Diabetes & Metabolic Syndrome: Clinical Research & Reviews 10 (2016) 161–165

Contents lists available at ScienceDirect

Diabetes & Metabolic Syndrome: Clinical Research & Reviews

journal homepage: www.elsevier.com/locate/dsx

# Insulin glargine versus insulin degludec in patients failing on oral therapy in type 2 diabetes: A retrospective real world comparative data from India

Samit Ghosal [a,*], Binayak Sinha [b], Kalyan Kumar Gangopadhyay [c]

[a] Nightingale Hospital, Kolkata, India
[b] Department of Endocrinology, AMRI Hospital, Salt Lake, Kolkata, India
[c] Department of Endocrinology, Fortis and Peerless Hospital, Kolkata, India

ARTICLE INFO

*Keywords:*
Diabetes
Plasma glucose
Glargine
Degludec
Hypoglycemia

ABSTRACT

*Objective:* To compare the changes in various glycemic parameters in insulin-naïve type 2 diabetes mellitus (DM) patients who were initiated on insulin glargine or insulin degludec in a real world setting.
*Methods:* Retrospective data were analyzed in consecutive type 2 DM patients in a real world setting, who failed oral therapy (at least 2 oral anti-diabetic drugs) and were initiated with either insulin glargine or insulin degludec. The parameters assessed were the changes in HbA1c, fasting plasma glucose, body weight, dose of Insulin and the total number of patient reported hypoglycemic episodes up to 6 months after initiation.
*Result:* At baseline, insulin glargine and insulin degludec groups were similar in terms of gender, age, weight, HbA1c and duration of diabetes. After 6 months follow up the change in HbA1c (−1.09 versus −1.45 $P = 0.124$), change in FPG (−72.81 mg/dl [−4mmol/L] versus −75.88 mg/dl [−4.2 mmol/L] $P = 0.755$), and the change in body weight (+1.65 versus +0.85 $P = 0.082$) were similar in glargine and degludec groups, respectively. Patients in insulin degludec group experienced significantly lesser patient reported hypoglycemic episodes (12 versus 40) and required significantly lesser dose (25.68 Units versus 18.61 Units per day; $P = 0.002$) compared to insulin glargine. 41% of the patients reached HbA1C target of ≤7% with insulin glargine compared to 69% with insulin degludec within the specified time period.
*Conclusion:* Results from this real world analysis suggest that among type 2 DM patients who were initiated on insulin degludec as compared to insulin glargine may be associated with significantly lesser patient reported hypoglycemic episodes and lesser dose of insulin while achieving similar glycemic control. This study is however limited by the retrospective nature of the data collection.


## 1. Background

Type 2 diabetes is a progressive disease with approximately 53% of patients requiring insulin initiation at 6 years post diagnosis [1]. Significant and continuing reduction in beta cell function in spite of therapy limits the effectiveness of oral drugs after only a few years of diagnosis [2]. This has led to the concept of adding basal insulin to the failing oral regimen.

Although the American Diabetes Association recommendation positions basal insulin as an option right after metformin, however in real life insulin is initiated much later. [3]. The oral anti-hyperglycemic armamentarium has strengthened significantly over the years with the introduction of gliptins and SGLT-2 inhibitors, which have a favorable impact on hypoglycemia and weight compared to the conventional agents like sulfonylureas and meglinitides [4]. As a result in reality, insulin is considered for patients only after 2 or 3 drugs have failed.

As far as insulin is concerned basal insulin is considered ahead of the pre-mix formulations in view of convenience of initiation and lower risk of hypoglycemia [5]. Recent mechanistic evidence

*Abbreviations:* DM, diabetes mellitus; HBA1C, glycated hemoglobin; SU, sulfonylurea; SGLT-2, sodium glucose cotransporter-2; RCT, randomized controlled trial; NPH, neutral protamine hagedorn; FPG, fasting plasma glucose; OAD, oral anti diabetic; IU, international unit.

* Corresponding author.
*E-mail addresses:* ramdasghosal@gmail.com (S. Ghosal), binayak.sinha@gmail.com (B. Sinha), jaykal69@hotmail.com (K.K. Gangopadhyay).

http://dx.doi.org/10.1016/j.dsx.2016.01.013
1871-4021/

documented greater risk of life threatening arrhythmias with hypoglycemic episodes, more so with nocturnal hypoglycemia [7]. This data was complimented with a 4 years prospective data documenting a higher risk of mortality predominantly driven by increased cardiovascular events in the group experiencing hypoglycemia versus the group that did not [8]. So, nocturnal hypoglycemia remains a huge concern [6].

This has led to the search for improved versions of basal insulin with flatter action profile and longer duration of action, with lesser variability and lesser chances of hypoglycaemia particularly nocturnal. The first in class was glargine followed by detemir. There was 42–48% lower nocturnal hypoglycemia with the first generation basal analogs compared to NPH [9]. Insulin degludec may be another improvement on the first generation insulin analogs with a flatter profile, longer duration of action and lesser glycemic variability compared to glargine [10]. Although the clinical trial results are promising the data from the real world practice is limited especially from India.

Retrospective real life data enriches the findings from randomized controlled trials. This study was conducted to assess the real life clinical difference between degludec and glargine in type 2 diabetic patients failing oral therapy. The aim of this study was to assess the efficacy and safety differences between the two arms and whether these differences were clinically meaningful endorsing the RCT data.

