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Original article

First time experience with Trulicity (Dulaglutide)as Add-on therapy for Type2 diabetes patients

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Abstract

Type 2 diabetes is a chronic progressive metabolic disease requires continues intensification of treatment in order to prevent its long-term complications, the use of GLP-1RA in combination with Ant hyperglycemic drugs has provided potent glucose lowering effect with less weight gain and hypoglycemia.Aim of the study:To study the effectiveness and safety of Trulicity (Dulaglutide) when added to existing therapy of obese Type 2 diabetes patient with poorly controlled long duration diabetes.Methods: Longitudinalstudycarried out among adult T2DM persons attending the Outpatients' Department, National Centre for Diabetes Tripoli, Libya according to selection criteria. At the initial visit, patient vital parameters (Weight, BMI,Pulseand BP) and biochemical parameters related to the study taken. Patients followed monthly, and study parameters assessed after 3moths and 6 months.Results: 40 patient included in the study (34 Female85%, 6 Males 15%), mean Age 55 (±9.90) years , mean diabetes duration 14.7 (± 6.20) year , mean body weight 99.16 (±14.23) Kg ,mean BMI 38.29 (± 4.73)Kg/m2 ,mean HbA1c 10.08 (±1.17)% , mean total insulin dose 61.2 (±24.22) units , mean Urea 28.55 (± 11.74) mg%, mean Creatinine 0.67 (±0.22)mg% , mean Total Cholesterol 157 .43 (± 40.32) mg% , mean LDL-c96.99 (± 36.92)mg% , mean Systolic Blood Pressure 136.25 (± 16.28)mmgh , mean Diastolic Blood Pressure 82.62(± 0.81)mmgh and mean Pulse 75.80 (± 7.92) Beat/min . After 3 months , 6 months of treatment the results respectively as following : The mean HbA1c reduced to 7.60 ±1.12 % , 7.01 ±0.94 (P value 0.000), body weight decreased to 95.28 ±36.96 Kg , 92.47 ±14.78 Kg (P value 0.000), total insulin dose reduced to 45.26 ±17.1 , 42.94 ±20.86 units (P value 0.000). Mean FBG 135.43 ±32.10 mg%, 128.94 ±29.64 mg% (P value 0.010), PPG 161.10 ±42.61, 144.84 ±29.71 mg% (P value 0.050). Conclusion: Adding Trulicity to the existing therapy of obese, long duration Type 2 diabetes patientswith high HbA1c resulted in lowering of HbA1c, weight reduction,and decrease total insulin dose without significant gastrointestinal and hypoglycemiaevents, the study reported significant lowering effects on lipid profile, preserved Kidney function.

Key words:Trulicity, Type 2 Diabetes,HbA1c, Weight

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Introduction

Recent guidelines for type 2 diabetes treatment from the American Diabetes Association, the AmericanAssociation of Clinical Endocrinologists, the American College of Endocrinology, and the American College ofPhysicians recommend A1C targets in the range of 6.5–8 % (1–3)The harmful consequences of high A1C levels from the Diabetes &Aging Study data reveal increased risk of microvascular complicationsin patients with A1C >9% (4). Data showing the relationship between the increased risk of microvascular disease and increased burden of cardiovascular disease intype 2 diabetes people (5).The UKPD Study showed that lowering A1C by 1% was associated witha37%reductioninmicrovascular complications risk. (6)A number of studies have shown that medications stimulate b-cell function, like sulfonylureas and dipeptidyl peptidase 4 inhibitors, is associated with B-cell exhaustion and worsening of glycemicControl (7, 8).The need to address multiple aspects of T2DM has been a powerful driver of the search for new treatment, Zinman and colleagues (2012) recommending the achievement of an HbA1c target of < 7%, with no weight gain and no hypoglycaemia as a clinically relevant composite outcome in the modern T2DM management .(9)Glucagon-like peptide 1 receptor agonists (GLP-1 RAs) are recommended as first injectable therapy for the most of type 2 diabetes patients (1,2) owing to their glycemic efficacy and lack of association with weight gain and hypoglycemia. (10)Dulaglutide(Trulicity) is a Long-acting GLP-1 RAs act via glucose-dependent stimulation of insulin secretion; delayed gastric emptying effect. (10)Dulaglutide indicated in adults with type2 diabetes patients to improve glycemic control as Add-on therapy in combination with other glucose-lowering medications including insulin, when these, together with diet and exercise, do not provide adequate glycaemic control. As add-on therapy, the recommended dose is 1.5 mg once weekly (11, 12)The efficacy and safety profile of Dulaglutideinvestigated through a comprehensive clinical trial programme: the AWARD (Assessment of Weekly Administration of LY2189265 in Diabetes) programme comprises six completed phase 3 trials (AWARD-1, AWARD-2, AWARD-3, AWARD-4, AWARD-5, and AWARD-6. (12-17)Rational of study to have real life experience with this medication as it's used for the first time among our patients , up to our knowledge this is the first study about Trulicity carried on among Libyan patients .
Aim of the study: To study the effectiveness and safety of Trulicity (Dulaglutide) when added to existing therapy of obese (BMI > 30 Kg/m2) Type 2 diabetes patient with poorly controlled (HbA1c>9%) and long duration (>5years) diabetes.

