# First experience with insulin analogues in type 1 diabetes mellitus in Tripoli diabetic hospital

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**Abstract:** The current study aims to determine the efficacy of insulin analogue on blood sugar control in patients with type 1 diabetes mellitus, this study is a cross sectional study and was carried out in Tripoli diabetes hospital during the period (Nov/2009-April-2010). One hundred patients with Type 1 diabetes mellitus on basal-bolus insulin injections (after consent taken), were enrolled in this study, insulin glargin taken as basal single dose at night (mostly at 10 pm) and Lispro injection before each meal (3 times/day), initially the total daily requirement calculated according to body weight or previous daily insulin doses and adjusted according to blood glucose profile done by patients (SMBG), the results were a significant regarding increase of total daily doses and body weight, decrease in number of hypoglycemic episodes /month and HBA1c. The study concluded that insulin analogue (glargin & Lispro) administrations were associated with improve glycaemia control with reduction in hypoglycemia episodes in Type-1 diabetes mellitus.

***Key words**:* Type1 diabetes, insulin analogue, self-monitoring blood glucose

## Introduction

The global rate of DMI is escalating (1, 2), outcomes from the Diabetes Control and Complications Trial (DCCT) confirmed that intensified insulin treatment diminishes the risk of micro and macro-vascular events compared with conventional treatment (3-6). The DCCT evidently demonstrated that intensive insulin therapy, definite as three or more injections per day of insulin or continuous subcutaneous insulin infusion (CSII) (or insulin pump therapy), was a solution of a better metabolic and improved results (7, 8). The study was carried out with short- and intermediate-acting human insulin, even with improved micro-vascular effects, intensive insulin therapy was linked with a high rate of severe hypoglycemia (62 episodes per 100 patient-years of therapy). While the conclusion of the DCCT, a number of rapid-acting and long-acting insulin analogs have been appeared. These analogs are associated with less hypoglycemia than human insulin although present the identical reduction of A1C in cases with (9, 10).

Reducing A1C to 7% has been shown to diminish microvascular complications of diabetes, and if realized almost immediately following the diagnosis, is related with long-term decline in macro-vascular disease. So a sensible A1C target for many non-pregnant adults with DMI is, 7%. Providers might reasonably suggest HBA1C goals of 6.5% for choose cases, if can be attained with no considerable hypoglycemia or other adverse effects of treatment. Suitable cases might consist of those with a short duration of diabetes, a long life expectation, hypoglycemia responsiveness, and no CVD. HB A1C goals of 8.5% may be proper for cases with a history of

severe hypoglycemia, hypoglycemia unawareness, limited life expectancy, advanced micro-vascular /macro-vascular complications, or extensive comorbid conditions (11). Metabolic control for DMI at any age should be assessed based on regular SMBG (Self-Monitoring Blood Glucose) levels and CGM data, if accessible, and HB A1C to facilitate modifications in treatment. The DCCT established the advantages of intensive B sugar control on diabetes complications with SMBG as part of a multi-factorial role, signifying that SMBG is a vital part of efficient treatment. SMBG permits patients to estimate their individual reaction to treatment and evaluate if metabolic aims are being achieved. SMBG results are practical in avoiding hypoglycemia, regulating insulin dose (chiefly before meals), and appreciating the effect of suitable nutrition therapy and physical activity. More frequent SMBG is linked to lower A1C levels (12, 13) SMBG rate and time should be ordered by the patient's particular requirements and aims. While advising SMBG, giver must guarantee that patients get continuing education and standard assessment of their SMBG skill and their facility to utilize SMBG records. In cases with DMI should do SMBG before meals and snacks, at a least, and at further times, as after-meals to evaluate insulin-to-carbohydrate ratios; at bedtime; mid-sleep (3-4 a.m.); prior to, during, and/or after exercise; if there is symptom of hypoglycemia; after remedy of low/high B sugar ; preceding to serious duties like as driving; and at more frequent intervals during sickness or strain.

