 0.0 | -0.5 |
| Hypoglycaemia (insulin users), events/patient-year | | | | |
| All | 238 | 6.8 | 0.0 | -6.8 |
| Nocturnal | 2.6 | 0.0 | -2.6 |
| Major | 1.3 | 1.3 | 0.0 |
| Body weight, kg | | | | |
| Insulin naïve | 151 | 72.7 | 71.4 | -1.2 |
| Insulin users | 1 | 62.0 | 62.0 | 0.0 |
| Lipids and BP (insulin naïve) | | | | |
| SBP, mean (mmHg), (N, % <130 mmHg) | 231 | 130.0 (148, 64.1) | 120.8 (127, 83.0) | -9.2 |
| BP (insulin users) | | | | |
| SBP, mean (mmHg), (N, % <130 mmHg) | 195 | 120.0 (183, 93.8) | 120.0 (1, 100) | 0.0 |
| Quality of life, VAS scale (0-100) | | | | |
| Insulin naïve | 152 | 53.8 | 80.8 | 27.0 |
| Insulin users | 1 | 50.0 | 77.0 | 27.0 |

BP: Blood pressure, SBP: Systolic blood pressure, VAS: Visual analogue scale
group, similar to baseline. Quality of life improved after 24 weeks of treatment [Table 8 and 9].

Mean HbA1c and FPG values improved from baseline to study end in those who started on or were switched to basal + insulin aspart ± OGLDs for insulin naïve group.

**Insulin detemir ± OGLD**

Of the total cohort, 90 patients started on insulin detemir ± OGLD, of which 57 (63.3%) were insulin naïve and 33 (36.7%) were insulin users. After 24 weeks of starting or switching to insulin detemir, hypoglycaemic events reduced from 2.5 events/patient-year to 0.0 events/patient-year in insulin naïve and from 6.3 events/patient-year to 0.0 events/patient-year in insulin user groups [Table 10 and 11].

Mean HbA1c and FPG values improved from baseline to study end in those who started on or were switched to insulin detemir ± OGLDs for insulin-naïve group [Table 12].

---

**Table 3: Insulin dose**

| Parameter | N | Pre-study | Baseline | N | Week 24 |
|-----------|----|-----------|----------|----|---------|
| Insulin naive | 0 | 0.0 | 238 | 23.8 | 153 | 24.0 |
| Insulin users  | 238 | 28.8 | 238 | 25.2 | 1 | 24.0 |

**Table 4: Overall efficacy data**

| Parameter | N | Baseline | Week 24 | Change from baseline |
|-----------|----|----------|---------|---------------------|
| Glycaemic control (insulin naïve) | 153 | 8.3 | 7.4 | −0.9 |
| FPG, mean (mmol/L) | 152 | 8.6 | 7.0 | −1.5 |

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

| Parameter | N | Baseline | Week 24 | Change from baseline |
|-----------|----|----------|---------|---------------------|
| Hypoglycaemia, events/patient-year | 153 | 2.3 | 0.0 | −2.3 |
| Insulin naïve | 187 | 6.3 | 0.0 | −6.3 |
| Body weight, kg | 75 | 66.8 | 66.3 | −0.5 |
| Quality of life, VAS scale (0-100) | 76 | 54.0 | 81.2 | 27.2 |

**Table 6: Insulin dose**

| Parameter | N | Pre-study | Baseline | N | Week 24 |
|-----------|----|-----------|----------|----|---------|
| Insulin naive | 0 | 0.0 | 153 | 26.0 | 77 | 28.4 |
| Insulin users  | 187 | 30.0 | 187 | 26.7 | - | - |

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

| Parameter | N | Baseline | Week 24 | Change from baseline |
|-----------|----|----------|---------|---------------------|
| Glycaemic control (insulin naïve) | 77 | 8.3 | 7.4 | −0.9 |
| FPG, mean (mmol/L) | 77 | 8.6 | 6.9 | −1.7 |

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

| Parameter | N | Baseline | Week 24 | Change from baseline |
|-----------|----|----------|---------|---------------------|
| Hypoglycaemia, events/patient-year | 5 | 10.4 | 0 | −10.4 |

**Table 9: Insulin dose**

| Parameter | N | Pre-study | Baseline | N | Week 24 |
|-----------|----|-----------|----------|----|---------|
| Insulin users  | 5 | 38.4 | 5 | 34.0 | - | - |