Materials and Methods:

Longitudinalstudy carried out among adult T2DM persons attending the Outpatients' Department, National Centre for Diabetes Tripoli, Libya(February – September 2021)

according to selection criteria:Inclusion Criteria : T2DM , Age > 40years , DM2 duration > 5 years , HbA1c > 9% , BMI > 30 ,Using 2 or more Anti-diabetes drugs one of them Insulin , Exclusion Criteria : T1DM , GDM , Pregnancy , Lactation, H/O Pancreatitis ,H/O Thyroid Cancer , Family H/O Thyroid Cancer , Advanced Diabetic Retinopathy , ESRD , patients on dialysis, Advanced Liver disease , Patients with Arrhythmias .Written consent were taken from all included patients,Patients followed monthly, and assessed after 3moths and 6 months.

Evaluation:At the initial visit patient parameters taken: weight, BMI, BP, Pulse, and initial level of HbA1c, Urea, Creatinine, Total Cholesterol and LDL. Patient showed how to use Trulicity pen and provided with Glucometer and logbook in order to monitor their glucose at the required times. Weight taken by RGZ-160 Health Scale,BP measured by Mercury Sphygmomanometer, take Pulse measured manually , Biochemical parameters taken early morning on fasting state and analyses done in our laboratory by Integra machine. Patients scheduled for monthly visits and in each visit we monitor their weight, BP, Pulse, averages of FBG PPG, number of hypoglycemia episodes (BG ≥70 mg %), gastrointestinal side effects (nausea vomiting). Insulin dosses also titrated in each visit.After 3months, 6months follow-up we repeat HbA1c, Urea, Creatinine, Total Cholesterol and LDL.Data analysis: Data analyzed by using SPS Version 21 in to descriptive statistic; Count, percentage mean and standard deviations. Graph presentations by exile. Analytic statistics;compare mean was done by using Paired Sample Test. Significant P-value >0.05.

Results: 40 patient included in the study majority of them were Females (34 Female, 85%, 6 Males 15%), with mean Age 55± 9.90 years , most of the participants living in Tripoli , the average DM2 duration 14.7 ± 6.20 year , the average body weight 99.16 ±14.23 Kg while the mean BMI 38.29 Kg/m2± an 4.73 Kg/ and most of them (30) classified as Obesity Class 2 , 3 , the mean HbA1c at the start of the study was 10.08 (±1.17%) which reflects poorly controlled state of diabetes , the mean total daily insulin dose used was 61.2 units (±24.22units) .(Table 1)The averages of participants' baseline character and outcomes showed in (Table .2) After 3 months , 6 months of treatment the results respectively as following : The mean HbA1c reduced to 7.60 ±1.12 % , 7.01 ±0.94 (P value 0.000) , body weight decreased to 95.28 ± 36.96 Kg , 92.47 ±14.78 Kg (P value 0.000) , total insulin dose reduced to 45.26 ±17.1 , 42.94 ±20.86 units (P value 0.000). Mean FBG 135.43 ±32.10 mg%, 128.94 ±29.64 mg% (P value 0.010), PPG 161.10 ±42.61, 144.84 ±29.71 mg% (P value 0.050). The participants HbA1c reduced by 2.48 % after 3months of treatment and they could sustained further reduction by 3.07 % after 6months reaching to targeted HbA1c level , also after 3months there were significant weight reduction average of 3.88 Kg which also sustained with more average reduction to 6.69 Kg after 6months . Total insulin dose after 3moths reduced by average 15.9 unit and decreased to average 18.26 unit after 6 months.