The accessibility of insulin analogs has allowed insulin replacement that are planned to more intimately replicate natural insulin secretions. Particularly, pre-meal insulin analogs (lispro, aspart, glulisine) have action outlines nearer to normal, with resultant quicker initiation and neutralization of action to lower blood sugar in contrast with regular human insulin. Basal insulin analogs (glargine, detemir) have prolonged act, less variableness, more control, less hypoglycemia (especially nocturnal), and an encouraging result on weight (14). Basal-bolus regime permits for accurate insulin dose regulations to attain glycaemic goals (HBA1c) and a glycaemic profile as close to physiological as possible with a low risk of hypoglycaemia (15-27). The function of basal insulin (background insulin) is to maintain blood sugar at steady degrees while abstain from food, generally used 1-2 times a day. A bolus dose is insulin that is particularly used at mealtime to deal with B sugar levels after a meal (14). The advantages of multiple daily dose, permit closely mimic normal insulin secretion, flexibility in time of insulin injections, amount of carbohydrates intake each meal. Drawback of MDI, that more injections per day and weight gain (28).

## Materials and methods

A cross sectional study which included a hundred patients of DM I in Tripoli diabetic hospital from (Nov 2009 until April 2010).The data collected about patient's demographics, Some important points in clinical history, relevant investigations and then the patients were followed after 3 months. Data were analyzed by using the Statistical Package for the Social Sciences (SPSS) version 16 (compare means with paired samples t-test).

## Results

In National Diabetes Hospital in Tripoli – Libya where most of people with DM in west part of Libya receive their diabetes care, a total of 100

patients with DM-I, who attended outpatient clinic included in the study, 72% of them were female, their age range was between (13-53 years with mean age 27.4 ± 9.4 years, the duration of diabetes ranged from newly diagnosed to (31years ) of DM while 46% of them were controlling their diet (assessed by registered dietitian ), (73%) were testing their blood glucose at home (SMBG), with mean of total daily dose of human insulin (55 ± 21.7 IU), most of them on mixtard 30 twice daily, the remaining were on actrapid insulin +NPH in different combinations in four to two injections daily, number of daily doses (3 ± 1), history of hypoglycemic episodes (5.07 ± 5.1), include minor , major and nocturnal episodes, mean were weight (66.4 ± 13.4 Kg), BMI (24.7 ± 4.4), and HBA1c pre study mean (10.6 ± 2.2%) After starting insulin analoug (insulin glargin as single basal dose at night +ultra rapid insulin analogue lispro/Aspart befor the 3 main meals) regular follow up 3 month later**,** the total daily dose is significant increased (60.9 ± 25 IU, $p < 0.05$), the number of daily doses were 4 times , the number of hypoglycemic episodes/month were significantly diminished (1.1 ± 2.1,$p < 0.001$),the mean weight increased (67 ± 14.6 kg $p < 0.09$),their mean HBA1c significantly reduced (9.5 ± 2.3% $p < 0.001$).

**Table 1:** Mean and standard deviation for different variables on the study

| Variable | Mean ± SD at start (twice daily human insulin) | Mean ± SD (after) basal-bollus insulin analogue | p-value |
|---|---|---|---|
| Total daily dose | 55 ± 21.7 | 60.9 ± 25 | 0.05 |
| Hypoglycemia episods | 5.07 ± 5.1 | 1.1 ± 2.1 | 0.00 |
| Body Weight | 66.4 ± 13.4 | 67.7 ± 14.6 | 0.09 |
| HBA1c | 10.6 ± 2.2 | 9.5 ± 2.3 | 0.00 |

