

**[neiss]**

11<sup>th</sup> International Conference on  
Advanced Technologies & Treatments  
**for Diabetes**  
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**Vienna**  
Austria



Rx

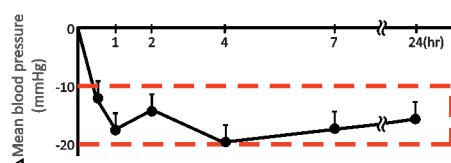
# Bencv $\frac{4}{8}$

Benidipine 4mg /8mg tablet

Rs. 8/  
Tablet

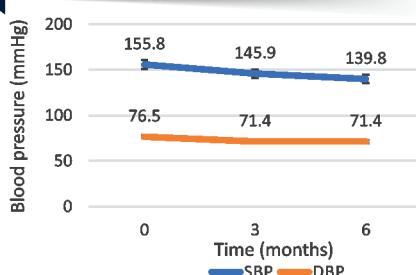
## Double Digit Reduction...CV Protection

### Blood Pressure reduction



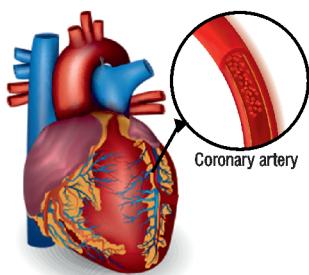
- Diffuses rapidly to the DHP binding sites.<sup>2</sup>
- Double digit BP reduction over 24 hours.<sup>2</sup>

### Switching from Cilnidipine to Benidipine



- Switching from cilnidipine to benidipine reduces BP by 16/5 mmHg in 6 months.<sup>1</sup>

### CV Protection



- Marked increase in coronary blood flow.<sup>2</sup>
- Vascular selectivity and enhanced nitric oxide production shows cardiovascular protective effect.<sup>2</sup>

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# Burden of severe hypoglycemia and ketoacidosis in patients with type 1 diabetes: Association with morbidity, mortality and costs

Cozzolino P, D'Angiolella LS, Bosi E, Scavini M, Mantovani LG.

Type 1 diabetes (T1DM) is associated with certain serious metabolic disorders, such as hypoglycemia and diabetic ketoacidosis. These metabolic disorders increase not only the risk of other vascular complications but also the risk of death and thus incur a massive burden on healthcare systems. In this context, a study was conducted to evaluate the mortality risk and burden of severe hypoglycemia and diabetic ketoacidosis in patients with T1DM as compared to those without acute events.

Through a data warehouse (DENALI), which matches with a probabilistic record-linkage data of individuals in a particular geographic region, records were obtained for patients with T1DM ( $n = 33,774$ ) during the years 2000 to 2010. Hypoglycemia and diabetic ketoacidosis were defined using the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9 CM) codes. Further, the data was analyzed for direct cost estimation. The results divulged the following:

- Among a total of 33,774 patients with T1DM, 958 patients had diabetic ketoacidosis and 363 patients had comorbid hypoglycemia
- Data of T1DM patients with diabetic ketoacidosis and those with hypoglycemia were compared with 32,453 patients with T1DM without events
- Patients with hypoglycemia had a higher mean age and more number of comorbidities as compared to the other groups
- Patients with hypoglycemia and diabetic ketoacidosis were observed to have remarkably higher risk of death as compared to T1DM patients without event
- Moreover, 5-year survival probability of patients with hypoglycemia was lower than those with diabetic ketoacidosis and T1DM patients without acute event ( $p < 0.05$ )
- Cost analysis revealed that patients with hypoglycemia during the years before and after the acute event had up to 50% higher cost burden than patients with diabetic ketoacidosis and T1DM without acute event.

Hypoglycemia accounts for considerable morbidity, hospitalizations and mortality among patients with type 1 diabetes; it is also associated with marked increase in costs of diabetes care more than in patients with diabetic ketoacidosis or those without acute event

Findings of the study helped conclude that hypoglycemia accounts for considerable morbidity, hospitalizations and mortality among patients with T1DM; it is also associated with marked increase in costs of diabetes care more than in patients with diabetic ketoacidosis or those without acute event.

# **Effect of low carbohydrate diets on pregnancy outcomes in women with gestational diabetes**

*Watanabe H, Matsumoto M, Iida M, Ikuta Y, Nagai Y.*

Nutrition therapy is an essential part of the management of gestational diabetes mellitus (GDM). Diet is the leading treatment of patients with GDM; however, role of diet in maternal and newborn outcomes is not well acknowledged. Therefore, in the present study, researchers aimed to assess the effectiveness of low carbohydrate diets on pregnancy outcomes in women with gestational diabetes mellitus in a particular geographic region.

**A low carbohydrate diet may be considered a crucial part of the nutritional management of pregnant women with gestational diabetes mellitus**

The researchers enrolled in the study a total of 337 women who had been newly diagnosed with GDM through a 75-g oral glucose tolerance test. The participating women were provided with either a low carbohydrate diet with 40–50% of energy supply obtained from carbohydrates ( $n = 322$ ) or balanced diet ( $n = 15$ ). Various data including maternal characteristics, delivery characteristics, and neonatal characteristics were obtained and subjected to statistical analyses.

The results divulged the following:

- As compared to the balanced diet group, the median percentage of kilocalories obtained from carbohydrate was significantly lower in the low carbohydrate diet group ( $p < 0.01$ )
- However, no change was observed between the groups in pre-pregnancy body mass index (BMI) and glucose concentrations before implementation of the diet regimen
- Besides, there were no differences observed between the groups in the obstetric and perinatal outcomes.

Thus, findings of the study suggest that low carbohydrate diets are not associated with perinatal abnormalities and may be considered effective and well-tolerated. This further suggests that a diet with limited carbohydrate content may be considered a crucial part of the nutritional management of pregnant women with GDM.