Table 1 Baseline characteristics of the participants(N=40).

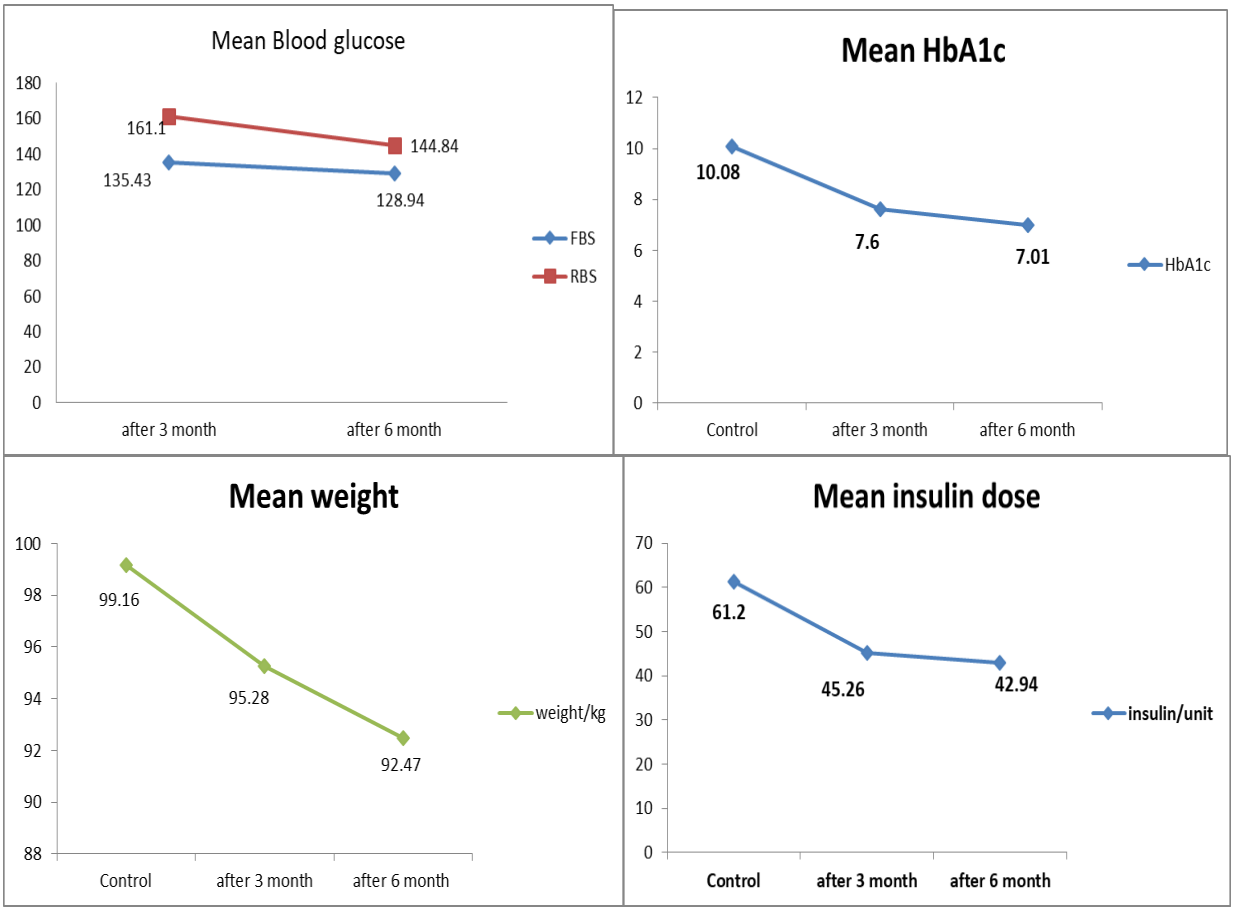
Character	NO	%
Age (mean ±SD 55.82±9.90years		
45-55	19	47.50%
56-65	13	32.50%
66-75	8	20%
Gender		
Female	34	85%
Male	6	15%
Address		
Inside Tripoli	31	77.50%
Outside Tripoli	9	22.5%
Duration of diabetes (mean duration)14.87 ±6.20 year		
5-10 years	10	25%
≥11years	30	75%
BMI groups		
30-34.9	10	25%
35-39.9	12	30%
≥40	18	45%
Associated Chronic illness		
Hypertension	21	52.5%
Hypertension & IHD	4	10%