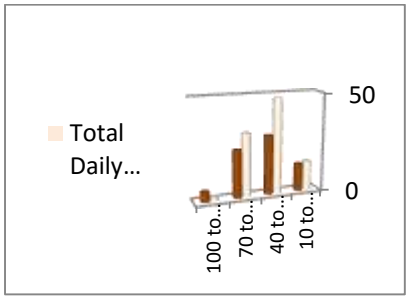


**Figure 1:** The total daily dose difference at start &after 3 month of study

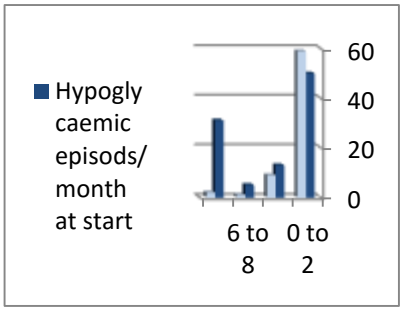


**Figure 2:** The total daily episodes before &after 3month of study

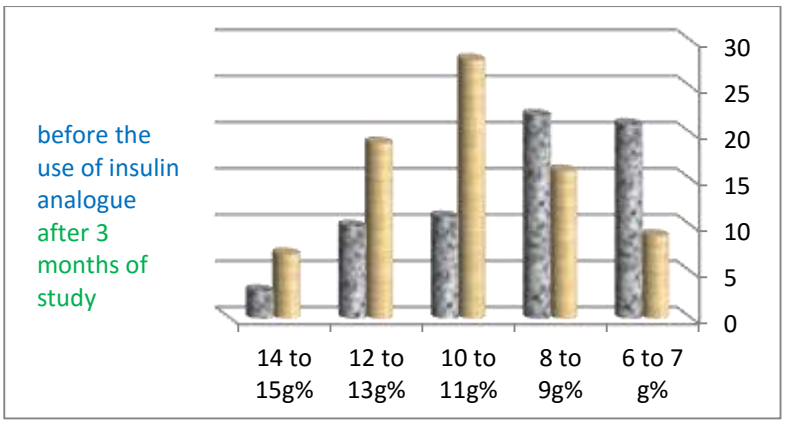


**Figure 3:** Difference in HBA1c levels before and after 3 months of study

## Discussion

Regular human insulin and intermediate-acting neutral protamine Hagedorn (NPH) insulin are conventional insulin. But both do not mimic the outline of basal and post-meal physiological insulin release. Insulin analogues are adapted human insulin attend to overcome this restriction (29). Insulin lispro in comparison with regular human insulin leads to a slightly lesser HB $A_{1c}$ concentration (weighted mean difference - 0.09%, 95% CI -0.16% to -0.02%), a lower risk of severe hypoglycemia (relative risk 0.80, 95% CI 0.67 to 0.96) and a lower rate of nocturnal hypoglycemia (rate ratio 0.51, 95% CI 0.42 to 0.62). Usually, patients chosen rapid-acting insulin analogues over regular human insulin for the reason that flexibility of the dose in relation to meal (30-34). Several reports shown that considerable enhancement in quality of life and patient pleasure with the utilize of rapid-acting insulin analogues, while further studies established no differentiation (30-34). Insulin glargine (Lantus ) in contrast to, neutral protamine Hagedorn insulin (NPH), offered a small but statistically important reduction in HBA1c (weighted mean difference - 0.11%, 95% CI - 0.21% to - 0.02%), as well, the main hazard decline in night-time hypoglycemia support of insulin glargine (Lantus) use (relative risk 0.64, 95% CI 0.47 to 0.87) (42).

For diabetic morbidity or mortality, still, incomplete statistics to compare insulin analogues and conventional insulin (42).

In this study, we compare between the utilization of insulin analogue (insulin Glargin as basal and Lispro or Aspart as bolus doses) and human insulin (insulin Mixtard 30 twice daily, NPH and soluble insulin with different regimes) in the same patients with DMI, concerning with blood sugar control, incident of hypoglycemia, and weight gain. We concluded that insulin analogues provide a scientific benefit over human insulin for glycaemic control in DMI, with less hypoglycemia especially nocturnal and may be considered a first choice for patients with recurrent hypoglycemia in spite of modification of conventional insulin treatment. ***Inconclusion****:* The study shows that insulin analogues (glargine, lispro) improved the glycaemic control in patients with DM-I (i.e. HBA1c), with decrease in the number of hypoglycemic episodes/month; however, both total daily dose and mean body weight are increased.

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