## **Appraising the association between type 2 diabetes and depression**

*Grinberg K, Amzaleg M, Panadha M, Mahamid R.*

Type 2 diabetes is one of the most common chronic disorders throughout the world. Alarmingly, the incidence of type 2 diabetes is increasing every year, especially within developed countries. Depression is one of the most important comorbidities associated with type 2 diabetes that markedly affects the health and well-being of the affected individual. In this context, a study was conducted with an aim to appraise the association between type 2 diabetes and depression levels with regards to five main variables that are age, education level, socio-economic level, perception of the disease and performance of physical activity.

A total of 91 participants with type 2 diabetes were enrolled in the study that were required to fill out two questionnaires; the sociodemographic questionnaire, and the Beck Depression Inventory (BDI) questionnaire. The data obtained from the filled-in questionnaires were subjected to statistical analyses including Pearson and Spearman correlations. Findings of the study divulged the following:

- An association was observed between the perception of the disease and depression ( $p < 0.05$ )
- Socio-economic level and depression were also found to be associated with each other ( $p < 0.05$ )
- However, no remarkable association was observed between the performance of physical activity, age, education level and depression.

**Lifestyle modifications associated with type 2 diabetes impair daily routine of the affected patients that in turn may affect their well-being as regards the depressive symptoms**

Thus, it could be concluded that various lifestyle modifications associated with type 2 diabetes impair the daily routine of the affected patients that in turn may affect their well-being as regards the depressive symptoms. This underscores the need to promote programs that may aid in identifying depressive symptoms and also devise management plans to address it. Considering that the socioeconomic status has a substantial effect on coping with the disease, studies should be conducted to evaluate the weaker segments of the population that are more prone to develop symptoms of depression.

## Appraising the association between visceral fat and Finnish Diabetes Risk Score in individuals with diabetic parents

Padhye DA, Sharma H, Kulkarni M, James A, Pathare N.

Growing evidence suggests a strong correlation of visceral fat mass with diabetes and pre-diabetes. The Finnish Diabetes Risk Score (FINDRISC) is a screening tool that helps to identify the 10-year risk of developing diabetes and pre-diabetes. In the present study, researchers worked on the premise that visceral fat has robust association with FINDRISC along with its obesity parameters such as BMI and waist circumference and aimed to evaluate the association between visceral fat and FINDRISC in individuals with diabetic parents who were treated at a diabetes care centre in India. They further aimed to analyze the contribution of association between visceral fat and FINDRISC in prediction of pre-diabetes and diabetes.

In this prospective analysis of 222 individuals over a one year period, visceral fat was determined through bioelectrical impedance analysis; FINDRISC was also determined. According to FINDRISC, study participants were categorized into two risk groups; low-slightly elevated (< 7 to 11) versus moderate-high (12 to > 17), and association between variables was evaluated.

The results divulged the following:

- When study participants were categorized according to FINDRISC, those at higher risk ( $> 12$ ) were found to have higher values for components that add points to the score, such as blood pressure ( $p < 0.0001$ ), visceral fat ( $p < 0.0001$ ), age ( $p = 0.010$ ), BMI ( $p < 0.0001$ ) and waist circumference ( $p < 0.0001$ )
- Pearson's correlation analysis demonstrated a significant association of FINDRISC with BMI ( $p < 0.0001$ ), waist circumference ( $p < 0.0001$ ) and visceral fat ( $p < 0.0001$ ).

Thus, it could be concluded that visceral fat is significantly associated with an increase in FINDRISC in individuals with diabetic parents. Findings of the study further suggest that early identification of high risk population for pre-diabetes or type 2 diabetes using bioelectrical impedance analysis for visceral fat along with FINDRISC may be a promising approach for preventive diabetes medicine. This would allow for timely lifestyle interventions along with counselling that in turn would facilitate self-management in high risk individuals.

**Early identification of high risk population for pre-diabetes or type 2 diabetes using bioelectrical impedance analysis for visceral fat along with FINDRISC (Finnish Diabetes Risk Score) may be a promising approach for preventive diabetes medicine**

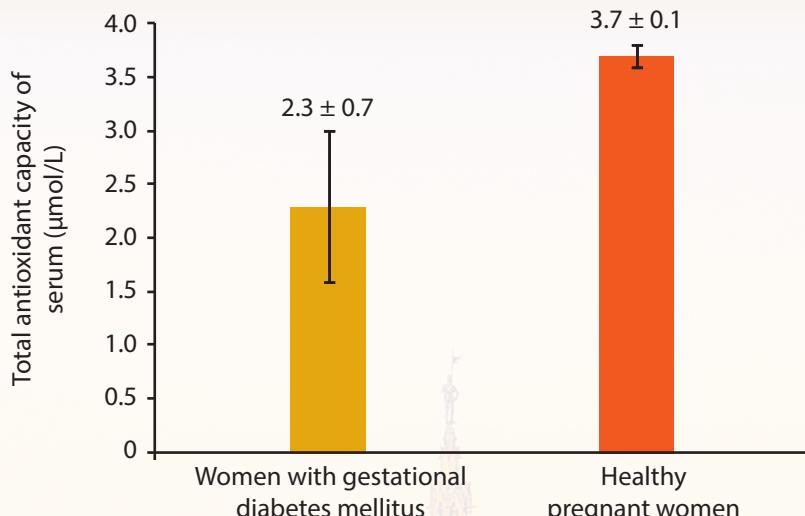
## Association of antioxidant status with gestational diabetes mellitus

Paknahad Z, Parast VM.

Gestational diabetes mellitus refers to glucose intolerance during pregnancy. Additionally, oxidative stress is considered to play a pivotal role in the development of diabetic complications. However, the association between GDM and oxidative stress is not well-recognized. The significance of oxidant/antioxidant equilibrium in the clinical presentation of GDM and its complications need further explanation. With an objective to compare antioxidant capacity and antioxidant nutrient intake between healthy pregnant women and those with GDM, a study was conducted. Demographic data were obtained from interviews conducted among the study participants and dietary intakes were recorded with the help of a semi-quantitative Food Frequency Questionnaire. Total antioxidant capacity (TAC) of serum was evaluated using the ELISA technique.