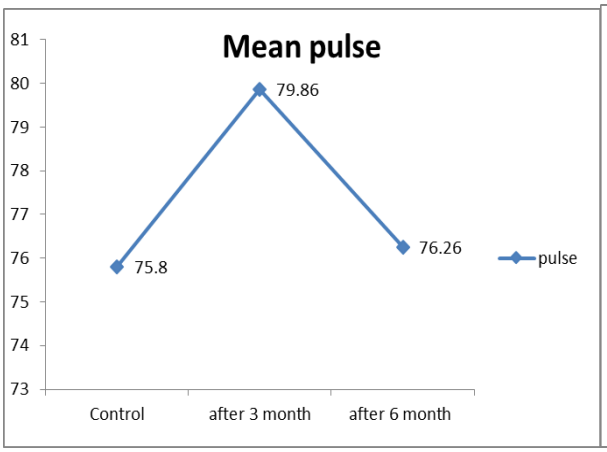
Table 2. Participants Baseline character and outcomes

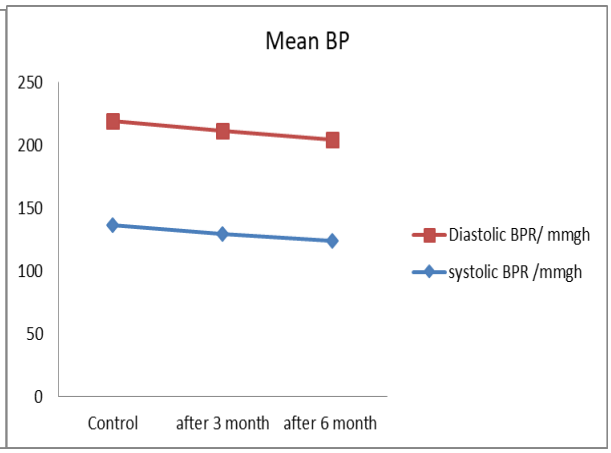
Character	Control	After 3 months	After 6 months	P value
Weight	99.16±14.23/kg	95.28±36.96/kg	92.47±14.87/kg	0.000
HbA1C	10.08±1.17%	7.60±1.12%	7.01±0.94%	0.000
FBG	-	135.43±32.10mg/dl	128.94±29.46mg/dl	0.010
PPG	-	161.10±42.61mg/dl	144.84±29.71mg/dl	0.050
Total Insulin dose	61.20±24.22 unit	45.26±17.1 unit	42.94±20.86unit	0.000
Total Cholesterol	157.43±40.32mg/dl	139.58±35.23mg/dl	125.38±43.20mg/dl	0.000
LDL-c	96.94±36.92mg/dl	74.25±22.15mg/dl	72.35±20.15mg/dl	0.000
Urea	28.55±11.74mg/dl	29.23±12.29/mg/dl	29.31±13.65mg/dl	0.061
Creatinine	0.67±0.22mg/dl	0.72±0.24mg/dl	0.70±0.36mg/dl	0.121
Systolic BP	136.25±16.28mmgh	129.33±16.17mmgh	124.21±16.43mmgh	0.000
Diastolic BP	82.62±.81mmgh	81.83±7.93mmgh	80.26±9.20mmgh	0.000
Pulse	75.80±7.92/minute	79.86±7.85/ minute	76.26±7.70minute	0.010