## 2. Methods

Retrospective analysis of data from three centers in Kolkata, India were conducted in consecutive patients who failed on oral anti diabetic drugs and were initiated on either insulin glargine or insulin degludec injected at bedtime.

Inclusion criteria:

1. Type 2 DM with HbA1C >7% on two or more oral antidiabetic drugs.
2. Initiation of insulin in the time period from 1st September 2013 to 30th September 2013.
3. Availability of HbA1C, FPG data at the time of initiation of insulin and at six months post initiation.

Exclusion criteria:

1. Pregnancy.
2. Any prior insulin use.
3. Initiation with basal insulin other than glargine and degludec.

Lack of follow up at 6 months post insulin initiation

Primary end point:

1. Change of HbA1C at 6 months

Secondary end point:

1. Change in FPG at 6 months.
2. Number of patient reported hypoglycaemic episodes.
3. Daily insulin dose requirement at 6 months.
4. Change in body weight.

All the patients had received advice regarding insulin injection technique, monitoring of blood glucose by glucometer and maintaining blood glucose measurement dairy and recognizing hypoglycaemic symptoms. The hypoglycaemic symptoms were patient reported, and as is usually the case in real life situations, could not always be verified by plasma laboratory glucose measurement. Nevertheless it was ensured that the patients included in this study used glucometers, which were plasma calibrated.

**Table 1**
Baseline characteristics.

| Baseline information | Group I ($n=33$) | Group II ($n=31$) | *P* value |
|---|---|---|---|
| Age in years | 56.09 ± 13.59 | 58.97 ± 11.32 | 0.363 |
| Gender (M:F) | 19:14 | 18:13 | 0.968 |
| Weight (kg) | 65.27 ± 9.32 | 65.87 ± 10.17 | 0.807 |
| BMI (kg/m$^2$) | 25.19 ± 2.90 | 25.61 ± 3.71 | 0.621 |
| HbA1c | 8.58 ± 1.35 | 8.42 ± 0.89 | 0.573 |
| FBS (mg/dl) | 182.88 ± 37.25 | 182.35 ± 34.85 | 0.954 |
| Metformin monotherapy | 31 (93.9%) | 31 (100%) | |
| OADs at screening metformin | | | |
| SU | 19 (57.6%) | 22 (70.9%) | 0.264 |
| DPP | 29 (87.8%) | 26 (83.8%) | 0.645 |
| TZD | 3 (9.1%) | 2 (6.5%) | 0.694 |
| Duration of diabetics | 12.15 ± 7.19 | 9.93 ± 3.98 | 0.136 |

The patients were asked to ring up the respective centers every week with their FPG levels and the dose of basal insulin (glargine or degludec) was titrated by ±2 Units to try and attain a FPG value between 100 and 120 mg/dl. There was no further dose adjustment for OAD during the course of this study.

Descriptive and inferential statistical analysis was carried out in the present study. Results on the continuous measurements are presented on mean ± SD and the results on categorical measurements are presented in number (%). Significance is assessed at 5% level of significance. Student *t* test (two tailed, independent) has been used to find the significance of the study parameters in continuous variable and chi square test/Fischer extract test has been used to find the significance of study parameters on categorical scale between two groups. Statistical software SAS 9.2, SPSS 15.0 was used for analysis of data.

## 3. Results

Data from 33 patients who were initiated on insulin degludec and 31 patients who were initiated on insulin glargine were analyzed. Overall, the treatment groups were matched at the baseline (Table 1).

At 6 months of follow up the observed mean HbA1C concentration was similar for insulin glargine and insulin degludec (7.32%) and (7.12%), respectively as well as the mean change in HbA1C (1.09%) and (1.45%), respectively (Table 2, Fig. 1). Similarly, the change in the fasting plasma glucose and change in the body weight were found to be similar between both the groups (Table 2, Figs. 2 and 3).

**Table 2**
Change in vital parameters at the end of 6 months.

| Variables | Group I | Group II | *P* value |
|---|---|---|---|
| HbA1c | | | |
| Baseline | 8.58 ± 1.34 | 8.42 ± 0.89 | 0.573 |
| 6 months | 7.12 ± 0.64 | 7.32 ± 0.72 | 0.247 |
| Difference | 1.45 ± 1.17 | 1.09 ± 0.55 | 0.124 |
| *P* value | <0.001** | <0.001** | – |
| FBS (mg/dl) | | | |
| Baseline | 182.88 ± 37.25 | 182.35 ± 34.85 | 0.954 |
| 6 months | 107.00 ± 19.25 | 109.55 ± 24.20 | 0.642 |
| Difference | 75.88 ± 40.15 | 72.81 ± 37.71 | 0.755 |
| *P* value | <0.001** | <0.001** | – |
| Weight (kg) | | | |
| Baseline | 65.27 ± 9.32 | 65.87 ± 10.17 | 0.807 |
| 6 months | 66.12 ± 8.96 | 67.52 ± 9.65 | 0.551 |
| Difference | 0.85 ± 1.43 | 1.65 ± 2.12 | 0.082 |
| *P* value | <0.001** | <0.001** | – |

** Statistically significant