**Women with gestational diabetes mellitus have lower antioxidant capacity possibly due to lower intake of vitamin E and zinc. Enhancement of the antioxidant status during pregnancy may play a significant role in the prevention of gestational diabetes mellitus**

**Figure 1: Total antioxidant capacity of serum in women with gestational diabetes mellitus as compared to healthy pregnant women**



Results divulged the following:

- TAC of serum was reported to be significantly lower in women with GDM as compared to healthy pregnant women ( $2.3 \pm 0.7$  vs.  $3.7 \pm 0.1 \mu\text{mol/L}$ , respectively) ( $p < 0.001$ ) (Figure 1)
- Intakes of vitamin E ( $11.8 \pm 3.1$  vs.  $16.2 \pm 3.1 \text{ mg}$ ,  $p < 0.001$ ), selenium ( $81 \pm 26$  vs.  $95 \pm 36 \mu\text{g}$ ,  $p < 0.05$ ) and zinc ( $7.4 \pm 1.9$  vs.  $9.1 \pm 1.7 \text{ mg}$ ,  $p < 0.001$ ) were found to be significantly lower in women with GDM than in healthy pregnant women
- No significant differences were observed in the intake of vitamin C,  $\beta$ -carotene, selenium, and fruits and vegetables among both groups.

Findings of the study helped conclude that women with GDM have lower antioxidant capacity possibly due to lower intake of vitamin E and zinc. Therefore, enhancement of the antioxidant status during pregnancy may play a significant role in the prevention of GDM.

## Importance of continuous glucose monitoring in patients with type 2 diabetes and associated hypoglycemia

Gomez AM, Carillo DCH, Lucia T, Dario P, Rondon M, Maira GJ, et al.

A retrospective observational study was conducted in a group of patients with type 2 diabetes to detect the clinical variables and indices of glycemic variability associated with low blood glucose levels. Patients attending a university hospital diagnosed with type 2 diabetes and a history of hypoglycemia were included in the study wherein continuous glucose monitoring (CGM) was indicated. Demographic

variables, glycated hemoglobin ( $\text{HbA}_{1c}$ ), previous antidiabetic therapy, diabetic complications, glomerular filtration rate and all measures used to evaluate glycemic variability by CGM were assessed. Interstitial glucose levels  $\leq 54$  mg/dL for at least 20 minutes was used to define hypoglycemia. Bivariate and logistic regression analyses were performed. Results demonstrated the following:

- Out of a total of 166 patients, 31.3% were reported to have hypoglycemia
- Percentage of coefficient of variation (CV%) was associated with hypoglycemia. CV% was analyzed to be the best predictor of hypoglycemia (OR 1.31 IC 95% 1.20 – 1.44) with a cutoff point of CV% above 33%
- No association was found between demographic variables, diabetic complications and pharmacological management with the presence of hypoglycemia ( $< 70$  mg/dL).

Findings of this study implicate that CV% is the only clinical variable associated with hypoglycemia, thereby suggesting the importance of CGM in patients with type 2 diabetes with a history of hypoglycemia.

**Continuous glucose monitoring plays a significant role in preventing hypoglycemia in patients with type 2 diabetes**

## Role of continuous glucose monitoring in sustained reduction of severe hypoglycemia in patients with type 1 diabetes

Slattery D, Iftikhar M, Brackenridge A, Hopkins D, Amiel S, Choudhary P, et al.

Continuous glucose monitoring is recommended for patients with type 1 diabetes with problematic hypoglycemia regardless of optimized medical management. CGM is considered to be effective in improving glycemic control and minimizing the frequency of hypoglycemic episodes. A survey was conducted in a group of adult patients with type 1 diabetes to assess the effect of CGM on  $\text{HbA}_{1c}$ , severe hypoglycemia (SH) and hypoglycemia awareness. Authors of the survey included a total of 75 patients with type 1 diabetes wherein CGM was performed for at least a year. Data on  $\text{HbA}_{1c}$ , SH and awareness status measured by Gold score were recorded. The mean age of the patients was  $46.7 \pm 12.8$  years and the mean duration of diabetes was  $31.8 \pm 13.9$  years. The median duration of follow-up was 46 months.

**Continuous glucose monitoring plays a significant role in reduction of rates of severe hypoglycemia in patients with type 1 diabetes with benefits sustained up to 7 years**

Results divulged the following:

- Mean SH rate reduced from  $7.69 \pm 33.74$  to  $0.95 \pm 4.1$  ( $p < 0.001$ ) after 1 year of CGM
- The benefits of CGM therapy in reduction of SH was maintained for up to 7 years ( $0.08 \pm 0.29$ )
- No significant deterioration in  $\text{HbA}_{1c}$ , SH and hypoglycemia awareness status were reported during the follow-up duration.

Results of this survey thereby suggest that CGM plays a significant role in reduction of rates of SH with benefits sustained up to 7 years, without deterioration of glucose control.

## Assessment of therapeutic and adverse effects of SGLT2 inhibitors on patients with diabetes

Chandran SR, Lim AYL, Bee YM, Goh SY.

Sodium-glucose co-transporter 2 inhibitors (SGLT2i) are a novel class of oral hypoglycemic drugs. These agents are considered to exhibit beneficial effects on weight and blood pressure (BP) regulation in addition to  $\text{HbA}_{1c}$ . However, these drugs are reported to cause urogenital infections (UI) and ketosis. In order to evaluate the therapeutic and adverse effects of SGLT2i, a survey was conducted. The electronic health records of patients on SGLT2i like dapagliflozin, canagliflozin and empagliflozin were obtained. Demographic data, weight, BMI, systolic and diastolic BP (SBP and DBP), episodes of diabetic ketoacidosis (DKA) and UI were collected for 6 months prior to the use of SGLT2i and 12 months thereafter. Changes in  $\text{HbA}_{1c}$ , weight, BMI, SBP and DBP were evaluated as the difference between the average/last pre-prescription measure and the average/last post-prescription measure. Additionally, episodes of ketosis (urine or blood), DKA and UI were compared. A total of 1201 individuals receiving SGLT2i were included who were diagnosed with type 1/type 2 diabetes, latent autoimmune diabetes, post-pancreatectomy diabetes and other subtypes. Results demonstrated the following:

**Use of SGLT2 inhibitors was significantly associated with reduction of  $\text{HbA}_{1c}$ , weight and blood pressure in patients with diabetes. Few patients who developed diabetic ketoacidosis were found to have additional precipitating factors**

- Use of SGLT2i was associated with significant reduction in  $\text{HbA}_{1c}$  ( $1.2 \pm 1.3\%$ ), weight ( $2.3 \pm 2.5$  kg), SBP ( $5.0 \pm 14.5$  mmHg) and DBP ( $2.8 \pm 7.2$  mmHg) ( $p < 0.001$ )
- Patients who developed ketosis while on SGLT2i had a significantly lower age ( $47 \pm 10$  years vs.  $55 \pm 9$  years,  $p < 0.05$ ) and higher  $\text{HbA}_{1c}$  ( $10 \pm 1.6\%$  vs.  $8.9 \pm 1.3\%$ ,  $p < 0.05$ )
- Patients who developed DKA (0.4%) were found to have additional precipitating factor(s)
- About 1.1% patients were reported to develop UI while on SGLT2i.

Findings of this survey helped conclude that SGLT2i were significantly associated with reduction of  $\text{HbA}_{1c}$ , weight and BP in patients with diabetes. Diabetic ketoacidosis was reported in patients who had additional precipitating factors.

## **Results from a 12 month real life study monitoring patients with type 2 diabetes using liraglutide**

*Rios C, Abreu A, Balcazar CM, Castan O, Casanova ME, Muriel A, et al.*

With the increasing global prevalence of T2DM, newer molecules are being used to establish various essential treatment options. Liraglutide, a glucagon-like peptide-1 (GLP-1) receptor agonist has demonstrated to be efficacious in decreasing the HbA<sub>1c</sub> levels and weight of the patients with diabetes. Hence, to analyze these effects of liraglutide a descriptive, retrospective cohort study was conducted on 85 outpatients (mean age = 59 years) between January 2013 and June 2016. These patients were followed up for 5 times in a year in a specialized care centre. The patients included in the study were on a daily subcutaneous dose of 1.8 mg of liraglutide, in addition to their standard treatment. A comparison between the value variables of HbA<sub>1c</sub>, glycemia, weight, BMI and blood pressure at the time of admission and at the 5<sup>th</sup> visit (12 months) were made. In this study, the paired t-test was compared in addition to generalized estimation equations and quadratic predictions with confidence intervals. The results of this study demonstrated that liraglutide decreased the HbA<sub>1c</sub>, basal glycemia, body weight, BMI, and systolic blood pressure of the patients by 1.8% (95% CI, 1.52–2.04; p < 0.0001), 73 mg/dL (95% CI, 60.29–84.88; p < 0.0001), 5.1 kg (95% CI, 4.66–5.53; p < 0.0001), 1.6 points (95% CI, 1.44–1.71; p < 0.0001) and 6.7 mmHg (95% CI, 0.90–12.45; p = 0.024), respectively. However, the largest decrease in HbA<sub>1c</sub> was evident between the first and second visits (3 months), and was stabilized over time. Adverse events like nausea, abdominal pain and hypoglycemia were also reported in 27%, 18% and 14% of the patients, respectively.

Hence, results of this study suggested that patients with T2DM on a daily dose of 1.8 mg liraglutide in combination with standard therapy demonstrate a decrease in HbA<sub>1c</sub> levels along with metabolic control.

**Patients with type 2 diabetes on a daily dose of 1.8mg liraglutide in combination with standard therapy demonstrate a decrease in glycated hemoglobin levels along with metabolic control**

## **Improvement of full closed loop post-prandial glycemic control in young adult patients with type 1 diabetes on dapagliflozin add-on therapy**

*Biester T, Nieswandt A, Biester S, Remus K, Dovc K, Bratina N, et al.*

In the recent times, dapagliflozin (DAPA), an SGLT2i, is increasingly being used as an adjunct therapy in the treatment of patients with T1DM. The DreaMed Substance Administration System with fuzzy logic closed loop algorithm has proven to be safe and efficacious in hybrid closed loop settings and full closed loop (FCL) settings. However, in FCL settings postprandial time is always considered to be a

phase of high glucose excursion. Hence, a trial was conducted with an aim to investigate the effect of DAPA on glucose levels after an unannounced meal under FCL conditions. In this monocentric, double blind, randomized, placebo-controlled cross-over trial, 15 eligible patients (mean age = 19 years) with T1DM, slope indices of inequality (SII), HbA<sub>1c</sub> 8.3 % (7.1–10.4) and non-severe obesity were admitted for 24 hours of FCL on two occasions. These patients were administered 10 mg DAPA or placebo twice a day and two mixed meal tests were performed for them. The glucose control for these patients was achieved by DreaMed FCL and 'time-in-range' (TIR) of 70–180 mg/dL was considered to be the primary outcome of the trial. The results of this study demonstrated that TIR with DAPA increased significantly overall and during the postprandial phase. In addition to this, a three-fold increase in the urinary glucose excretion was also seen (Table 1). The time above 180 mg/dL was also seen to be significantly decreased in the patients without an increase below 70 mg/dL. However, no serious ketosis was observed in any patient.