**Table 10: Insulin detemir±oral glucose-lowering drug safety data**

| Parameter | N | Baseline | Week 24 | Change from baseline |
|-----------|----|----------|---------|---------------------|
| Hypoglycaemia, events/patient-year | 57 | 2.5 | 0.0 | −2.5 |
| Insulin naïve | 33 | 6.3 | 0.0 | −6.3 |
| Body weight, kg | 47 | 87.7 | 84.6 | −3.2 |
| Quality of life, VAS scale (0-100) | 47 | 53.5 | 80.7 | 27.2 |

**Table 11: Insulin dose**

| Parameter | N | Pre-study | Baseline | N | Week 24 |
|-----------|----|-----------|----------|----|---------|
| Insulin naive | 0 | 0.0 | 57 | 18.1 | 47 | 20.3 |
| Insulin users  | 33 | 20.9 | 33 | 14.2 | - | - |

**Table 12: Insulin detemir±oral glucose-lowering drug efficacy data**

| Parameter | N | Baseline | Week 24 | Change from baseline |
|-----------|----|----------|---------|---------------------|
| Glycaemic control (insulin naïve) | 47 | 8.3 | 7.3 | −1.0 |
| FPG, mean (mmol/L) | 47 | 8.7 | 7.1 | −1.6 |

HbA1c: Glycated haemoglobin A1c, FPG: Fasting plasma glucose
Insulin aspart ± OGLD

Of the total cohort, 37 patients started on insulin aspart ± OGLD, of which 26 (70.3%) were insulin naïve and 11 (29.7%) were insulin users. After 24 weeks of treatment, hypoglycaemic events reduced from 14.2 events/patient-year to 0.0 events/patient-year in insulin users whereas, hypoglycaemic events remained nil in insulin users, similar to baseline. Quality of life improved at the end of the study [Table 13 and 14].

Mean HbA1c and FPG values improved from baseline to study end in those who started on or were switched to insulin aspart ± OGLDs for insulin naïve group [Table 15].

**CONCLUSION**

Our study reports improved glycaemic control (HbA1c, FPG) 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. Quality of life improved in the total cohort. Major hypoglycaemic events decreased from 0.5 events/patient-year to 0.0 events/patient-year in insulin naïve group while no change from baseline (1.3 events/patients-year) was observed for insulin user group. SADRs were not reported in any of the study patients. Overall, body weight reduced in insulin naïve group whereas no change in body weight was observed for insulin users. 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 Rajasthan, 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, Chalkarwar 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 13: Insulin aspart±oral glucose-lowering drug safety data**

| Parameter                  | N  | Baseline | Week 24 | Change from baseline |
|----------------------------|----|----------|---------|----------------------|
| Hypoglycaemia, events/patient-year |    |          |         |                      |
| Insulin naïve              | 26 | 0.0      | 0.0     | 0.0                  |
| Insulin users              | 11 | 14.2     | 0.0     | -14.2                |
| Body weight, kg            |    |          |         |                      |
| Insulin naïve              | 26 | 63.7     | 63.8    | 0.1                  |
| Insulin users              | 1  | 62.0     | 62.0    | 0.0                  |
| Quality of life, VAS scale (0-100) |    |          |         |                      |
| Insulin naïve              | 26 | 54.2     | 80.0    | 25.7                 |
| Insulin users              | 1  | 50.0     | 77.0    | 27.0                 |

VAS: Visual analogue scale

**Table 14: Insulin dose**

| Insulin dose, U/day | N  | Pre-study | N  | Baseline | N  | Week 24 |
|---------------------|----|-----------|----|----------|----|---------|
| Insulin naïve       | 26 | 0.0       | 26 | 22.3     | 26 | 21.5    |
| Insulin users       | 11 | 28.0      | 11 | 25.4     | 1  | 24.0    |

**Table 15: Insulin aspart±oral glucose-lowering drug efficacy data**

| Glycaemic control (insulin naïve) | N  | Baseline | Week 24 | Change from baseline |
|----------------------------------|----|----------|---------|----------------------|
| HbA1c, mean (%)                  | 26 | 8.3      | 7.4     | -0.9                 |
| FPG, mean (mmol/L)               | 25 | 8.4      | 7.3     | -1.1                 |

HbA1c: Glycated haemoglobin A1c, FPG: Fasting plasma glucose

Cite this article as: Joshi A, Meenawat A, Patni R, Sharma DC, Panicker S. Clinical experience with insulin detemir, biphasic insulin aspart and insulin aspart in people with type 2 diabetes: Results from the Rajasthan cohort of the A1chieve study. Indian J Endocr Metab 2013;17:S526-9.

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