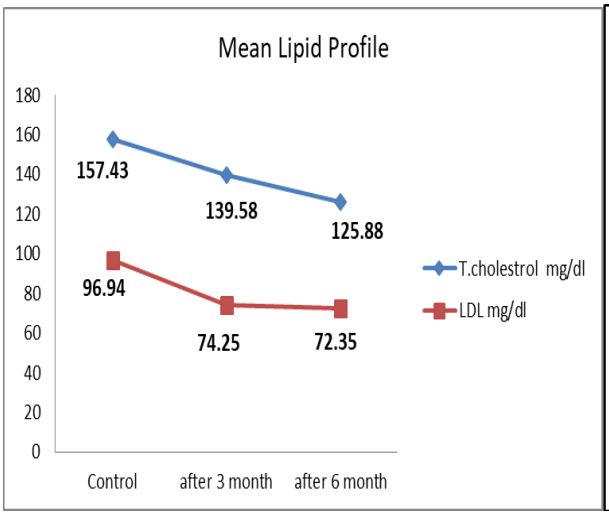
Table .3 Side effects

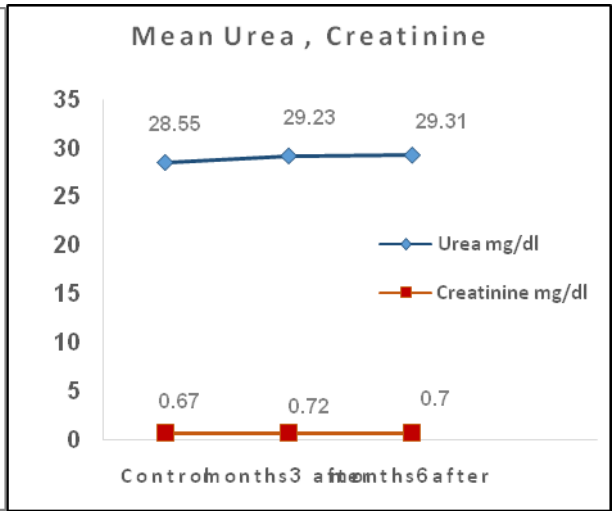
Side effect	NO	%
Hypoglycemia (episodes) mean 0.39±0.89 , P value 0.78		
No episodes	35	70.50%
Once	3	7.5%
Frequent	2	5%
Gastro intestinal symptoms		
No	37	92.50%
Nausea	2	5%
Vomiting , Diarrhea	1	2.5%











Discussion

Recommended HbA1C targets for Type 2diabetes are between 6.5 and 8%; Patients with HbA1C > 9% are at increased risk for micro- and macrovascular complications and require treatment intensification to improve glycemic control as soon as possible. (1,4)That is why in our study we include those patients with HbA1C >9%.Long diabetes duration and A1C < 9% are indicative of decreased β-cell function, the requirement for intensive treatment not only to prevent complications, but also further deterioration of β-cell function.Ideally, clinicians should select agents that do not act through a β-cell overstimulation and can help β-cell rest (18-20).These characteristics individuals who may be at risk for β-cell failure include long duration of type 2 diabetes (>8 years), high A1C (> 9%) (18,19), and previous use of insulin secretagogues (20).In our studydiabetes, duration was 14.87 ±6.20 years and our selected participants were using 2 or more diabetes medications

including insulin The study patients achieved average HbA1c 7.6% after 3 months and they sustained that reduction even more; HbA1c 7.1 after 6 months, significant reductions from baseline observed in both fasting and postprandial glucose levelsOverweight and obesity are associated with multiple co-morbidities including type 2 diabetes, cancer and cardiovascular diseases. Body-mass index (BMI) is risk factor for various causes of death, including ischemic heart disease, stroke, and cancers. (21,22).Researches regarding BMI showed that each 5 kg/m2 higher BMI was associated with nearly 30% higher all-cause mortality and upper range of BMI (25-50 kg/m2) was strongly associated with mortality related to diabetes. (23).The average BMI of the participants in our study was 38.29 Kg/m2and most of them (NO.30) classified as Obesity Class 2, 3, and that subjects them to more risks. One of our targets was weight reduction. That achieved after 3months with significant weight reduction average of 3.88 Kg,and the reduction was more after 6months with average reduction of 6.69 Kg.The results of this study indicate that the Trulicity found to be effective as it improves studyparameters; HbA1c FBG PPG,weight, total insulin dose, lipid profile and safe as there were no significant side effects:hypoglycemia, nausea and vomiting reported during this study.

Disclosure: None

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