**Sodium-glucose co-transporter 2 inhibitors are considered to be well-tolerated and effective adjuncts in patients with type 1 diabetes**

**Table 1: Comparison of dapagliflozin with placebo on the basis of primary and secondary outcomes**

Variable ITT (n = 15)	Dapagliflozin	Placebo	p-value
<b>Primary</b>			
<b>Time within 70-180 mg/dL (%)</b>			
24 hr	68.40 (60.68, 70.66)	50.35 (45.56, 56.16)	< 0.001
7 am - 7 pm	41.67 (33.23, 47.22)	18.75 (14.04, 29.83)	< 0.001
11 pm - 7 am	100.00 (93.17, 100.00)	90.63 (77.27, 100.00)	0.123
<b>Secondary</b>			
Time below 70 mg/dL (%)	1.39 (0, 4.11)	0 (0, 2.53)	0.064
Time above 180 mg/dL (%)	29.17 (26.39, 36.84)	45.49 (42.45, 54.21)	< 0.001
Mean glucose levels (mg/dL)	154.20 (144.74, 174.55)	186.61 (172.53, 201.03)	0.001
Bolus insulin (U)	9.65 (8.13, 12.46)	16.00 (13.41, 19.16)	< 0.001
Basal insulin (U)	17.33 (14.50, 21.78)	22.51 (15.38, 27.14)	0.008
Urinary glucose excretion (mg/25 h)	149331 ± 42.57	48520 ± 22618	< 0.001

Hence, the results of this study concluded that, young adults with T1DM who took effort from DAPA combined with FCL demonstrated an average increase in TIR by 2.8 hours compared to placebo despite consuming two unannounced meals. Apart from this, the bolus and basal insulin levels were found to be reduced in FCL thus, proving SGLT2 inhibition to be well-tolerated and effective in full closed loop settings.

# Appraising the role of continuous glucose monitoring as a gold standard tool in patients with type 2 diabetes

Levit S, Ginossar G, Zivony A, Barnea R, Korek-Abadi I, Hanna RC.

Remission in patients with T2DM is no longer considered to be a myth. Recent studies have demonstrated that these remissions can be achieved quite quickly as the therapeutic objectives have shifted from blood glucose (BG) normalization to metabolic purposes (BMI reduction). Hence, a study was conducted on 18 uncontrolled T2DM patients (mean age of  $58.8 \pm 10.6$  years) with T2DM for about  $14.4 \pm 8.4$  years. These patients were initially treated with insulin combined with metformin and other oral antidiabetic medications. The average duration of insulin therapy for these patients was estimated to be about  $7.5 \pm 6.9$  years. Continuous glucose monitoring (CGM) recording was done before metabolic (gravicentric) intervention and immediately after complete insulin discontinuation for these patients. Since, the intervention was aimed at weight reduction, liraglutide was started in all the patients. However, in five patients SGLT2i was also added. The results of this study demonstrated reduction in BMI and  $\text{HbA}_{1c}$  values from  $34.1 \pm 5.6$  to  $29.0 \pm 4.1$  ( $p = 0.005$ ) and from  $8.5 \pm 1.3$  to  $6.9 \pm 0.6\%$  ( $p = 0.0002$ ), respectively. This demonstrated a dramatic improvement in the metabolic state and facilitated insulin discontinuation. The CGM recordings, mean amplitude of glycemic excursion (MAGE) recordings and the standard deviation demonstrated a significant reduction in the coefficient of variability (CV) from  $27.0 \pm 8.0\%$  to  $20.0 \pm 6.0\%$  ( $p = 0.004$ ),  $82.9 \pm 30.6$  to  $64.8 \pm 23.4$  mg% ( $p = 0.002$ ) and from  $48.6 \pm 18.4$  to  $31.5 \pm 11.3$  mg% ( $p < 0.001$ ), respectively. In addition to this, significant reduction in parameters, like continuous overall net glycemic action (CONGA), lability index (LI), low blood glucose index (LBGI), high blood glucose index (HBGI), glycemia reduction approaches in diabetes effectiveness study (GRADE), mean of the daily differences (MODD), median value (MVALUE) and mean absolute glucose change (MAG) were also evident in the patients participating in the study. However, the hypoglycemia indexes remained unchanged demonstrating a strong positive correlation between CV and MAGE.

**Coefficient of variability appears to be the most easily accessible and informative criteria for confirming metabolic recovery in patients with type 2 diabetes thus making continuous glucose monitoring a 'gold standard' tool**

Hence, the results of this study concluded metabolic recovery and insulin weaning to be accompanied by dramatic reduction in all the parameters reflecting glucose variability in patients with T2DM; without any change in the hypoglycemic indices. Coefficient of variability appears to be the most easily accessible and informative criteria for confirming metabolic recovery in patients with T2DM thus making CGM a 'gold standard' tool.

# Elderly patients with type 2 diabetes: Role of exenatide

Abreu A, Rios C, Balcazar C, Milla'n W, Bastidas O, Casanova ME, et al.

Type 2 diabetes mellitus is a progressive metabolic disease characterized by the presence of persistent hyperglycemia. Patients over 60 yrs of age having T2DM pose a therapeutic challenge to physicians worldwide. Glucagon-like peptide-1 (GLP-1) receptor agonists are used to treat T2DM as monotherapy or in combination with other antidiabetic drugs. These drugs exert favorable effects on patients due to their ability to modify various cardiovascular risk factors. Exenatide is one such GLP-1 receptor agonist that has improved patient adherence due to its weekly dosing schedule.

The present study, a descriptive, retrospective cohort study, was conducted for three years in a specialized care centre. A total of 39 patients with poorly controlled T2DM were recruited for the study. Patients were administered exenatide at a subcutaneous dose of 2 mg every week in addition to the standard therapy, and were scheduled for one year follow-up with 4 visits. Repeated measurements of HbA<sub>1c</sub>, baseline glycemia, weight, BMI and BP were made over time. Statistical analysis was done using paired t-test, generalized estimation equations, and quadratic predictions with confidence intervals.

The mean age for recruited patients was 71 years and the onset of T2DM was 7.6 years old. The results divulged the following:

- An average significant decrease in HbA<sub>1c</sub> of 1.7% (8.9% of admission value and 7.2% at 12 months) with the use of exenatide in combination with standard therapy
- An average significant decrease in baseline glycemia of 106 mg/dL with the use of exenatide in combination with standard therapy
- An average significant decrease in systolic-BP of 15.6 mmHg and diastolic-BP of 5.8 mmHg with the use of exenatide in combination with standard therapy
- The largest decrease in HbA<sub>1c</sub> average occurred between first and second visit
- No serious adverse events were observed.

In conclusion, exenatide exerted a favorable effect on blood pressure with no serious adverse effects. Additionally, the weekly dosing schedule ensured adequate adherence to the treatment. Exenatide therefore, can be considered a favorable therapeutic option in patients with diabetes who are over 60 years of age.

**Exenatide exerted a favorable effect on blood pressure with no serious adverse effects**

# Type 2 diabetes mellitus in geriatric patients: Focus on health status and glycemic control

Libiseller A, Lichtenegger K, de Campo A, Wiesinger T, Stolletz N, Cuder G, et al.

The global prevalence of type 2 diabetes has been rising in geriatric population. Up to 25% of people older than 70 years of age suffer from type 2 diabetes. Diabetes guidelines underline the need to individualize glycemic goals and to modify treatment approaches with the chief focus on avoiding hypoglycemia in geriatric patients. The study was directed to assess glycemic control in patients with type 2 diabetes in geriatric care facilities based on the individual health status.

The study included 170 medical records of geriatric patients with type 2 diabetes in 4 geriatric care facilities (64.7% female, age  $80 \pm 9$  years, HbA<sub>1c</sub>  $51 \pm 16$  mmol/mol, BMI  $27.9 \pm 5.8$  kg/m<sup>2</sup>), which were retrospectively assessed. Patients were allocated to three groups based on health status:

- Healthy (n = 27)
- Complex (n = 86)
- Poor (n = 57)

**Individualization of diabetes therapy is highly recommended considering the needs of geriatric patients**

The results revealed that overall blood glucose value was highest in the poor health group with  $10.4 \pm 2.6$  mmol/L as compared to those in the complex group ( $9.3 \pm 2.3$  mmol/L) and those in the healthy group ( $8.3 \pm 1.9$  mmol/L). Moreover, 1.4% of all blood glucose values in the healthy group were below 90 mg/dL as compared to 1.6% in the poor group and 2.8% in the complex group. Furthermore, 37.2% (poor) vs. 23.4% (complex) vs. 18.5% (healthy) received insulin as the main diabetes therapy, but only 14.3% (poor) vs. 30% (complex) vs. 40% (healthy) were treated with basal insulin (Table 2).

**Table 2: Assessment of glycemic control in patients with type 2 diabetes in geriatric care facilities**

Parameters	Healthy	Complex	Poor
Overall blood glucose value (mmol/L)	$8.3 \pm 1.9$	$9.3 \pm 2.3$	$10.4 \pm 2.6$
Proportion of optimum blood glucose values (< 90 mg/dL)	1.4%	2.8%	1.6%
Patients treated with basal insulin	40%	30%	14.3%

It could be inferred that overall blood glucose values were higher in the poor and complex group. There were few low blood glucose values in all groups. However, basal insulin therapy is still underused despite being recommended by international guidelines and having low complexity and low hypoglycemic risk, especially in the poor-health group. This underscores the need of individualization of diabetes therapy, which could be solved in part by implementing electronic decision-support systems considering geriatric needs.

# Determination of glucose variability and glucose status correlating with cardiometabolic risk factors in patients with type 2 diabetes

Morosanu A, Morosanu M.

Among the latest parameters of glucose control, glucose variability is associated with oxidative stress in type 2 diabetes. However, its influence is yet to be determined. Oxidative stress, through the production of reactive oxygen species, has been proposed as the root cause underlying the development of insulin resistance,  $\beta$ -cell dysfunction, impaired glucose tolerance and type 2 diabetes. This study investigated the association between cardio-metabolic risk factors (CMRF) and glucose parameters evaluated by continuous glucose monitoring (CGM) in individuals with type 2 diabetes.

In this study, researchers included 30 persons with T2DM who were stratified as follows:

- 8 women and 22 men
- 14 persons with insulin therapy and 16 with oral treatment
- Mean diabetes duration: 11.43 years
- Mean age: 56.59 years

**Awareness of familial cardiovascular risk factors is associated with better glucose control in patients with higher exposure to hypoglycemia**

Furthermore, CMRF included body weight, BMI, waist circumference, physical activity, smoking, alcohol consumption, lipid profile [total cholesterol, HDLc, triglycerides (TG), LDLc], blood pressure (systolic-SBP, diastolic-DBP), personal and family history of CVD, family history of diabetes. Glucose parameters included HbA<sub>1c</sub>, glucose variability (GV), mean amplitude of glucose excursions (MAGE), number of glucose values (time), area under the curve (AUC, glucose exposure), mean glucose values (glucose amplitude) on domains-hypoglycemic (< 70 mg/dL), intermediate (70–180 mg/dL), hyperglycemic (> 180 mg/dL), optimal (90– 130 mg/dL). The study participants were assessed by CGM.

The results revealed the following:

- Body weight was inversely associated with GV and MAGE
- Individuals with SBP > 130 mmHg had lower percent of hypoglycemic values and hypoglycemic exposure, higher total glucose exposure, higher diurnal and nocturnal glucose exposure and higher glucose amplitude (mean)
- TG values were directly associated with diurnal glucose exposure and inversely related to nocturnal AUC
- HDLc was directly associated with the magnitude of intermediate glucose exposure (70-180 mg/dL)
- Individuals with family history of diabetes had higher time spent and total glucose exposure to hypoglycemia
- Individuals with family history of CVD had lower HbA<sub>1c</sub> values.

However, the other assessed data were not significant, even if the direct relation between worse metabolic control and hyperglycemic exposure was close to statistical significance. The final conclusion suggested SBP to be lower in persons with higher hypoglycemic exposure and was directly correlated with total glucose status. Furthermore, TG and HDLc were also directly correlated with total glucose status. Lastly, awareness of familial cardiovascular risk factors was associated with better glucose control with higher exposure to hypoglycemia.

## Assessment of short-term glucose variability change in type 2 diabetes by continuous glucose monitoring

Morosanu A, Morosanu M.

Glucose status is the chief determinant factor for diabetes development on short-term and long-term periods. Glucose fluctuations are related to oxidative stress in a higher extent than sustained hyperglycemia in type 2 diabetes. Glycemic variability refers to swings in blood glucose levels, has a broader meaning because it alludes to blood glucose oscillations that occur throughout the day, including hypoglycemic periods and postprandial increases, as well as blood glucose fluctuations that occur at the same time on different days. This study evaluated prospectively the relation between glucose variability (GV-standard deviation of glucose values), mean amplitude of glucose excursions (MAGE) and HbA<sub>1c</sub>, anthropometric parameters, gender, diabetes treatment in persons with type 2 diabetes assessed by continuous glucose monitoring.

The study included 30 subjects with type 2 diabetes [8 women/22 men, median age 64 (39–69) years, mean diabetes duration 14 (0–17) years, insulin therapy-14, oral therapy-16] performed blinded CGM for 3 days. Further, 10 of the insulin treated subjects performed a second CGM after 3 months. Various parameters were assessed including HbA<sub>1c</sub>, body weight, BMI, waist circumference, glucose variability (GV - standard deviation of glucose values), MAGE, number of glucose values (time), area under the curve (AUC, glucose exposure), mean glucose values (glucose amplitude) on domains-hypoglycemic (< 70 mg/dL), intermediate (70–180 mg/dL), hyperglycemic (> 180 mg/dL), optimal (90–130 mg/dL).

**Short-term glucose fluctuations were directly related to long-term glucose status (HbA<sub>1c</sub>) and hyperglycemic exposure, while inversely related to parameters of normoglycemia, and body weight**

The results of the study were as follows:

- GV and MAGE were considerably higher in insulin treated persons and women at the first visit
- HbA<sub>1c</sub> was higher in women and in insulin treated persons. GV and MAGE were directly associated with HbA<sub>1c</sub> initially and after 3 months
- GV and MAGE were inversely associated with body weight initially and after 3 months. GV and MAGE were directly related to hyperglycemic exposure, and inversely related to normoglycemic exposure

- HbA<sub>1c</sub>, GV and MAGE decreased after three months, likely due to specific treatment adjustments based on continuous glucose monitoring.

Thus, it was concluded that short-term glucose fluctuations were directly associated with long-term glucose status (HbA<sub>1c</sub>), and hyperglycemic exposure, while inversely related to parameters of normoglycemia, and body weight.

## Simplifying insulin regimens in type 2 diabetes

Taybani Z, Bo'tyik B, Katko' M, Gyimesi A.

Multiple daily insulin injections (MDI) are often required for patients with type 2 diabetes presenting with severe hyperglycemia. On resolving glucose toxicity, the regimen can potentially be simplified. However, there are no guidelines regarding simplifying the regimen which consequently leads to long term continuation of MDI for such patients. The present study therefore examined the safety and efficacy of switching from MDI to a simplified regimen of once daily IDegLira in relatively well controlled subjects with type 2 diabetes (HbA<sub>1c</sub> < 7.5%) using low total daily insulin dose (TDD). IDegLira is a fixed-ratio combination of insulin degludec and liraglutide.

A total of 30 adults with type 2 diabetes, treated with MDI along with metformin were enrolled in the study. The patients had a mean age of 62.9 yrs and duration of diabetes of 10.8 yrs. Baseline mean HbA<sub>1c</sub> was 6.34%, BMI was 32.90 kg/m<sup>2</sup>, bodyweight was 92.57 kg, and TDD was 40 units. Previous insulins were stopped and once daily IDegLira was started for all study participants. IDegLira was titrated every 3 days with 2 dose steps (each dose step contains 1 unit of insulin degludec and 0.036 mg of liraglutide) by the patients to achieve a self-measured pre-breakfast plasma glucose concentration of < 6 mmol/L. Additionally, Metformin was continued and titrated up to the maximal tolerated dose. Study results revealed the following:

- Good glycemic control was maintained after 94.4 days of average follow-up while BMI and bodyweight decreased significantly
- Mean HbA<sub>1c</sub> changed by 0.12% to 6.22%, bodyweight changed by 4.38 kg to 88.19 kg and BMI changed to 32.01 kg/m<sup>2</sup>
- IDegLira+metformin combination therapy was generally well-tolerated.

Overall, switching from low dose MDI to IDegLira in patients with well-controlled type 2 diabetes achieved similar glycemic control and was found to be well-tolerated. Additionally, it may induce some weight loss. Therefore switching to a simplified regimen in everyday clinical practice is well-tolerated and effective.

**Switching from low dose multiple daily insulin injections to IDegLira in patients with well-controlled type 2 diabetes achieved similar glycemic control and was found to be well-tolerated**

## **Association between use of basal insulin and risk of hypoglycemia in patients with type 2 diabetes**

*Meneghini L, Zhou FL, Bosnyak Z, Berria R, Jimenez J, Bailey T.*

The Lightening study was conducted with an objective to evaluate rates of hypoglycemia in patients with T2DM who were prescribed first or second generation basal insulin (BI) analogs, including glargine 100 U/mL (Gla-100), detemir (IDet); and, degludec (IDeg), glargine 300 U/mL (Gla-300), respectively. In this context, the BI treatment data between April 1, 2015 and December 31, 2016 were gathered. The primary analysis was focused on patients switching BIs to validate findings from previous real-world Gla-300 studies. Treatment endpoints included severe hypoglycemia event rate and HbA<sub>1c</sub> change from baseline to 76–180 days follow-up.

**Gla-300 is associated with lower rates of severe hypoglycemic events, in comparison to those with first generation insulin analogs in patients with type 2 diabetes mellitus**

Results revealed that there were markedly reduced rates of severe hypoglycemia in patients switching from any BI to Gla-300 in comparison to those switching to Gla-100 or IDet. Interestingly, treatment outcomes were similar to those switching to IDeg. Overall, it can be inferred that Gla-300 is associated with lower rates of severe hypoglycemia in comparison to the first generation BIs, in patients with T2DM switching from any previous BI. These results mirror the findings of earlier randomized controlled trials and other real-world analysis of Gla-300. Further analysis is required to correlate the variable incidence of severe hypoglycemia with clinical and economic outcomes.

## **Arachidonic acid and lipoxin A4 may prevent diabetes**

*Undurti D.*

The increased production of pro-inflammatory cytokines and reactive oxygen species (ROS) in type 1 and type 2 diabetes mellitus stimulates apoptosis of beta cells and cause peripheral insulin resistance; the degree of their increased production is however, greater in type 1 diabetes in comparison to type 2 diabetes mellitus. It is believed that the methods intended to suppress inflammatory events may prove to be beneficial in diabetes as well. In this regard, in vitro and in vivo studies were conducted with an aim to determine the plausible endogenous anti-diabetic molecules, with focus on low molecular weight lipid molecules.

**Both type 1 and type 2 diabetes mellitus can be prevented by arachidonic acid and lipoxin A4; these lipid molecules may therefore function as endogenous anti-diabetic molecules**

The outcomes divulged that there were low plasma concentrations of arachidonic acid (AA) and lipoxin A4 (LXA4) in alloxan-induced type 1 diabetes mellitus in preclinical studies and in individuals with type 2 diabetes mellitus. The in vitro studies suggested that AA and LXA4 could prevent alloxan and streptozotocin-induced cytotoxicity to pancreatic beta cells. Of note, alloxan and streptozotocin-induced type 1 and type 2 diabetes mellitus could be prevented by AA and LXA4 by suppressing production of inflammatory cytokines, expression of NF- $\kappa$ B and preserved beta cell function. The authors of the study concluded that both type 1 and type 2 diabetes mellitus can be prevented by AA and LXA4, thereby suggesting that these lipid molecules may function as endogenous anti-diabetic molecules.

## Efficacy of IDegLira in patients with poorly controlled type 2 diabetes mellitus

Didangelos T, Kontoninas Z, Tziomalos K, Margaritidis C, Stergiou I, Tsotoulidis S, et al.

A study assessed the clinical outcomes of combination therapy with insulin degludec (IDeg) and liraglutide (Lira) in patients with long-established, poorly controlled T2DM. The patients in the study were earlier treated with sulfonylureas, GLP-1 receptor agonists, dipeptidyl peptidase-4 (DPP-4) inhibitors, metformin, SGLT2 inhibitors and/or insulin. All patients following initiation of IDegLira were on metformin and a few of them were on fast insulin analogs. They were treated with IDegLira for minimum 3 months.

Results showed that there was an improvement in the mean HbA<sub>1c</sub> ( $8.9 \pm 1.6\%$  vs  $7.3 \pm 0.7\%$ ) with concomitant weight loss. In addition, there was a reduction in the mean systolic blood pressure [(BP); ( $135.6 \pm 19.4$  vs  $130.7 \pm 16.4$  mmHg)], but not in the mean diastolic BP with IDegLira. Mean dose of IDegLira was  $35.9 \pm 13.8$  U/24h. There was no significant alteration observed in the measured glomerular filtration rate (mGFR) ( $74.7 \pm 17.4$  vs  $72.6 \pm 22.8$  ml/min/1.73 m<sup>2</sup>). Besides, there were no episodes of severe hypoglycemia during treatment with IDegLira.

Hence, it can be inferred that switching to IDegLira from regimens including insulin in conjunction with oral anti-diabetics, in patients with type 2 diabetes, may improve glycemic control with decreased systolic BP and weight loss.

**Switching to IDegLira from regimens including insulin in conjunction with oral anti-diabetics, in patients with type 2 diabetes, may improve glycemic control with decreased systolic blood pressure and weight loss**

# Usability, benefits and safety of an implantable continuous glucose monitoring system

Chen XO, Addaguduru S, Mdindi C, Rastogi R, DeHennis A.

Continuous glucose monitoring (CGM) over longer durations can possibly prevent hypoglycemia. There exists a long-term implantable CGM system with an implant fluorescence-based glucose sensor that lasts up to nearly 3 months, a wearable smart transmitter and a mobile app which display real-time glucose readings. An analysis ascertained its user adherence, adverse events and glucose variability in patients with diabetes. It included individuals with diabetes ( $n = 50$ ) who had three cycles of sensor use or were on their 3<sup>rd</sup> sensor (up to 270 days) between September 2016 and September 2017. Total 13,500 sensor days were analyzed.

The long-term implantable continuous glucose monitoring system demonstrates increased usability and appears to be safe with numerically reducing patients' time in severe hypoglycemia

Results showed an increase in user adherence in all sensor use cases. The number of adverse events appeared to decrease till 3<sup>rd</sup> sensor use. Of note, the average glucose between sensor uses remained similar; whereas, there was a numerical decline in percent time in both hypoglycemia and severe hypoglycemia. The authors of the study concluded that the long-term implantable CGM system demonstrates increased usability and appears to be safe for approximately 270 days with numerically reducing patients' time in severe hypoglycemia.



# Insuwell



Methylcobalamin 1500 mcg, ALA 100 mg, Vitamin D 200 IU,  
Vitamins & Trace minerals Tablets

**Intensifies Nutrition... Impedes Complication**

## Intensifies Nutrition

- Vitamins improve plasma glucose and lipid profile in type 2 diabetes.<sup>1</sup>
- Minerals improves glucose homeostasis & enhances insulin sensitivity.<sup>2</sup>
- Berberine helps to reduce weight.<sup>3</sup>

## Impedes Complication

- Vitamin D reduces insulin resistance & improves symptoms of neuropathy.<sup>4</sup>
- Alpha lipoic acid reduces symptoms of Pain & burning sensation.<sup>5</sup>
- Mecobalamin reduces symptoms of numbness & paresthesia.<sup>5</sup>

**Recommended: 1 Tablet Daily**

Reference:

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